Introduction to Organometallic Chemistry

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Lecture - 21

Metathesis reaction

In this lecture, we will discuss catalytic metathesis, metathesis as we have discussed the last lecture it is a change in place.

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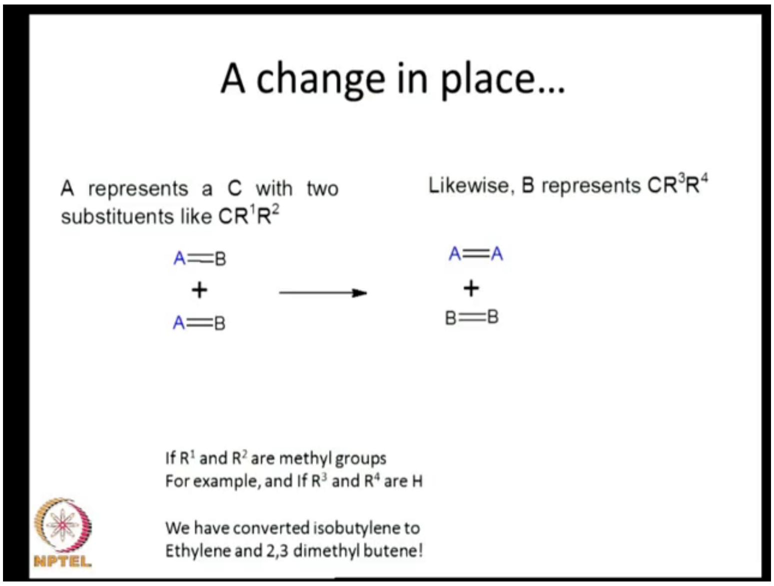

A change in place...

A represents a C with two substituents like CR^1R^2

Likewise, B represents CR^3R^4

$$A{=}B + A{=}B \longrightarrow A{=}A + B{=}B$$

If R^1 and R^2 are methyl groups
For example, and If R^3 and R^4 are H

We have converted isobutylene to
Ethylene and 2,3 dimethyl butene!

In the case of olefins, when you have alkylidene groups and if alkylidene group change places, then you would have a metathesis reaction. In the slide that is, before you will notice that two alkenes and their same alkene A B, which is basically indicative of two alkylidene groups joined together. If we do a metathesis of this A B olefin, then you can get both A A and B B band. If you remember, this allows for a change in the size of the olefin. So, if you take a small olefin and you do metathesis, you can get a bigger olefin and a smaller olefin and this is very useful for the petroleum industry. In fact, metathesis was originally discovered in the industry.

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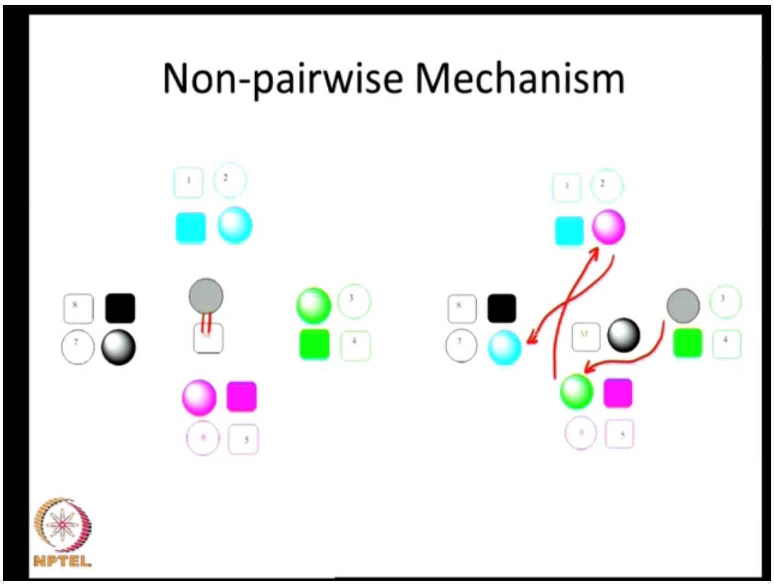

Non-pairwise Mechanism

Eventually, it was understood better through the work of Showen and he discovered what is called the non pair wise mechanism for the metathesis. We will just briefly revise what we have discussed earlier and I have before me, a set of four olefins which are represented by these green magentablue and black alkylidene groups. The alkaline groups that are going to be exchanged are the ones which are shown in round as a round figure and the alkylidene groups, which are stationary or will remain in the same place are the ones which are in square shape.

So, you will notice that if you take four different olefins you can have a complete random distribution of these olefins. The great round figure which is attached to the metal which is basically having M double bond C H 2 here is going to be the exchanged with the green one to start with. Then the green alkylidene group is exchanged with the magenta and the magenta is exchanged with the one on the trans in the transposition. So, you will notice that the round magenta has gone here the green one has come here and the blue which was here has come over to this position. So, this is just to indicate that you can have a completely random distribution of the alkylidene groups.

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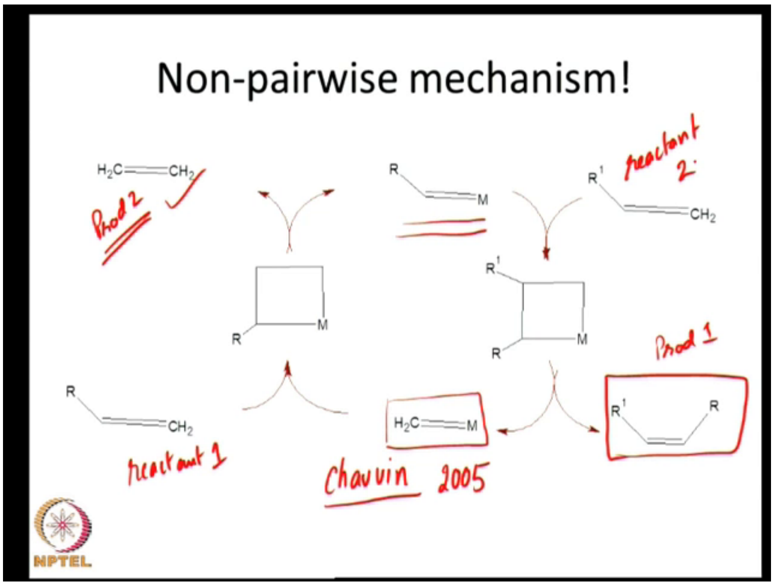

Non-pairwise mechanism!

This non pair wise mechanism was suggested by Chauvin and you will recollect that Chauvin got the Nobel Prize in 2005 for this very reason for discovering the actual mechanism that was behind this famous metathesis reaction.

Pictured here, is the mechanism you start with M C H 2 M double bond C H 2 and then you can exchange it with another olefinin such a way that you can eliminate ethylene and that is what is happening. Here, ethylene is eliminated and a new alkylidene metal system is generated which can interchange with another alkylidene group of another olefin in order to finally generate a completely new olefin.

So, these are the two products, this is product one and this is product two and these two olefins are generated. Starting with two olefins which is the reactant one and reactant two, this is reactant one and this is reactant two. So, based on this type of a non pair wise mechanism it was possible to explain all the reactions that were observed from the metathesis reaction.

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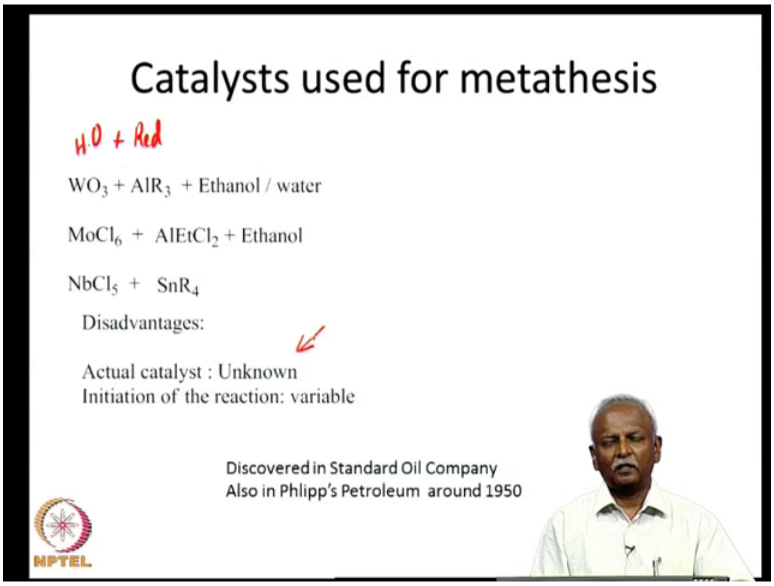

Catalysts used for metathesis

H.O + Red

$WO_3 + AlR_3$ + Ethanol / water

$MoCl_6 + AlEtCl_2$ + Ethanol

$NbCl_5 + SnR_4$

Disadvantages:

Actual catalyst : Unknown
Initiation of the reaction: variable

Discovered in Standard Oil Company
Also in Phlipp's Petroleum around 1950

So, what we have not discussed in the last lecture where we discussed the mechanism of this process is a fact that the catalysts required for the metathesis were often very complex. Originally, it was discovered by the standard oil company and patented also by Phillips petroleum for a specific case. Most of these companies used very complex mixtures for carrying out metathesis.

In general, it could be said that a early high oxidation state metal ion or a metal complex an oxide or a chloride was used and this was followed by a reducing agent. So, a high oxidation state metal, so this is the high oxidation state metal that I am talking about and then this was combined with a reducing agent, very often this was an aluminumalkyl species aluminumalkyl oraluminium alkyl chloride.

Then surprisingly, small amounts of ethanol or water were required in order to initiate the reaction. There were several disadvantages for this particular mixture. One was the fact that the catalytic species was not known it could be a variety of different species which were generated starting from this mixture. So, the catalytic species itself could not be modified, it was an unknown species and there was very often an initiation period that was required in order to start the reaction.

So, the reactions were slow to begin with, before they took off this means that the reaction itself would lead to in terms of when you have reactions, which lead to polymers you have a large range in molecular weight. We will talk about this little later on during the course of this lecture also. So, this is a big disadvantage, but nevertheless the petroleum companies found it extremely useful to do metathesis reaction. In order to generate more useful fractions from the petroleum fractions that was isolated directly from crude. So, it was a useful reaction, but then the catalyst was not known.

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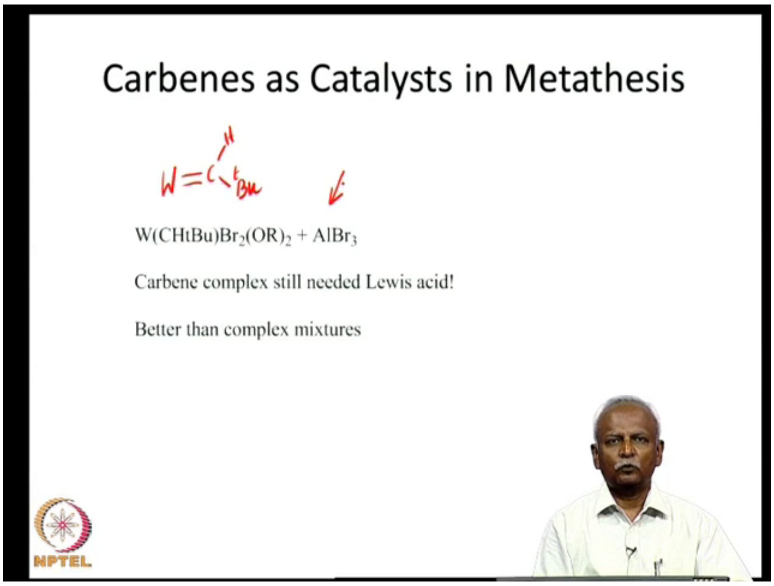

Carbenes as Catalysts in Metathesis

$W(CHtBu)Br_2(OR)_2 + AlBr_3$

Carbene complex still needed Lewis acid!

Better than complex mixtures

After Chouven unravel the mechanism of the reaction, it was clear that one needed a carbene and, so this carbene catalyst was used or was one of the first ones which were rationally designed. You will notice that this species, this carbene species was the catalyst. But it was still in a high oxidation state and it required an aluminium alkyl species aluminium halide, in order to activate this species.

So, a Lewis acid was apparently for some reason it was required in order to carry out this reaction forward. This Lewis acid activation is presumably to generate a vacant coordination site on the tungsten, so this is better than complex mixtures. The complex mixtures that were originally known for carrying out metathesis reactions were extremely complex this was better it were two components. But still it was not as good as what one would desire.

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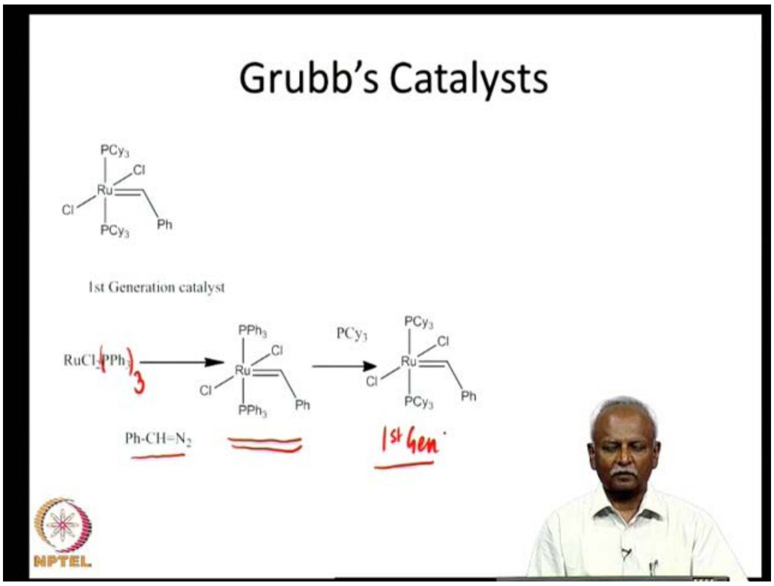

Grubb's Catalysts

1st Generation catalyst

$RuCl_2(PPh_3)_3$

$Ph\text{-}CH{=}N_2$

PCy_3

1st Gen

So, the first breakthrough came from the work of Schrock and Grubb. We will discuss these two in detail, we will take Grubbs catalyst first and then we will talk about the Schrock catalyst. Grubbs catalyst was a modification of the carbene systems that were known, which were derived from fisher carbene. Fisher carbenes were those species where you had a lead transition metal along with a carbon bearing a hetero atom. However, when you replace the hetero atom with all alkyl groups the carbine became lot more reactive and especially, reactive towards the metathesis reaction itself.

So, this catalyst which was first made by Grubbs, which is called the first generation catalyst on the Grubbs group, is extremely important for several reasons. First of all, it was the first single component catalyst which means that did not require another species in order to initiate the reaction. Secondly, it was a precursor for several other second generation. Third generation Grubbs catalyst this is also important and the fact that it could be easily generated in the reaction that is used for making this complex is shown here.

In fact, R u C l 2, P P h 3 thrice is the starting material and this starting material can now be reacted with adaizo carbene precursor. This leads to transfer of the carbene to the ruthenium and this molecule is a stable molecule which can be isolated and characterised. This species which is generated by attaching a carbeneto the R u C l 2, P P h 3 thrice turns out to be less reactive it is not as good a metathesis catalyst.

But when you replace that triphenyl phosphine with tricyclo hexyl phosphine, very simple substitution reaction you end up with the first generation catalyst. This is the first generation, first generation catalyst from the Grubbs group and it turns out be a good metathesis catalyst. So, there are advantages for this catalyst system, first of all it can be readily synthesised, very easily synthesised in the laboratory.

It is a stable system which can be stored and used again and again without difficulty you do not have to make it fresh every time you want to do the reaction. So this is the primary advantage and it is a single component catalyst and as I said that is a major advantage of the Grubbs catalyst.

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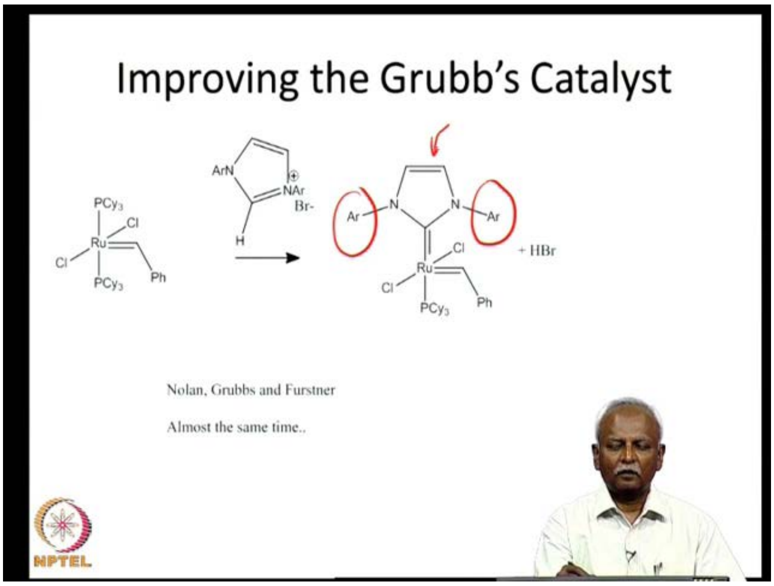

Improving the Grubb's Catalyst

Nolan, Grubbs and Furstner

Almost the same time..

Now, after Grubbs declared the synthesis of this catalyst, it turns out that several people wanted to make better metathesis catalysts. Something that would be more reactive than the first generation catalyst which could not be used with several substrates, three people, Nolan, Grubbs and Furstner discovered that if you can attach N heterocyclic carbene, this is the N heterocyclic carbine which we have encountered earlier.

If we can attach N heterocyclic carbeneto the ruthenium replacing one tri cyclo hexyl phosphene on the ruthenium with the carbene, then the catalyst turns out to be much more reactive much more useful. Presumably, the electron density on the ruthenium is increased and it is also true that you have large arial groups which protect the ruthenium centre from unnecessary reactions and decomposition. Now, all three of them published this about the same time, but following this initial results Grubbs showed that.

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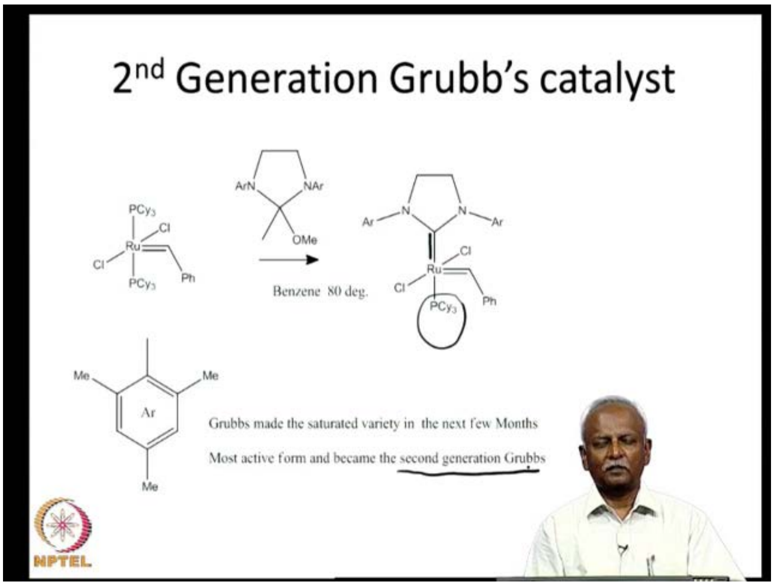

2nd Generation Grubb's catalyst

Grubbs made the saturated variety in the next few Months

Most active form and became the second generation Grubbs

If you replace the unsaturated N heterocyclic carbene in the present system you have an unsaturated heterocyclic carbene. If you replace it with a saturated variety of N heterocyclic carbine, then it turns out that the reaction is much, much better. The variety that Grubbs made actually had simple methyl groups to protect eryleto give steric protection to the ruthenium and you have a stable ruthenium complex. In fact, for the sake of understanding we will convert that single bond into double bond because we normally talk of this as carbine and carbene coordination to the ruthenium is one that promotes the reactivity of this centre.

During the course of this reaction, it is usually P C y 3 which leaves and generates a vacant coordination sight on the ruthenium. In general if you want a catalyst to function the resting state you would have a ligand with an extra ligand and which leaves and generates a vacant coordination site which initiates the reaction. Grubbs published the synthesis of this compound and its reactivity just a few months after he published unsaturated variety.

But it was very clear that unsaturated variety was the most active form and, so it became what was called popularly. As a second generation, Grubbs catalyst, the second generation Grubbs catalyst turns out to be a lot more reactive stable and useful for carrying out metathesis reactions.

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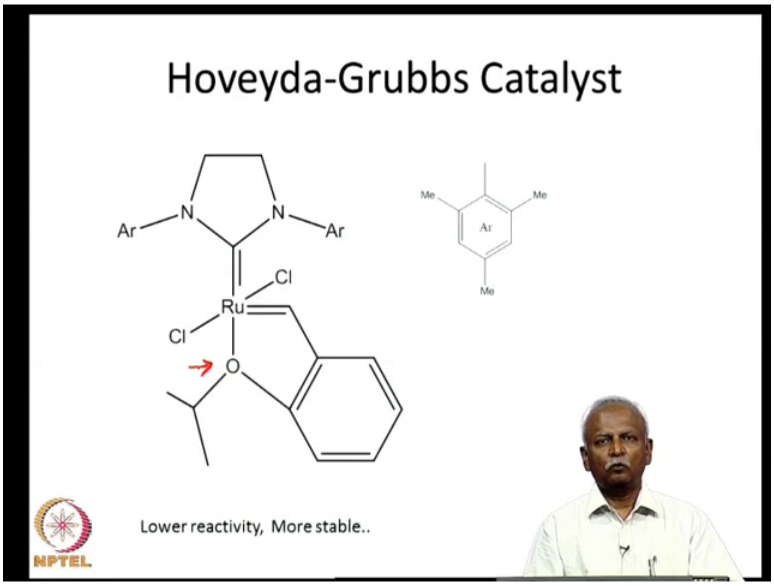

Hoveyda-Grubbs Catalyst

Lower reactivity, More stable..

Now, during the course of this study if there were other attempts to modify the N heterocyclic of being in such a way that it would give you a system which would generate a very reactive catalyst. This time mention should be made about the Hoveyda Grubbs catalyst this was the combination of the Grubbs catalyst system. Basically, you had N heterocyclic carbene which was saturated variety and you also had a carbine which was the essential reactive component of the metathesis catalyst. But, the P C y 3 was replaced with a pendant group on the on the alkylidene such that it coordinated to the ruthenium and blocked that site.

So, the vacant coordination site at the ruthenium was very readily generated by loss of this R u O bond. So, this R u O bond was lost initially and that led to a reactive form of the catalyst. Now, this turns out to be a little more useful it is less reactive, but it is more stable because of internal coordination of the alkylidene. So, when you design a catalyst it is very important that you design a catalyst that is as reactive as possible. But, at the same time it has a long shelf life and that is what we considered by more stability.

However, these two things are very often working at cross purposes because if you make the complex very stable then it will be less reactive. So, let us proceed further after

Hoveyda made this modification for the Grubbs catalyst. Grubbs second generation catalyst was the one which was most useful, but it was not very reactive.

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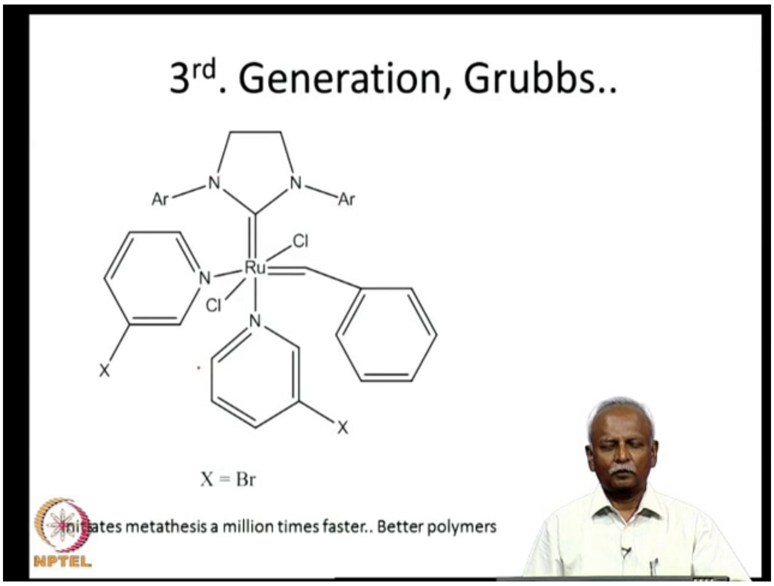

3rd. Generation, Grubbs..

X = Br

Initiates metathesis a million times faster.. Better polymers

Grubbs showed that if you replace the pendant group with a peredene unit a substituted peredene. If you react the Grubbs second generation catalyst with a peredene specifically, bromo peredene then it turned out to be an extremely useful catalyst it was extremely reactive. In fact, it initiates metathesis a million times faster than the second generation catalysts this like I said earlier it turns out be an extremely important fact for polymerisation.

If you do polymerisation, metathesis polymerisation which will talk about in a few minutes if you do metathesis polymerisation. If there is a long initiation time for the catalyst to start functioning, then you will end up with polymers with a variety poly dispersity which is undesirable. So, it is important to have as low poly dispersity as possible that means the molecular weight range is very small then you get much better polymers.

Polymers with better physical characteristics and, so it is important to have a catalyst which is extremely fast which has no lag time for the initiation of reaction. So, this catalyst which is called the third generation catalyst and it is an extremely fast catalyst which initiates metathesis a million times faster than the second generation catalyst.

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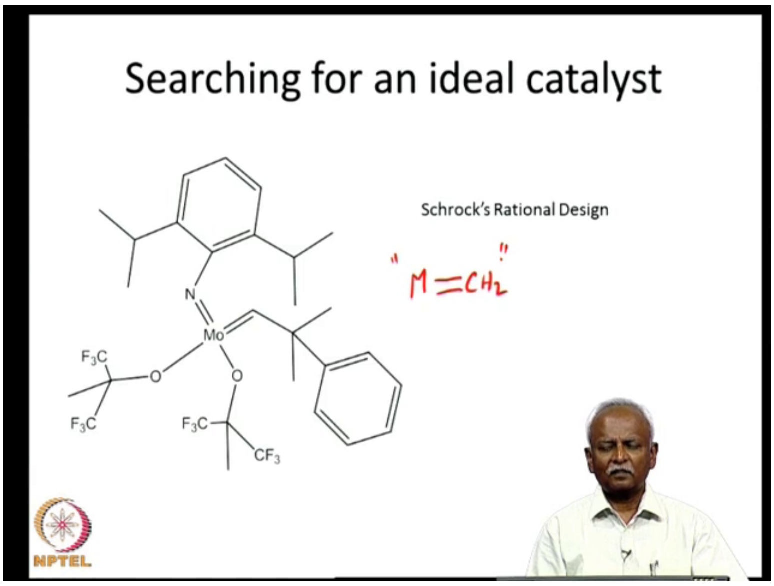

Searching for an ideal catalyst

Schrock's Rational Design

"$M=CH_2$"

So, let us take a look at the Schrock's design, Schrock was a person who was working with early transition metals and high oxidation state carbene compounds. If you remember the metathesis catalysts that were initially designed, that were known in the patents were all early transition metals oxides or chlorides. Which were activated with an alkylating agents either a tin R 4 tin compound or it was an A l R 3 compounds something that would alkalate an early transition metal. So, Schrock's design is quite natural; it starts with albidums pieces which are in then the high oxidation state. He showed that if you take a carbene, a Schrock carbene which surprisingly has no heteroatom to stabilise it.

If you take the Schrock carbene and if you attach two alkoxide units then it can function as a metathesis catalyst, but surprisingly the alkoxy groups which are attached to the metal have to bear some electron withdrawing groups. If they are not electron withdrawing when they are not as reactive as one would like them to be, so the Schrock's catalyst the most celebrated form of Schrock catalyst is what I have shown here. This has got two tri fluoro methyl groups attached to the butaoxy that is attached to the molybdenum.

So, this is a Schrock's catalyst which turns out be the most useful form of the catalyst it has got an alkylidene group. So, M double bond C H 2 is still the basic unit which is a catalytically active units are metathesis. That remains common for both the Grubbs catalyst and Schrock's catalyst the only difference is the fact that the molybdenum catalyst that is the basis for Schrock's catalyst has got two alkoxy groups, which are electron withdrawing in nature.

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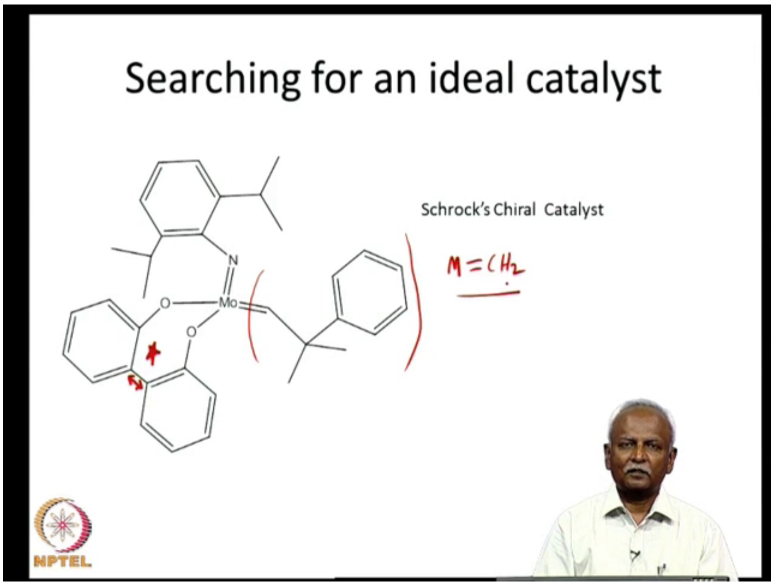

Searching for an ideal catalyst

Schrock's Chiral Catalyst

$M = CH_2$

Now, Schrock's catalyst also had another advantage and that advantage is shown here and that is the fact that you can generate a chiral Schrock's catalyst. Now, if you remember if you remember the catalyst centre has got two alkoxy units and binol which is tanaxially chiral with an axially chiral molecule which means that there is no single carbon which bears a symmetric unit. The chirality comes from the fact that you cannot rotate these molecules around this carbon carbon bond very easily. So, the chirality resides in the fact that these two planar rings are oriented in such a way that they have a helical axis to them.

So, now you have two alkoxy groups this is the binol unit which is attached to the molybdenum and it bears chirality at the molybdenum and now if you can do a catalysis metathesis catalysis using this alkylidene unit with the molybdenum centre which is carrying out metathesis always has a chiral centre. So, whenever you have the possibility for generating some stereo selective carbon carbon bond formation, then it would be possible to do it in a selective way when you have this chirality or this handedness on the molybdenum centre.

So, the Grubbs catalyst at the moment at least the ones that I have shown you do not have the chirality inbuilt in them whereas, the Schrock's chiral catalyst has this major advantage in that. It is chiral centre which is attached to the molybdenum and which is retained right through the reaction and so it turns out to be an extremely useful centre for inducing chirality.

So, let us see how these systems are being used, so we have discussed the catalysts in detail, but in all the cases it is only the m double bond C H 2 that is really important for carrying out reaction. So, it is only M double bond C H 2 that is the catalytically active centre and whatever we have described the rest of the paraphernalia. That is attached to the metal purely provides assistance in terms of a stabilising the molecule stabilising the catalyst or providing the right electronic input into the metal, so that the catalysis can be carried out.

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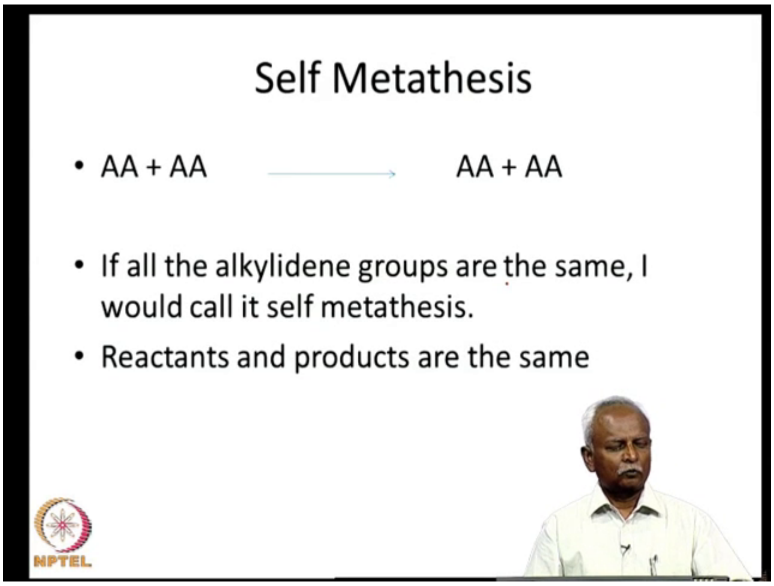

Self Metathesis

- AA + AA ⟶ AA + AA
- If all the alkylidene groups are the same, I would call it self metathesis.
- Reactants and products are the same

So, let us go to the actual examples where reactions can be carried out I would call self metathesis as the first example. Suppose you just have a two alkylidene groups which are identical and you carry out metathesis you would end up with reactants and products which are same, I would call this self metathesis. There is no thermodynamic loss or gain in this whole process and there is no effective reaction also, this is not of a great it is not of great utility to have the self metathesis.

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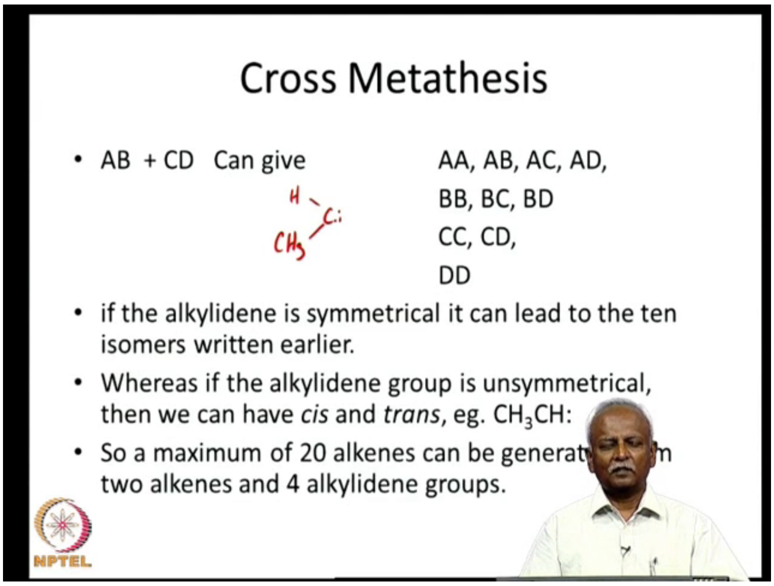

Cross Metathesis

- AB + CD Can give
  AA, AB, AC, AD,
  BB, BC, BD
  CC, CD,
  DD
- if the alkylidene is symmetrical it can lead to the ten isomers written earlier.
- Whereas if the alkylidene group is unsymmetrical, then we can have *cis* and *trans*, eg. CH_3CH:
- So a maximum of 20 alkenes can be generat m two alkenes and 4 alkylidene groups.

So, the more useful reaction is the one where you have cross metathesis. Now, let us imagine the extreme scenario where you have four different alkylidene groups attached to the olefin. So, in other words two olefins are undergoing metathesis and there are four different alkylidene groups I have labelled them as A B C D which means A is one alkylidene group B is a different alkylidene group.

Similarly, C D is a different olefin is now you just imagine the metathesis reaction carried out in this case will lead to almost ten different olefins because the alkylidene groups unless they have very strong electron withdrawing or donor groups on them. You will not have a major difference in the delta h of this reaction and goes from left to right after metathesis.

So, if you have A A B A B A, C and A D they are four different olefins that can be generated starting with the alkylidene group which is attached to the alkene. Then it is transferred to the metal and then it can be transferred to any one of the other olefins. Similarly, you can write out the remaining number for olefins that can be generated with each one of these alkylidines and you will realise that there are ten of them, so ten different alkenes can be generated. In the event that the alkylidene is asymmetrical you will have only ten, if you have an unsymmetrical alkylidene group which means that you have let us say C H 3 C H group.

So, the alkylidene for example, has got this type this is the alkylidene group that we are talking about then you can have both Cis and Trans olefin s generated from this alkylidene. So, a maximum of twenty alkanes can be generated just starting with two alkylidene alkenes and four alkylidene groups. This is the maximum that can be generated starting with four different alkylidene groups. Now, let us take a look at how one can utilise such a reaction which leads to a complex mixture of ten alkenes or twenty stereoisomers how can that be of any use.

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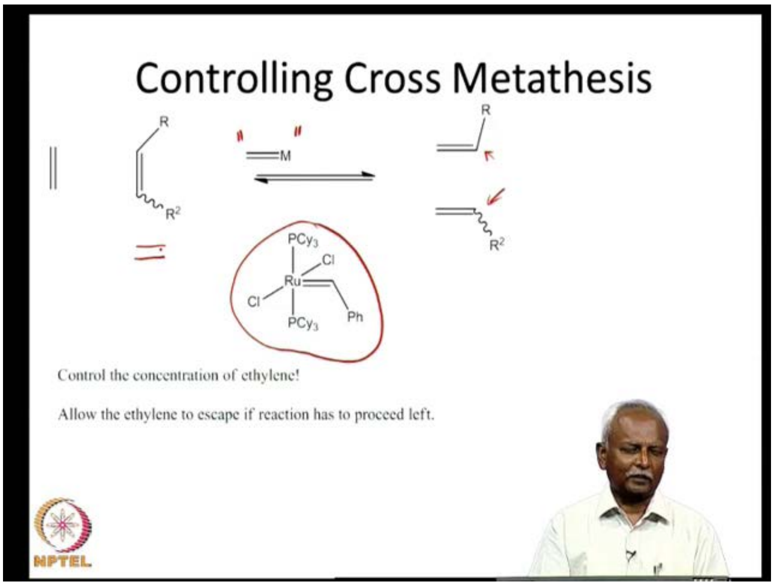

Controlling Cross Metathesis

Control the concentration of ethylene!

Allow the ethylene to escape if reaction has to proceed left.

So, this is something that we need to consider very often the cross metathesis reaction which is what we are talking about when you have different alkylidene groups is designed in such a way that it will give us the product which is of importance. The other product is conveniently eliminated from the reaction mixture either because it is volatile or in such a way that it can be isolated very easily. So, let us take a look at this reaction which I have indicated here weather it is sys or Trans alkenes if you can combine it with ethylene.

Let us say and carry out a metathesis reaction I have indicated the metathesis catalysts as alkylidene as a carbene metal carbene unit in principle. It can be either Schrock’s catalyst Grubbs catalyst, but in this in the case of olefins very often, it is convenient to just take the more readily available and the less air sensitive Grubbs catalyst and carry out the reaction and one will end up with these two alkenes during the course of this reaction.

If you want to control this reaction in such a way that I want to make only the alkylidene only the alkane which is pictured here I can push this reaction to the left very simply by allowing the ethylene to escape from the reaction mixture. So, this principle will be operating and one would go from the right side of this reaction to the left side and ethylene would be allowed to escape.

Suppose, I want to split a very large olefin which has got say A C eighteen olefin which has got the double bond in the middle and I want convert into two olefins which are smaller in size, then I can just have an high pressure of olefins. So, if I control the concentration of ethylene, I can move the reaction from left to right. If I increase the ethylene concentration I can very simply make the smaller olefins and move the reaction from left to right, so this turns out to be a useful way of controlling the metathesis.

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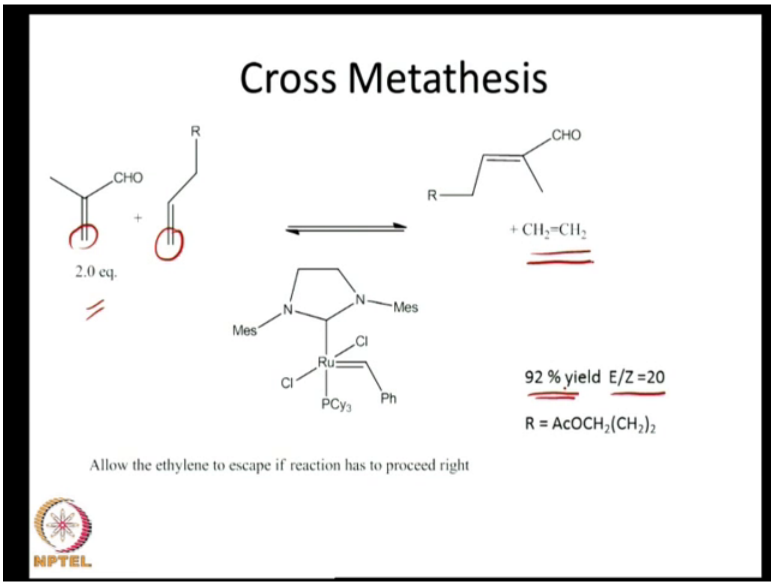

Cross Metathesis

2.0 eq.

+ $CH_2{=}CH_2$

92 % yield E/Z =20

R = $AcOCH_2(CH_2)_2$

Allow the ethylene to escape if reaction has to proceed right

Using the Le Chatliers principle, it is also known that there are some electronic factors which control the reaction here I have shown an example, where I have an electron withdrawing group on the olefins in which case then the reaction turns out to be a useful. If I have more amount of this electron withdrawing group attached olefin which is marked as this aldehyde the substituted neutral dehyde here. That is taken in a slightly larger amount and you will notice that this can again end up with elimination of the two C H 2 groups.

Ethylene is eliminated during the course of this reaction and very conveniently you have generated a useful aldehyde which is now having a much larger molecular weight and you will also notice that although you had a unsymmetrical alkylidene group. So in other words this alkylidene could end up with both sys and trans. You will notice that this reaction mixture ended up with the e by z ratio that means the trans compound the trans product was formed in a ratio of twenty is to one for the sys compound.

So, this turns out to be a very easy way of generating starting with here, I have shown this reaction was done with the Grubbs second generation catalyst and he ended up with a 92 percent yield just by adding two equivalents of the aldehyde. That you started out with and you ended up with an aldehyde which is more useful and a 92 percent yield. So, this was carried out with Grubbs second generation catalyst and it allows for a reaction where you have an aldehyde as a source too.

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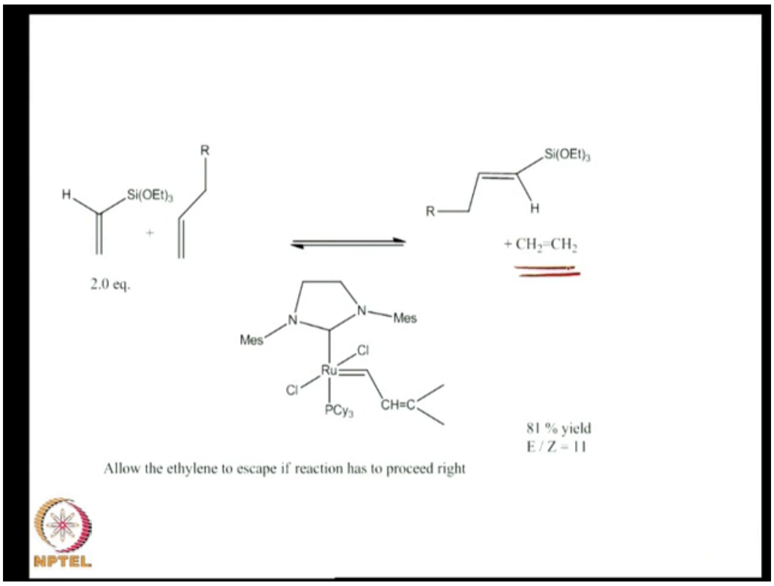

81 % yield
E / Z = 11

Allow the ethylene to escape if reaction has to proceed right

Now, a similar reaction with a modified Grubbs second generation catalyst here again you get a silent substituted alkene. This can also proceed from one side to the other side purely by removal of ethylene from the reaction mixture and you end up with 81 percent yield of the desired product and a E by Z ratio of 11.

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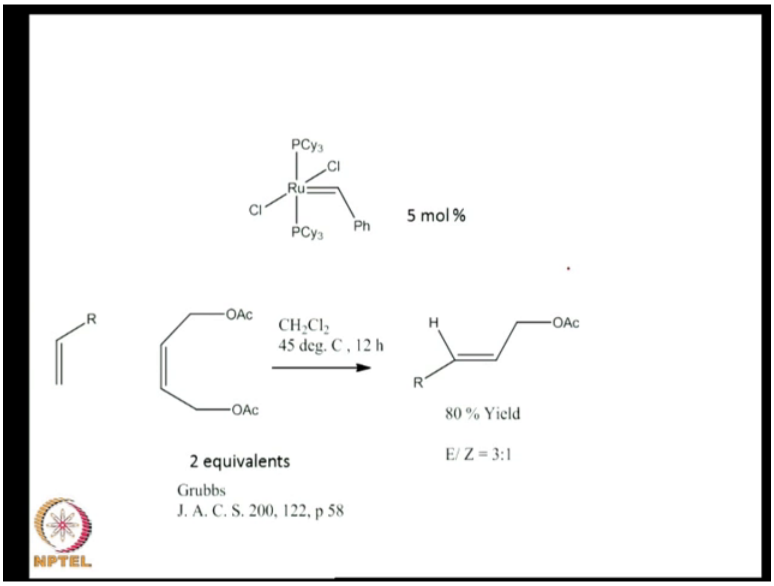

5 mol %

CH_2Cl_2
45 deg. C , 12 h

80 % Yield

E/ Z = 3:1

2 equivalents

Grubbs
J. A. C. S. 200, 122, p 58

So, in all these cases ethylene the amount of ethylene that was used was amount of ethylene that was removed from the reaction mixture was the key for pushing the reaction from left to right and generating the product that was useful. So, here I have shown you another example, where you ended up with a useful product 80 percent yield again with Grubbs first generation catalyst is only five more percent of the first generation catalyst very mild conditions. You can convert the compound which is of use in this particular case it is the side product is a product is reasonably volatile and can be removed from the reaction mixture.

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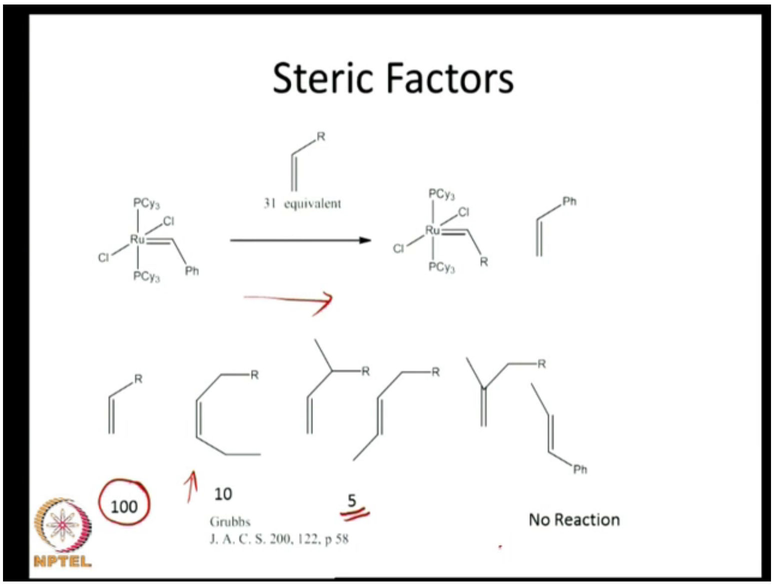

Steric Factors

31 equivalent

100

10

5

No Reaction

Grubbs
J. A. C. S. 200, 122, p 58

So, you can see that the Le Chatliers principle is that the key for generating useful products, so you can also have some steric effects during the course of this reaction. Now, you will remember that olefins have a tendency to coordinate two metal atoms to a lesser extent when they are substituted. So, since the olefins has to be coordinated to the metal during the course of the reaction the reaction works well when you have less subsidiary olefins here, I have shown you the first step in the whole metathesis process. That is the formation of the elimination of the alkylidene group which is attached to the ruthenium centre on reaction with the starting material.

So, here I biased the reaction in such a way that I end up with only the substitution initial substitution of the alkylidene group on the ruthenium. So, if you look at the rates of these reactions at the rate at which the reaction proceeds, this reaction proceeds from left to right, you notice that if I have a single substituent on the ethylene. So, that is the fastest that procedure the rate of say hundred arbitrary units then the moment you have two substituents on the olefin in a sys position.

Then the reaction slows down by almost ten orders one order of magnitude it comes down to ten units relative units. Similarly, if you have a heavily substituted alkene and if you have a trans substituted alkene then the reaction falls by another factor of two. So, you can see how the reaction goes slower and slower as you have greater and greater number of substituents and the sys substituent is substitution pattern is better than the trans substitution pattern. This turns out that if you have a heavily substituted olefin especially one with the phenyl group.

So, if you have a styrene then the reaction is practically a virtually nonexistent with when you have the Grubbs first generation catalyst. So, this gives you an idea about how it is important to have very reactive olefins and if you want to carry out reaction in a fast manner. So, there are various ways which allow you to control the reaction and these are used very effectively for doing cross metathesis.

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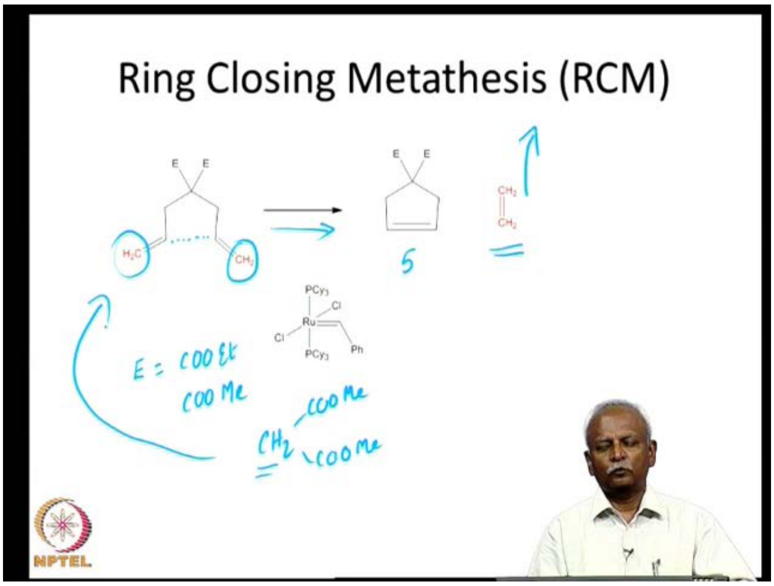

Ring Closing Metathesis (RCM)

Now, we come to a special class of action which is called ring closing metathesis reaction. Ring closing metathesis reaction is a special case when the two olefins which are undergoing metathesis belong to the same molecule. So, if I have two double bonds which are positioned in such a way that you can eliminate two alkylidene groups and form a ring. So, basically what we are doing in this particular case is, we are eliminating these two C H 2 groups and forming ethylenes.

As I told you earlier elimination of ethylene is very often a convenient way of pushing the reaction from one direction to the other direction. So, this itself drives this because ethylene is a volatile species which can be eliminated from the reaction mixture. More than that, the reaction is entropically favoured by having the two groups which are joining together from a single molecule. So, in other words two different olefins are not formed, a single olefin is formed and that leads to a five membered ring, which is entropically very favourable.

This is a five membered ring which is formed and the new bond that is formed in between these two carbons turns out to be a very favourable situation. So, Grubbs first generation catalyst is convenient for carrying out these types of reactions and you will notice that E is actually an electron withdrawing group. Very often, it is C O O E t or C O O M e and this you will recognise as a species which is coming from a dialkylation of diethyl malenates.

So, if you take C H 2, C O O M e dimethyl malenate and you alkalate this active carbon then you will end up with this particular starting material. It is a very convenient starting material and you can generate this five membered ring is very readily using any closing metathesis reaction. This turns out to be useful and it can even be done with larger sized ring not necessarily with a five member ring and once again the Le Chatliers principle is utilised, so that you can remove ethylene and form a very nice ring system.

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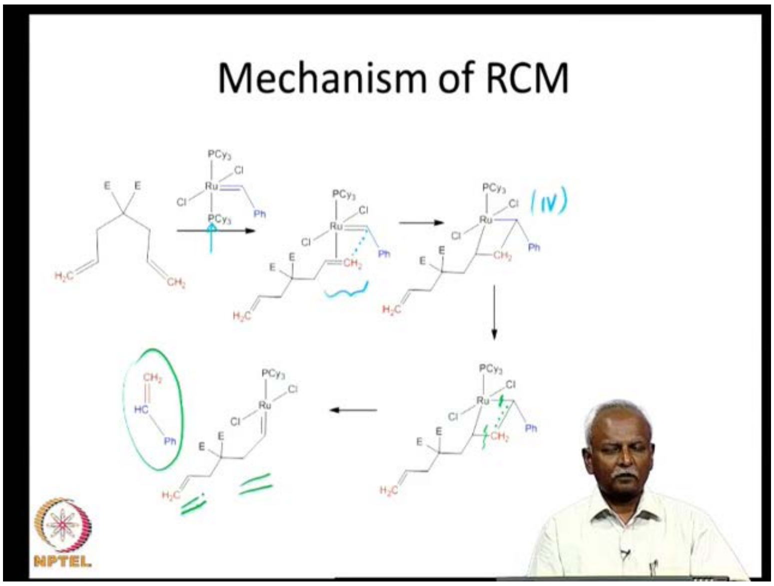

Mechanism of RCM

Let us take a look at the mechanism of the ring closing metathesis why is it that it is so convenient to carry out the metathesis reaction. I have colour coded the alkylidene group which is present of the ruthenium to start with. You will notice that the replacement of this P C y 3 on the ruthenium with the olefin from the starting material or the reactant lead to a ruthenium alkylidene alkene complex this is a key intermediate. Now, starting with a ruthenium two centre, you end up with formally a ruthenium four centres.

Here, you carried out what we call as an oxidative coupling reaction where the ruthenium undergoes formal oxidation and you have coupled two carbon centres. Basically, the two carbon centres which are coupled are marked here in the dotted lines and, so you end up with a new bond which is metallo cyclo butane. Ruthenium metallo cyclo butane is formed and this ruthenium metallo cyclo butane can now break in a different fashion. Earlier, you had the formation of a new carbon carbon bond between the C H 2 group which was coming from this starting material and the alkylidene group which is present on the metal.

Now, I can eliminate this alkene and I shall show it in a different colour, so that you can follow it very easily, I break these two bonds and form a new carbon carbon double bond. If I form a new carbon carbon double bond, then I end up with, this product is eliminated and I have an alkylidene group where the starting material is now coordinated to the ruthenium.

I have alkylidene group which can now carry out another metathesis reaction, now with this olefin which is attached to the same molecule. So, an alkylidene group which has got an alkene inside as an internal reactant turns out to be a very fast reaction and that is what we have written here.

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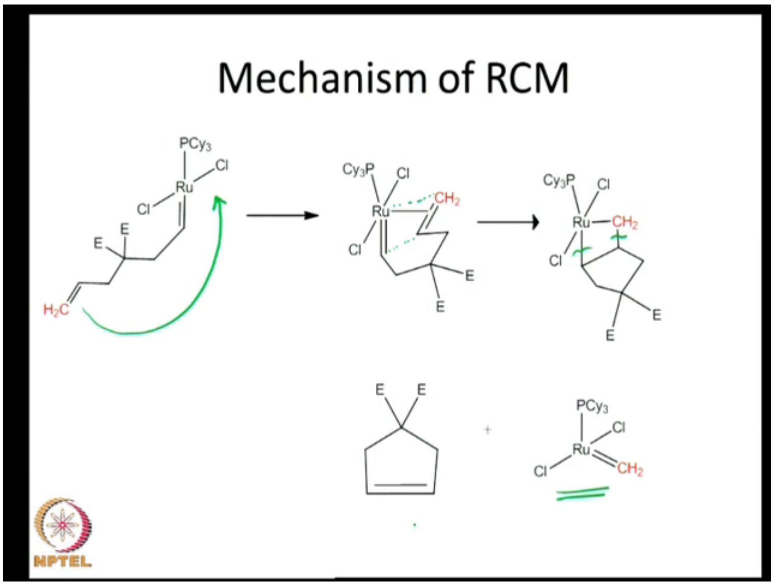

Mechanism of RCM

Now, we move this C H 2 double bond to this position. If you move it to this position then you end up with a cyclic intermediate and the cyclic intermediate once again forms a bond. This time the ruthenium carbon bond is formed here and the carbon carbon bond is formed here. The new carbon carbon bond the methyl, now again goes from plus 2 to plus 4 oxidation state. This can now eliminate can break in such a way that you form R u C H 2 as the final as the catalyst again is regenerated catalyst and the cyclic product which is listed here.

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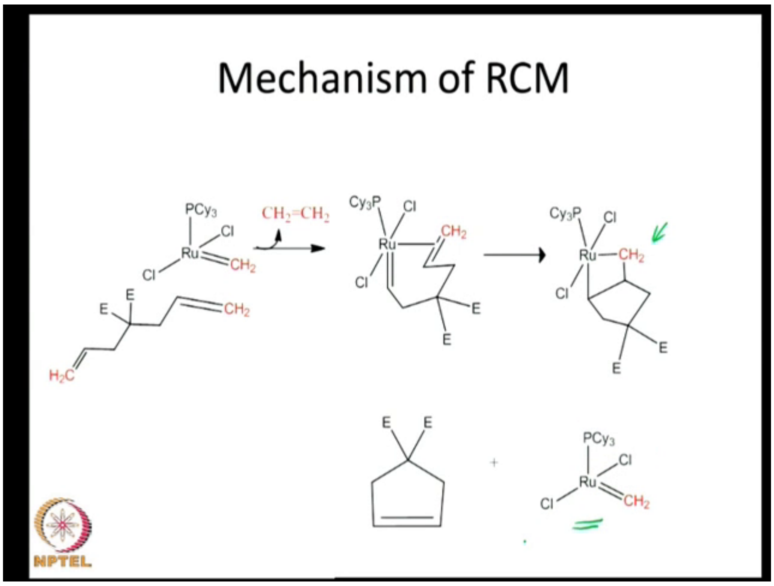

Mechanism of RCM

So, we can write these two systems together, now I will start with the R u C H 2 which I generated in the previous reactive set and now we can go through the catalytic cycle fast. You have the formation of ruthenium metallo cyclo butane which is listed here and I can eliminate the cyclo pentene which regenerates the catalytically active intermediate. So, this is the mechanism of the ring closing metathesis this is the mechanism of the ring closing metathesis.

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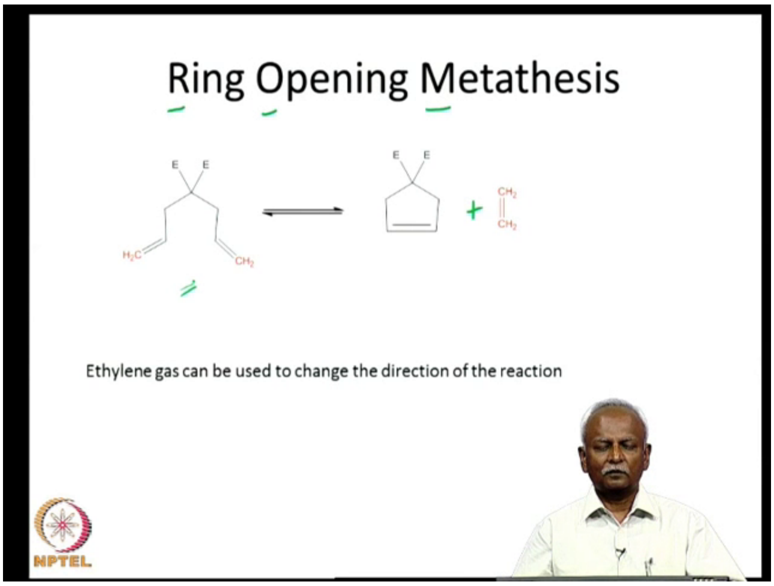

Ring Opening Metathesis

Ethylene gas can be used to change the direction of the reaction

Now, you will notice that the same reaction can be pushed in the opposite direction if you have a large amount of ethylene. Suppose, I have a high concentration of ethylene and I take the ring closed product, then I can have a ring opening metathesis. So, this is called RON the previous one is called RCM and this one is called ROM, and the ring opening metathesis can push the reaction from the ring closed system to the ring open system.

Now, exactly the same reaction can go back the same steps can be retraced in order to generate this product, in this particular instance this is the product. So, you realise how the reaction can be used to very effectively go from one direction in a very effective fashion to generate a wide variety as starting materials and products.

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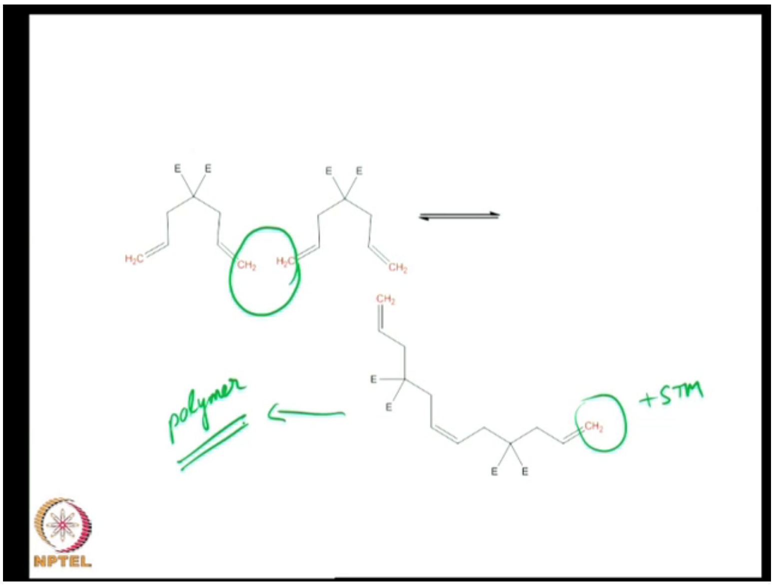

So, once again I can take the reactant which I had shown you earlier which is the diethyl malenate which has been di alkalated using two alkyle groups. That again is an easy step if I take these two di alkylated species, I can in fact eliminate ethylene once again from two different molecules. Now, that will lead to a new diene this time it will be actually triene, its triene because you have generated a new double bond in the process.

So, two dienes come together and form a triene and, now you will realise that you can keep adding these molecules together in such a fashion that you can form a polymer. So, I can remove two C H 2 units from one of these molecules and another one of the starting material, starting material and lead to a polymer. So, this is a polymerisation reaction which is executed through metathesis and in each step ethylene is eliminated. Because ethylene is a volatile molecule that can be quickly removed from the reaction mixture and you can have a very efficient way of polymerising a diene.

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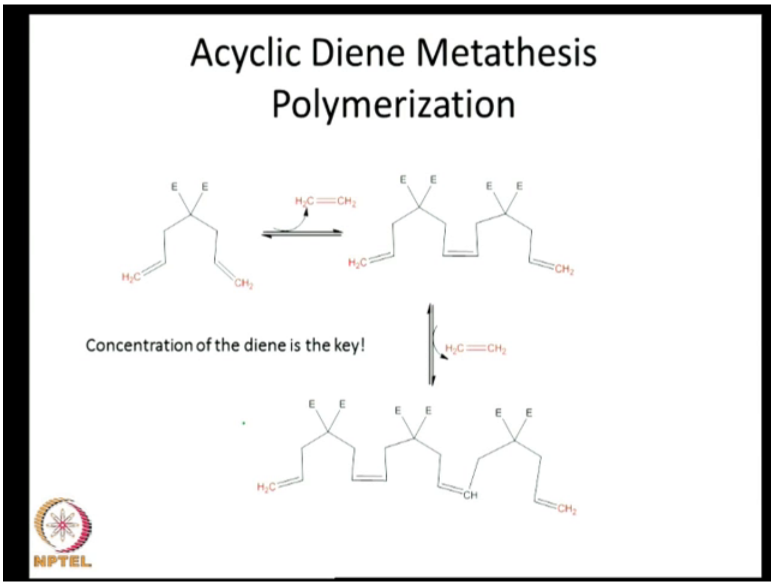

Acyclic Diene Metathesis Polymerization

Concentration of the diene is the key!

So, this is called acyclic diene metathesis polymerisation. Acyclic diene metathesis polymerisation is a system where you eliminate ethylene from a diene molecule in such a way that you form a polymeric molecule. How do you push the reaction the same reactant has been used for three different reasons, one is to do ring opening metathesis other is to do ring closing metathesis, another is to do acyclic diene metathesis polymerization. So, here the concentration of the diene is a key concentration of the diene if it is very high then the polymerisation results.

If you remove ethylene during the process then you can very effectively make a large high molecular weight polimer starting with an acyclic diene. Now, if you add a lot of ethylene to a cyclised product then of course, you can go from the ring closed product to the ring opened product. So, you can push the reaction in different directions based on the concentration of the reactant which is there.

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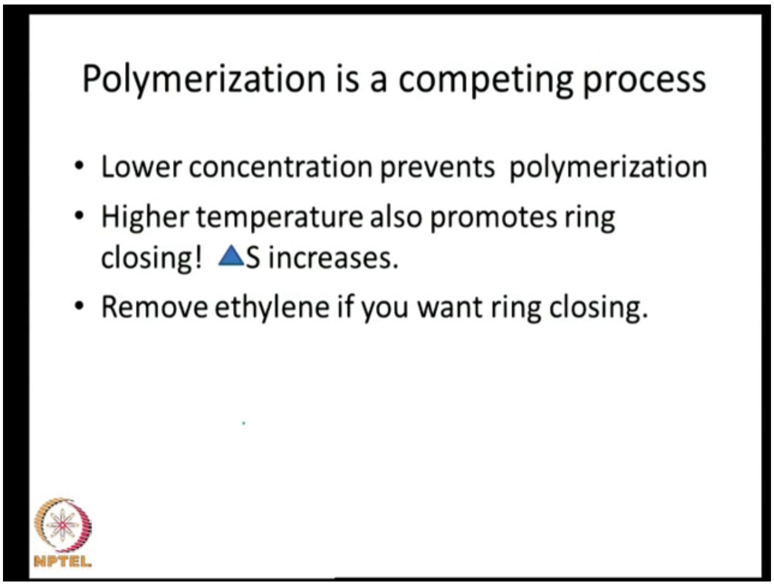

Polymerization is a competing process

- Lower concentration prevents polymerization
- Higher temperature also promotes ring closing! ▲S increases.
- Remove ethylene if you want ring closing.

Polymerisation is a competing process whenever you do ring closing metathesis polymerisation or a ring opening metathesis polymerisation. So, the lower concentration always prevents polymerisation if you have a large amount of the diene, large concentration of the diene. Then the possibility of the diene reacting with itself is higher and of course, leads to polymerisation. If you have high temperature, then the ring opening and the elimination of ethylene is promoted because the T delta S increases in the process and you can have larger free energy change negative free energy change as a result of the reaction.

So, that would be a more favourable process when you have the reaction proceeding in a forward direction that means you have ring closing during the whole system. If you remove ethylene of course, if you want to do ring closing reaction you should remove ethylene from the reaction mixture so that it does not come back and complete for the reaction.

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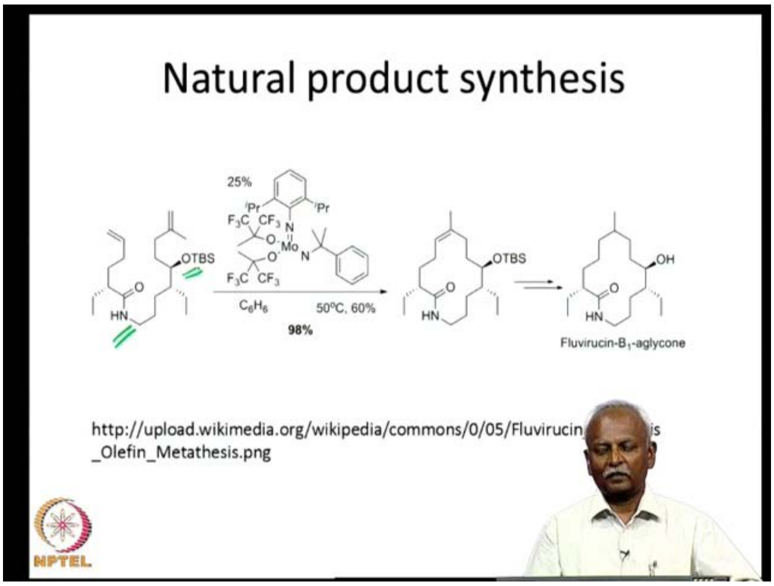

Natural product synthesis

http://upload.wikimedia.org/wikipedia/commons/0/05/Fluvirucin is
_Olefin_Metathesis.png

So, you can see that how this particular metathesis reaction is extremely useful and it has been used extensively for the synthesis of a variety of natural products. The natural product synthesis especially for unusual ring systems is being conveniently accomplished using the metathesis catalysis. Here Schrock, the Schrock ‘s catalyst has been used very effectively you have two reactive groups, you have an amide functionality which is a present here and you have an ether functionality.

In the presence of the functionalities, if you want to do a metathesis reaction it is convenient to do it with a Schrock catalyst. The Schrock catalyst carries out this whole reaction and 25 percent, 98 percent yield and if you need a large amount of the catalyst for this whole process to function. But nevertheless this is a very efficient way of making such a large ring natural product and very effectively you can generate ring system.

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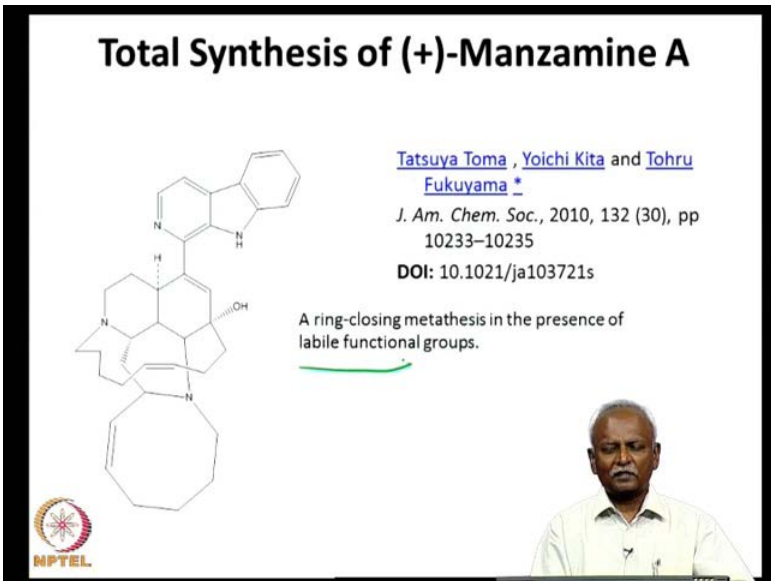

Total Synthesis of (+)-Manzamine A

Tatsuya Toma , Yoichi Kita and Tohru Fukuyama *

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A ring-closing metathesis in the presence of labile functional groups.

A recent synthesis of another natural product Manzamine, Manzamine A which is been isolated from a marine organism is shown here. This was accomplished by a ring closing metathesis in the presence of very labile functional groups. This is a very complex natural product with so many ring systems and in spite of all that the reaction could be carried out. Fukuyama and the co-workers have recently published the total synthesis of such a complex natural product. The last step is the ring closing metathesis which was accomplished, which led to the generation of this chiral natural product being synthesised very efficiently. So, with this I would like to end today's lecture, I will show you some of the keep options.

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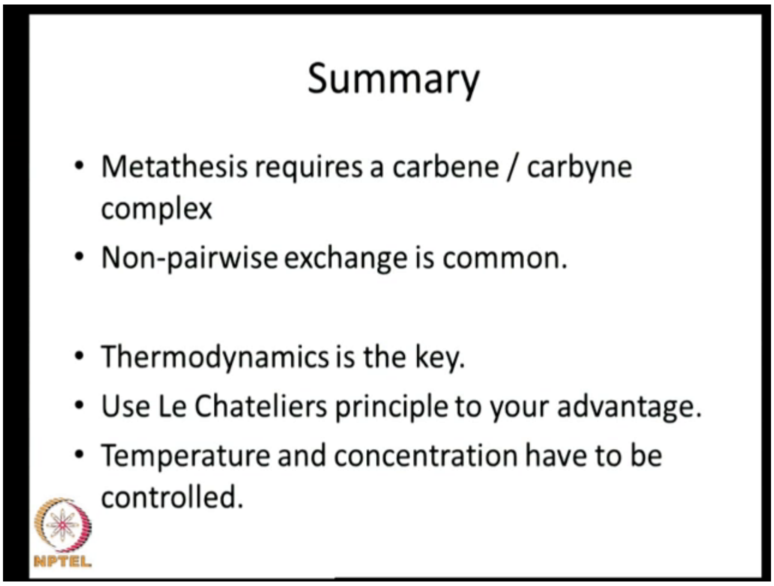

Summary

- Metathesis requires a carbene / carbyne complex
- Non-pairwise exchange is common.

- Thermodynamics is the key.
- Use Le Chateliers principle to your advantage.
- Temperature and concentration have to be controlled.

So, we will summarise today’s lecture by saying that metathesis requires a carbene complex. It can also be carried out with a carbyne complex with acetylenes they are not discussed this in today’s lecture, but it is also possible. The most important point is to note, is a fact that there is non pairwise exchange and this non pairwise exchange means that you will have a clutter of products in this whole reaction.

In order to carry out this reaction effectively, you need to utilise thermodynamics to the hilt. So, if you have to use the Le Chatliers principle that is the most important principle that can be used to advantage in order to push the reaction in the direction in which you want to carry out. The whole push reaction from the reactant to the product side you have to utilise Le Chatliers principle very effectively.

Temperature and concentration also are important when you carry out polymerisation reactions you can utilise the whole thing with efficiently when you use if you use high temperatures and T delta S is large. So, we can push the reaction to the side in which we want to carry out the reaction efficiently, so it is the metathesis reaction. Although, it seems to be such a nonspecific reaction, it generates a large number of products very easily.

You can use it very effectively if you remember that the importance of thermodynamics, you can push it in the direction which you want it to proceed. So, in the case of carbynes you can use the reaction with acetelenes and you can generate metathesis of carbynes.

That leads to acetelenes, poly acetelene which are very difficult to make otherwise and you can make very interesting materials which we shall cover in a future talk.