Transition Metal Organometallics in Catalysis and Biology
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Lecture - 26
Ring Closing Metathesis (Part-2)

Welcome to this course on Transition Metal Organometallics in Catalysis and Biology. We have been discussing about olefin metathesis reaction in the past few lectures and in particular, in the last two lectures we have been focusing on ring closing metathesis reaction. Now one thing which we have noticed that these olefin metathesis reactions are thermoneutral reactions in the sense that there is no, the energy released is almost equal to the energy needed for carrying out the reaction.

So there is no enthalpy gain during the course of the reaction and because of which this is not a enthalpy driven process. However, we had seen that there are various other factors which guide or drive the reaction forward for example, in the case of ring opening polymerization, it is the release of ring strain that drives the reaction forward.

Similarly, in case of the reverse ring closing metathesis what we had observed is the formation of large macrocycle where ring strain becomes insignificant and the formation of gaseous product like ethylene resulting from the two terminal alkene which gets reacted to each other as a process of olefin metathesis.

So that drives the reaction. So there are instances where the release of ring strain carries the reaction forward as in the case in ring opening metathesis whereas in ring closing metathesis it is the formation of ethylene molecule which drives the action forward because ethylene being gas quickly gets out of the reaction vessel. And the same thing is observed for other metathesis reaction.

For example in ring opening metathesis polymerization ROMP or even in some of the cross metathesis reaction that these evolution of ethylene is seen as a driving force for getting the reaction move forward. So with that let us now focus on ring closing metathesis reaction and in continuation with yesterday's or previous lecture, what we had observed that ring closing metathesis are mainly used for making rings which are large macrocycles.

And when there are possibility of forming more than one ring or there is a possibility of forming multiple rings what we had observed in our last discussion is the fact that the larger ring with lesser ring strain is the one which is favored and it is the one which is observed. So today we move on with some more examples of ring closing metathesis.

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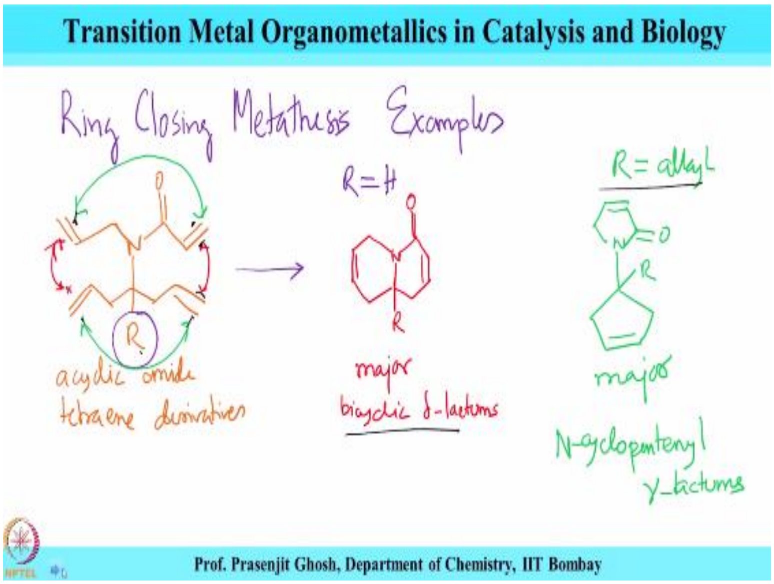

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Examples. For this substrate these are acyclic amide tetraene derivatives. So one can envision these having four double bonds has multiple choices for undergoing this ring closing metathesis and what we see that the one which should undergo the ring closing metathesis depends on the variety of factors including in this particular case, including the substituent which is present over here.

For example, if R is equals hydrogen then the major product of this reaction becomes bicyclic six membered ring as is shown over here. And that involves the ring closing metathesis occurring between these two alkanes to give the following bicyclic compound and this is the major product. And these are called bicyclic delta-lactam.

However, if R equals alkyl then what happens is strikingly different than the metathesis occurs between these two olefins which are on the nitrogen as well as these two resulting in two five membered rings as is shown over here. And these are called

N-cyclopentyl gamma-lactams. So what we see over here is that a story of differential reactivity in one case.

In the first case when R equals hydrogen then these two olefins undergo metathesis reactions, ring closing metathesis to give this bicyclic gamma-lactam. Whereas, when R becomes alkyl substituents more bulky than the olefins on the same amine ligands same side they undergo ring closing metathesis to give this N-cyclopentyl gamma-lactam.

So this is a very interesting bit and what we see this same story of differential reactivity occurring in many substrates which has multiple double bonds and in some cases the ones which would give larger macrocycle is what is observed than the smaller one. A nice example in continuation with this discussion is described below.

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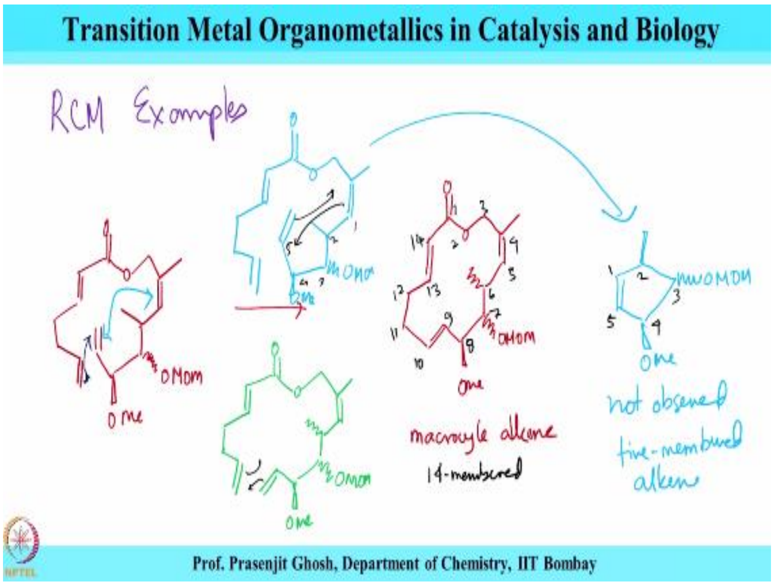

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This is for the substrate which has four double bonds and it is kind of complex structure, which I am going to draw over here. This is a protection group. Now for this, there is a possibility of various kind of ring closing metathesis that occur. But the one which is favored is the one which results in larger macrocycle and that is between these two olefin. So this can be sort of nicely written as is shown here.

So the metathesis sort of takes place between these two olefin resulting in the desired substrate product which is which has a larger macrocycle as is shown over here. So this is a large macrocycle and it is actually called macrocycle alkene. There exists other possibility as well. For example, one can think of metathesis undergoing between these two olefins and in that case one can think of a structure or orientation something like.

In this case, the other possibility is that one can think of a metathesis like this and that would result in a five membered ring and that would give a product which would be and so that would have the following carbons bearing as is shown over here. But fortunately a this product is not formed, not observed, this five membered alkene and this is possibly because of the issue of larger ring strain being present in small membered cyclic structure, than it is in the big cyclic structure.

So what we see which is becoming evident over and over again is that this RCM is a very powerful reactions, but they have a particular purpose and the purpose is that these are effective only for creating large macrocycles, which has very less ring strain. So for example, the one which is favored over here, this macrocyclic alkene is about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, so it is a 14 membered ring.

So what we see that this 14 membered macrocycle is favored as opposed to the other product which could have been formed from metathesis of different alkenes those structures are not favored in ring closing metathesis. Now, the ring closing metathesis also goes beyond the domain of achiral reactions to chiral reactions as is shown here in the few examples.

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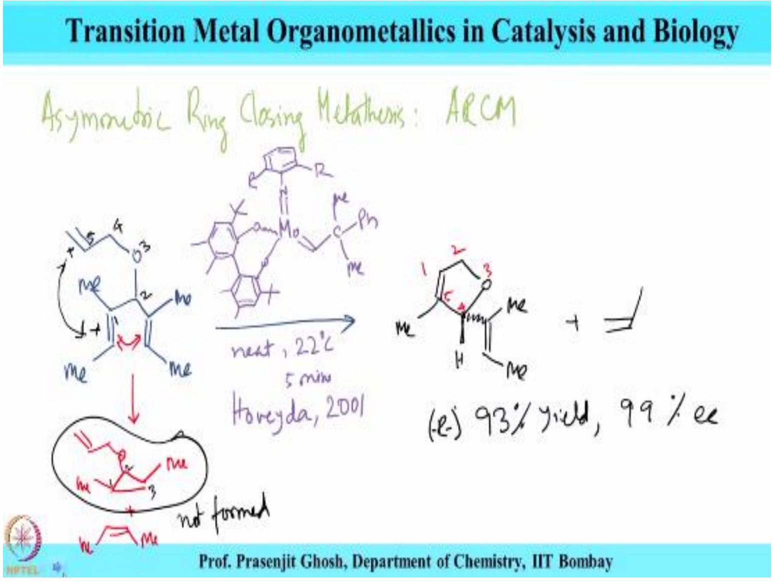

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Asymmetric Ring Closing Metathesis: ARCM

neat, 22°C
5 min

Hoveyda, 2001

(R) 93% yield, 99% ee

not formed

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And these are called asymmetric ring closing metathesis and in short they are called ACRM or ARCM. A nice example of this is demonstrated below. Now this the catalyst uses quite elaborate like in other catalyst, this one is quite it is a molybdenum imido carbene complex with tributyl dimethyl. So these two R's is a bulky group and then the carbene fragment which is also bulky with too methyls and one phenyl.

So this catalyst was reported by Hoveyda, 2001 and this reaction neat reaction at 22 degrees centigrade in 5 minutes gives the desired product which involves the metathesis between this olefin and this olefin resulting in the formation of a five membered ring 1, 2, 3, 4, 5. So the corresponding product is a cyclic ether plus vinyl alkene.

This reaction is highly stereospecific, results in R stereochemistry in 93% yield and 99% ee. Now to note here also is the fact that there exist a possibility of other ring closing metathesis reaction happening which is between these two olefin, but that would result in highly constrained cyclopropane ring, which would be something like this.

And these products, which will be is never observed not observed or not formed. So what we see in ring closing metathesis over and over again that there exist always a possibility of differential reactivity and the reaction which gives rise to product with or rings macrocycles with less or lesser ring strength is the one which is favored.

So here in this case we saw that ring with a five membered ring was favored as opposed to a three membered ring over here. So that is what highlights this ring closing metathesis reactions. We are going to take a look at another example of asymmetric ring closing metathesis or ARCM examples.

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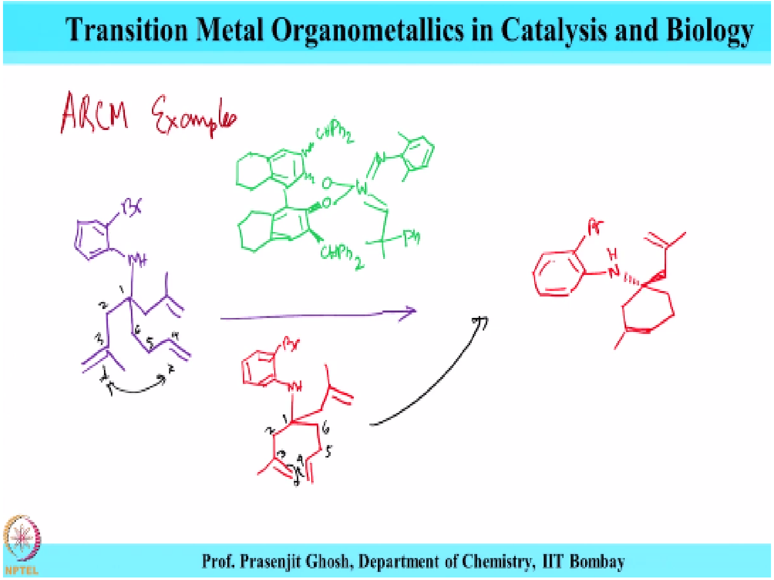

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ARCM Example

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Now this is for this particular alkene amine and this is also a imido carbene complex of tungsten as is drawn over here. These are elaborate ligand architectures a benzene ring and a cyclohexane ring fused. And also bulky CHPh 2 substituents bound to tungsten with a imido phenylimido moiety with two methyls and a phenyl ring and a carbene bound to tungsten with two methyl and phenyl.

So this is the elaborate carbene catalyst. And what the way it reacts is the reaction that occurs between these and this olefin resulting in a six membered ring which can be envisioned if I draw it in this presentation. And here the numbered atoms are so which will undergo metathesis to give the corresponding product as is shown over here, this macrocyclic compound.

So this is another example of asymmetric ring closing metathesis. And with this we come to the end of discussion of today's lecture on various aspects of ring closing metathesis. We have looked into various examples achiral as well as the chiral one. And we have also noted the main character feature which visible in all of the reaction is that the formation of a larger macrocycle through ring closing mechanism is favored in cases where there is less of a ring strain.

So in terms of getting products with respect to ring closing metathesis reaction, so one sees that when there are multiple opportunity of rink closing metathesis exist on a substrate with different alkenes the one which is favored will have comparatively less ring strain and larger macrocycles in that process. So with this we come to today's discussion, closing of today's discussion on ring closing metathesis reaction.

We are going to take it take this metathesis reaction in much more details, when we meet in the subsequent lecture. And with that, I once again thank you for being with me in this lecture and look forward to being with you in the next lecture when we take up various other examples of ring closing metathesis that exist and discuss them in great detail. Till then thank you and goodbye.