Transition Metal Organometallics in Catalysis and Biology

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Lecture - 25

Ring Closing Metathesis (Part-1)

Welcome to this course on Transition Metal Organometallics in Catalysis and Biology. We have been talking about ring closing metathesis. Ring closing metathesis reactions are in principle exactly opposite to that of ring opening metathesis reactions. And in this context we were sort of comparing all the specific attributes of ring closing metathesis with that of ring opening metathesis.

Now while drawing the completion between ring opening metathesis and ring closing metathesis, one sort of finds out that for ring opening metathesis the release of ring strain in the substrate is a key factor that guides the reaction forward towards ring opening metathesis. On the other hand, in ring closing metathesis it is exactly the opposite in the sense that the rings are found.

But these rings need not be under strain, because these rings are usually large macrocyclic rings and hence the strain issue which had been the guided factor for ring opening metathesis does not arise in ring closing metathesis despite the formation of rings is because of the fact that these rings are usually large macrocycles and hence they are not small rings. As a result, their strain is also too less.

So in this connection we are going to start more discussing about the ring closing metathesis particularly from the perspective of the mechanism for ring closing metathesis.

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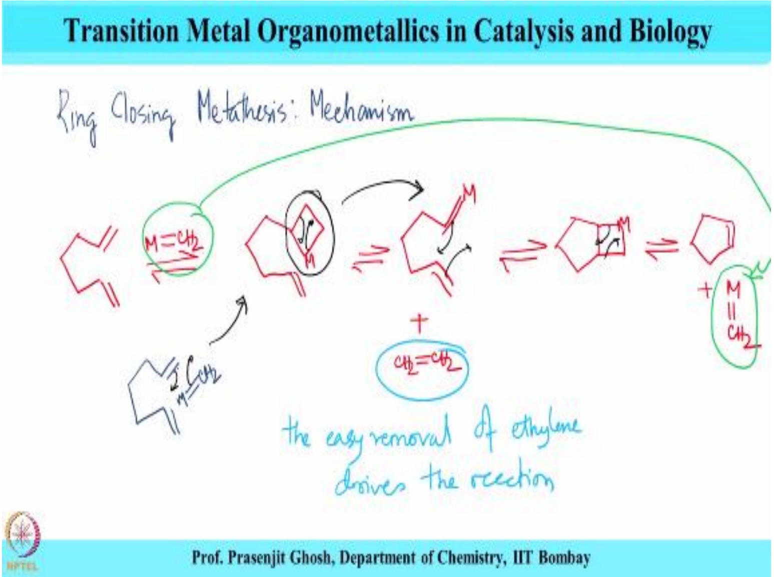

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Ring Closing Metathesis: Mechanism

the easy removal of ethylene drives the reaction

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This substrate it is a diene which reacts with the active species which is the metal carbene complex to form this metallocyclobutane intermediate and this is formed by the approach of this with MCH 2 leading to this metallocyclo butane intermediate that then results in the metal carbene ring along with the formation of ethylene and that is formed from this metallocyclobutane to give this product.

And then this further undergoes another metathesis reaction to give this intermediate bicyclic intermediate and that in general would give back cyclopentene with metal carbene species. So the active species is thus regenerated and in the course, the cyclopentene is formed and that is driven by the easy removal of ethylene drives the reaction. So this ethylene which is formed, it drives the reaction forward.

So we are going to take a look at some more applications in terms of examples that are being used for demonstrating the power of ring closing metathesis.

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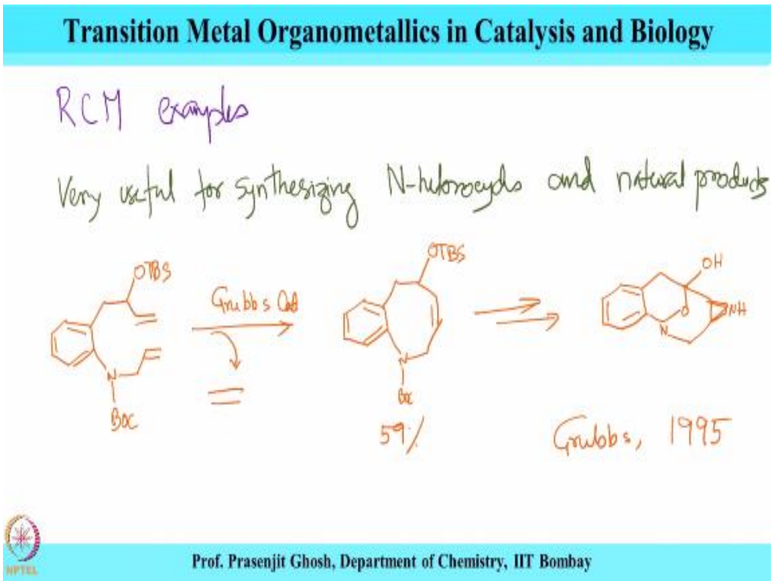

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RCM examples

Very useful for synthesizing N-heterocycles and natural products

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Examples. And this method is useful for synthesizing nitrogen based heterocycles and natural products. Very useful for synthesizing N-heterocycles and natural products. And this is shown by this interesting example. This in presence of Grubbs catalyst eliminates ethylene, which obviously is the driving force for the reaction to give this bicyclic compound and that can be, this was prepared in 59% yield.

And that can be used for synthesizing this natural product, complex natural product as is shown over here. And this was reported by Grubbs in 1995. The other examples of ring closing metathesis involves C2-symmetric ketals as in the one shown here.

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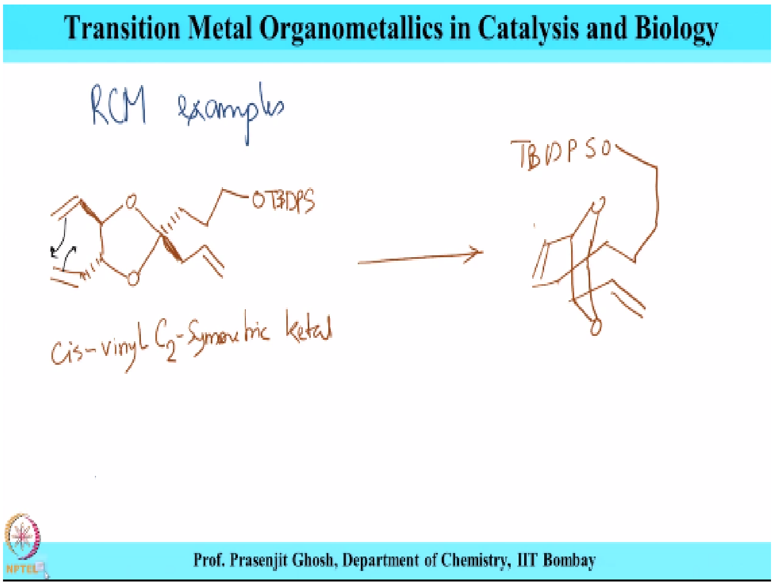

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RCM examples

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Examples involving vinyl C2-symmetric ketal. This is the 2 C2 symmetry of the vinyl group. So this is cis-vinyl C 2 ketal that undergoing ring closing metathesis as is shown over here to give between these two olefins to give giving this product. And so this undergoes the ring closing metathesis. The final product for this is as shown here. And this undergoes several type of rearrangements and this finally gets in there. Another example of ring closing metathesis is discussed here.

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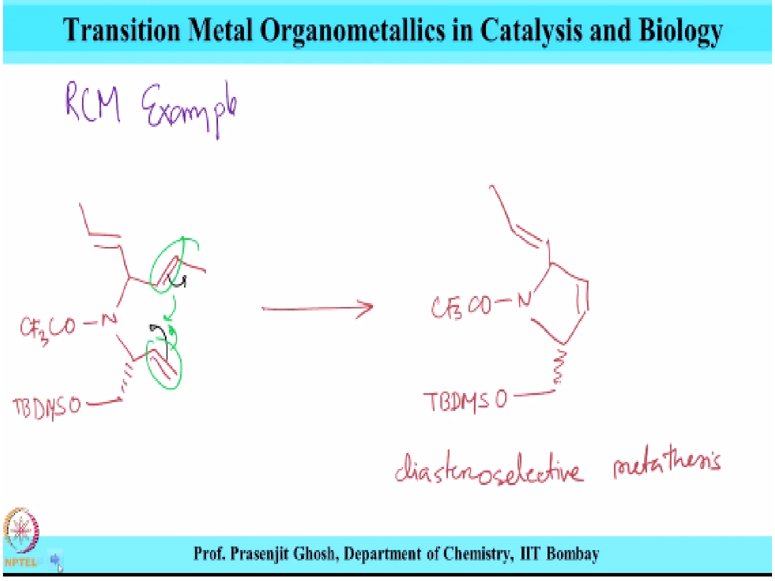

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RCM Example

diastereoselective metathesis

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So this is in this complex substrate nitrogen COCF 3 OS TBDM and this undergoes ring closing metathesis resulting in between these two olefin resulting in CO N, this five member ring OS TBDM. And this is a diastereoselective metathesis reaction. And here we see that the two olefins undergoes ring closing using these two olefinic bond. The other examples, we continue to give various examples of ring closing metathesis.

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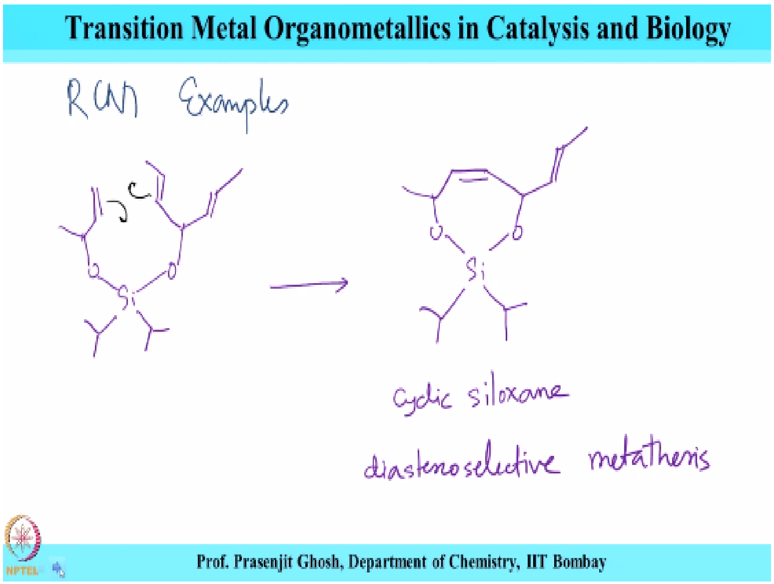

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RCM Examples

Cyclic siloxane

diastereoselective metathesis

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The next example involves CM examples. The next example involves this silyl ether. This silyl ether that undergoes intramolecular ring closing metathesis between the olefins, this leading to the formation of cyclic siloxanes as is shown over here. So the product is a cyclic siloxane and this is also another example of diastereoselective metathesis reaction. We continue to look at a few more examples of metathesis.

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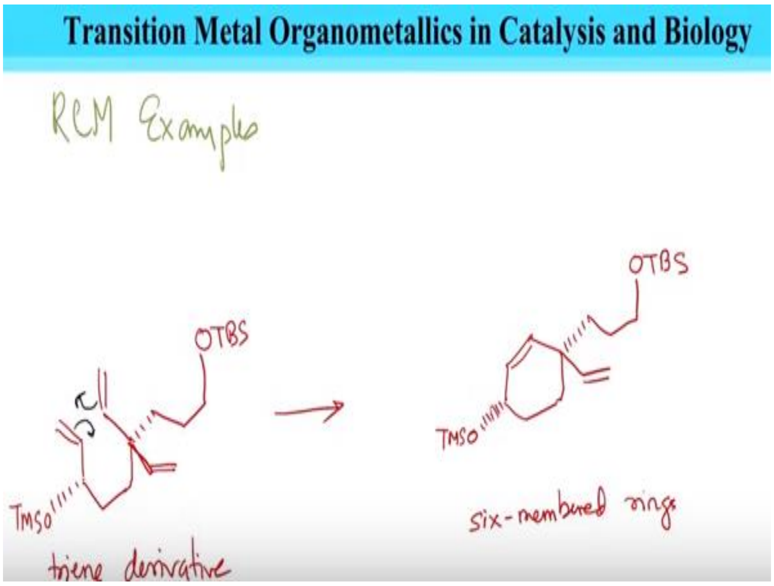

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RCM Examples

And this one involves a triene derivative as is shown over here, OTBS a triene derivative that undergoes metathesis intramolecular metathesis between the olefin shown over here to produce a six membered ring as is shown over here. TMSO OTBS and this provide. Now this is a triene and only a six membered ring which is favorable or ring closing metathesis of that ring occurs.

So this ring closing metathesis is not restricted to simple olefins but also can be applied to phosphonates. We are going to take a look at some of the examples of phosphonates.

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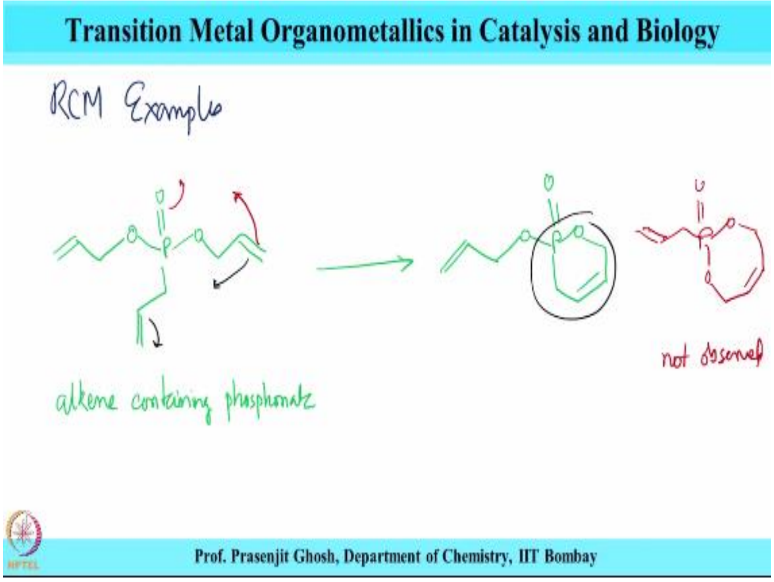

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RCM Example

alkene containing phosphonate

not observed

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This is alkene containing phosphonate that reacts to give this compound as is shown over here. Again a six membered ring and that is formed from these two olefin giving rise to this six membered ring and the other possibility of metathesis with a P-O bond as is shown over here that leading to the product this is not observed. So what we see is that there exists a selectivity in undergoing ring closing metathesis with carbon-carbon bond as opposed to undergoing with a P-O bond.

Another example of selectivity of ring closing metathesis is illustrated in this example to be discussed now.

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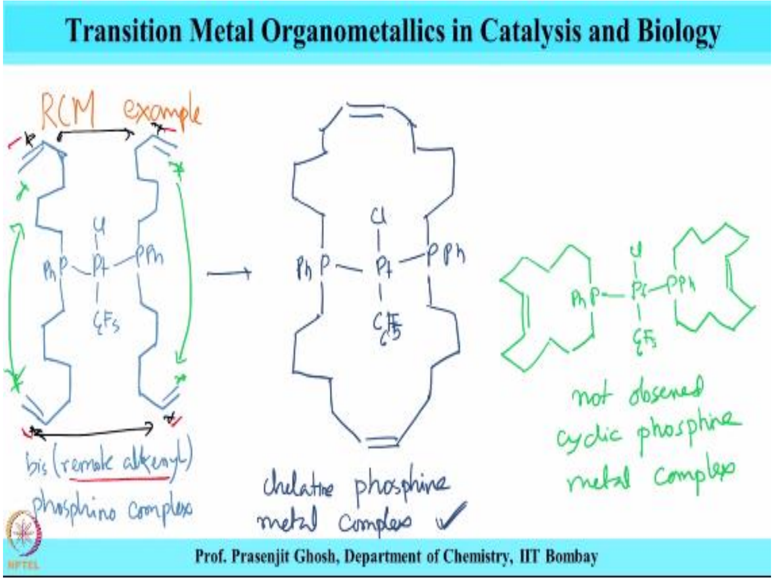

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RCM example

bis (remote alkenyl) phosphino complex

chelating phosphine metal complex ✓

not observed cyclic phosphine metal complex

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This is in observed in this Platinum complex chloride C 6 F 5 PPh as is shown here. PPh shown here. Now this is called this remote alkenyl phosphino complex. The name remote alkenyl refers to the alkene ring in the remote end and what was observed is the metathesis reaction between these olefins which are on the opposite side of the ligand resulting in the complex Pt Cl C 6 F 5 PPh PPh which is connected, connecting the two phosphine ligands.

And that happens between the RCM of this. And then what is observed is chelating phosphine metal complex and the other possibility of these two olefin reacting with each other, these two olefin reacting to each other to give the product F 5 PPh PPh to give this product does not observed cyclic phosphine metal complex. So what we see is the rings which are more macrocyclic in nature as is shown over here that is formed as opposed to the one which is slightly less microcyclic.

And hence, this may be probably because of less ring strength involved in forming larger macrocycles. So with this we come to the end of today's discussion on ring closing metathesis. What we have seen is that this ring closing metathesis is a powerful tool for preparing macrocycles which are large and also this can be used in a diastereoselective fashion for preparing various kinds of N-heterocycles and some of them can also be taken towards total synthesis of useful natural products.

So with this we come to an end of today's discussion on RCM. More as we meet when we take up RCM in the next lecture, look at various nitty gritty details about applications of ring closing metathesis. So I once again take the opportunity to thank you for being with me in this class. And I will very much look forward to discussing more on RCM when we meet next. Till then goodbye and thank you.