Introduction to Organometallic Chemistry

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Lecture - 37
C-H Activation

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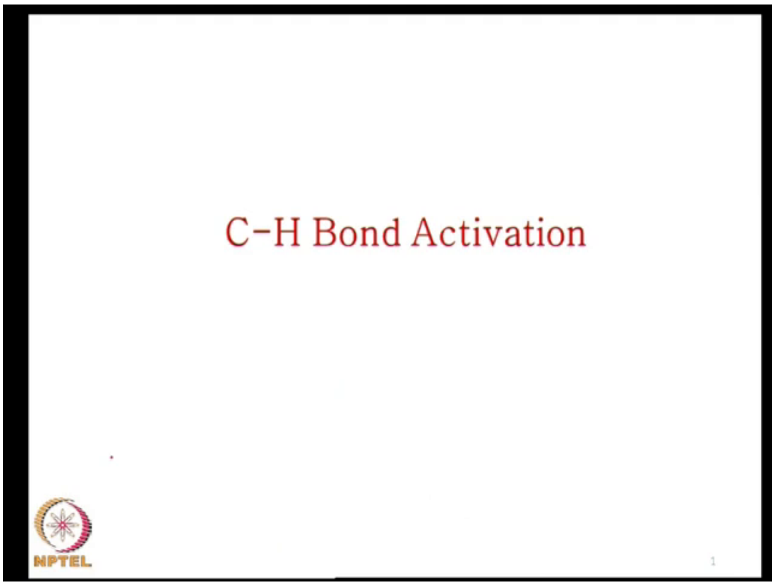

C–H Bond Activation

Today we will talk about C H bond activation. We have discussed in the past, the activation of c x bonds, where x is a heteroatom, but today we will talk about the C H bond, which is in fact in all organic chemistry. And so the chemistry of the C-H bond in the context of organometallic chemistry is quite important.

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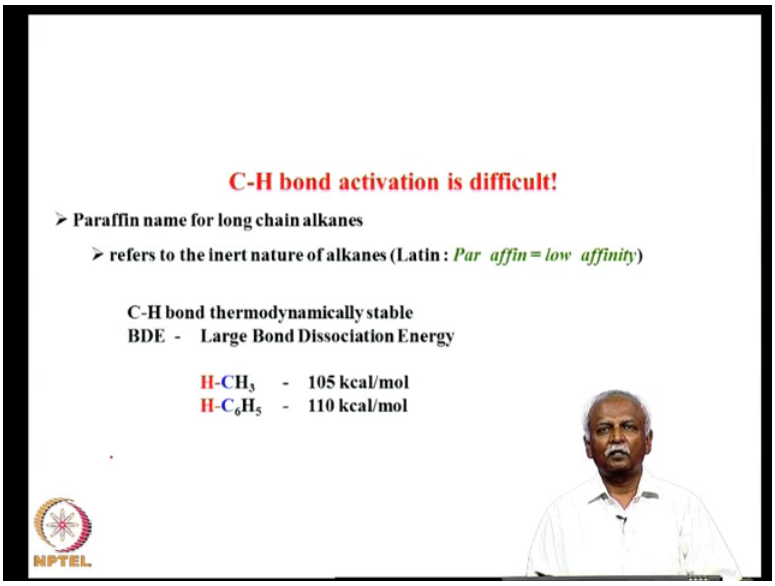

C-H bond activation is difficult!

- Paraffin name for long chain alkanes
  - refers to the inert nature of alkanes (Latin : *Par affin = low affinity*)

C-H bond thermodynamically stable
BDE - Large Bond Dissociation Energy

H-CH_3 - 105 kcal/mol
H-C_6H_5 - 110 kcal/mol

But yet, this has been a major difficulty, a major challenge for organometallic chemists. And one can trace this difficulty to the fact that the C-H bond is in fact a thermodynamically stable species, an extremely stable species which has got one of the highest bond energies that is accessible to carbon with any other element. And in fact, if you look at the name paraffin, which is, what is given for long chain alkanes where there is no other functional groups. You realize that, it is because of its low affinity for other chemical species. So, if the thermodynamics is working against you, it is in fact difficult to carry out any activation of that particular bond.

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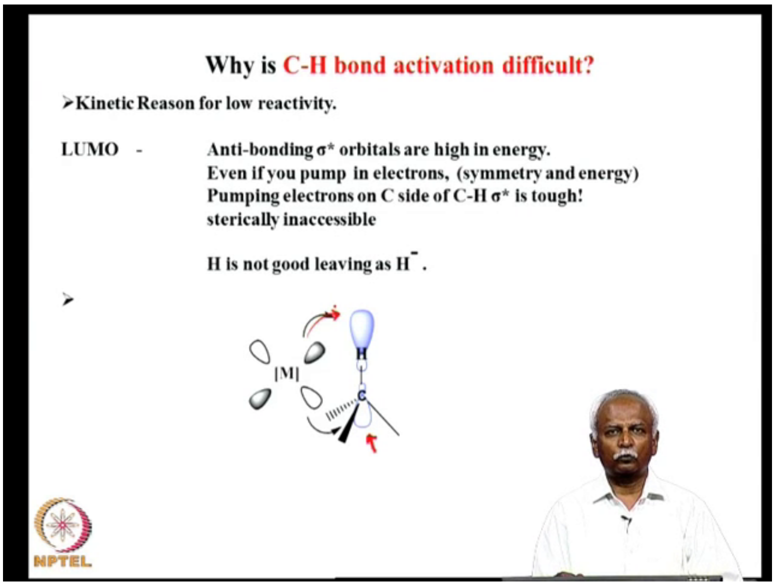

Why is C-H bond activation difficult?

- Kinetic Reason for low reactivity.

LUMO - Anti-bonding σ* orbitals are high in energy.
Even if you pump in electrons, (symmetry and energy)
Pumping electrons on C side of C-H σ* is tough!
sterically inaccessible

H is not good leaving as H^-.

-

So, let us take a closer look at why this activation is difficult. Now, if you look at the lowest unoccupied molecular orbital of the C-H bond, it would approximately have the shape. Now, we are not particularly concerned with the contribution of carbon and the contribution of hydrogen, in this particular molecular orbital. But just schematically we have represented it here. And we show that the anti-bonding orbital will have this symmetry and approximate shape.

Even if you match the C-H bond, the sigma star bond in terms of symmetry and energy pumping electrons into this MO, becomes a difficult task. The metal infact, has got orbitals of the right symmetry, but not often of the right energy, but if the energy is matched then indeed pumping electron should be possible. But even there you notice that, on the carbon side there are three bonds on the carbon, in an SP3 hybridized orbital there are three bonds on the carbon, which are in fact protecting the lobe, that is present on the C-H sigma star.

So in accessible. So this orbital that we are talking about is not accessible to the metal and that is the interaction, is shown by the arrow. It would be easier to pump in electron density on to the hydrogen, but if you just push in electron density into the hydrogen you would have to generate it as H, you have to dislodge it as H minus and that would also be an extremely difficult task.

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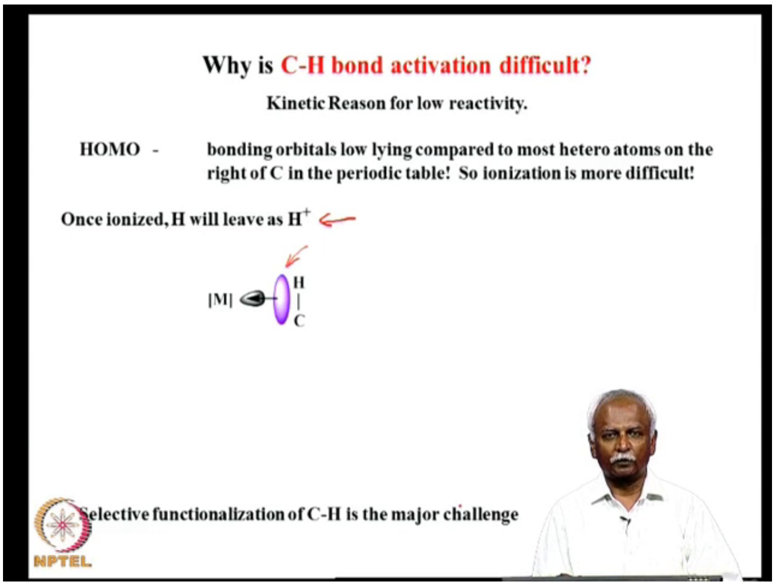

Why is C-H bond activation difficult?

Kinetic Reason for low reactivity.

HOMO - bonding orbitals low lying compared to most hetero atoms on the right of C in the periodic table! So ionization is more difficult!

Once ionized, H will leave as H^+

Selective functionalization of C-H is the major challenge

On the other hand, we might be able to remove an electron from the C-H bond. In fact the bonding orbitals are low lying, but nevertheless we could find an empty orbital, which is probably hopefully lower in energy level than the C-H bonded itself. But if you remove an electron, an electron from the C-H bond, the form of that is like a simple sigma bond. Then it would be possible, to find an empty orbital on the metal that would leave it as CH plus dot and it will ionize very readily as h plus. This in fact is a favorable situation and it might be quite feasible, but on the other hand because the C-H bond is selective functionalisation is a major challenge, which has to be countered.

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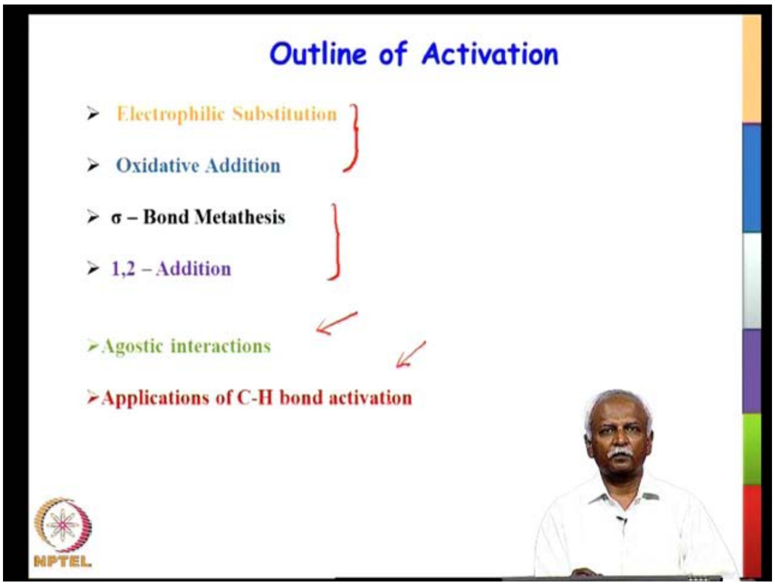

Outline of Activation

- Electrophilic Substitution
- Oxidative Addition
- σ – Bond Metathesis
- 1,2 – Addition
- Agostic interactions
- Applications of C-H bond activation

So, let us proceed with the outline of today’s discussion, we do have some situations where you have both electrophilic substitution and oxidative addition. These are the two major forms, by which C-Hactivation occurs. There are a few instances where, you do have a sigma bond metathesis and 1,2 addition. And finally, before we close the discussion, we will discuss two important aspects which is, one is the interaction of C-H bonds with metal atoms, which have mostly manifested themselves as interactions and one very recent development which is, which is an application of C-H bond activation, which seems to be very promising, now each one of these are, are these interesting applications, are color coded. Here, in this outline and they will continue to be color coded in the presentation as well.

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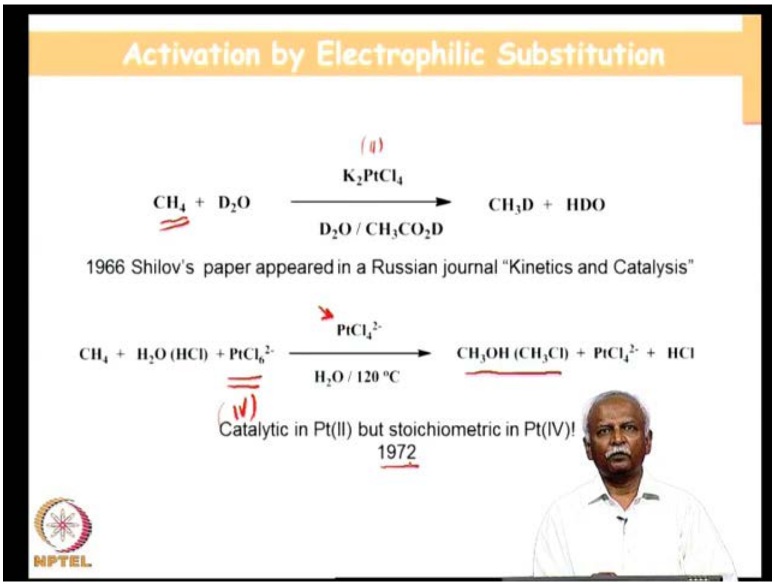

Activation by Electrophilic Substitution

(II)

$$CH_4 + D_2O \xrightarrow[D_2O\ /\ CH_3CO_2D]{K_2PtCl_4} CH_3D + HDO$$

1966 Shilov's paper appeared in a Russian journal "Kinetics and Catalysis"

$$CH_4 + H_2O\ (HCl) + PtCl_6^{2-} \xrightarrow[H_2O\ /\ 120\ ^\circ C]{PtCl_4^{2-}} \underline{CH_3OH\ (CH_3Cl)} + PtCl_4^{2-} + HCl$$

(IV)

Catalytic in Pt(II) but stoichiometric in Pt(IV)!
1972

So, let us take up electrophilic substitution. In fact, it is interesting to know that as early as 1966, Shilov in Russia published a paper in a Russian journal, in the Russian language, which made it reasonably inaccessible tomost of the chemists because at that time Russia was behind the. It was not obvious to many that, this very interesting paper on the direct activation of methane had been accomplished. And that was accomplished by a simple platinum catalyst, which was a platinum two, platinum, the platinum two oxidation state.

And it was an exchange of hydrogen for deuterium, this paper triggered a lot of attention later on when it became accessible to many people in the west. Round about a few years later, a little later Shilov himself published a second more significant paper. In which he clearly showed that a platinum four species, a platinum four species could be used in fashion to activate methane, to give either methanol or methyl chloride depending on the concentration of the chloride ion in the medium.

Now, this reaction although it is not extremely useful because you have to use amount of platinum four, platinum two is only a catalyst. Inspite of this, it turns out that this paved a way for understanding electrophilic aromatic substitution, electrophilic substitution. So this is published only in 1972about six years after the 1966 paper.

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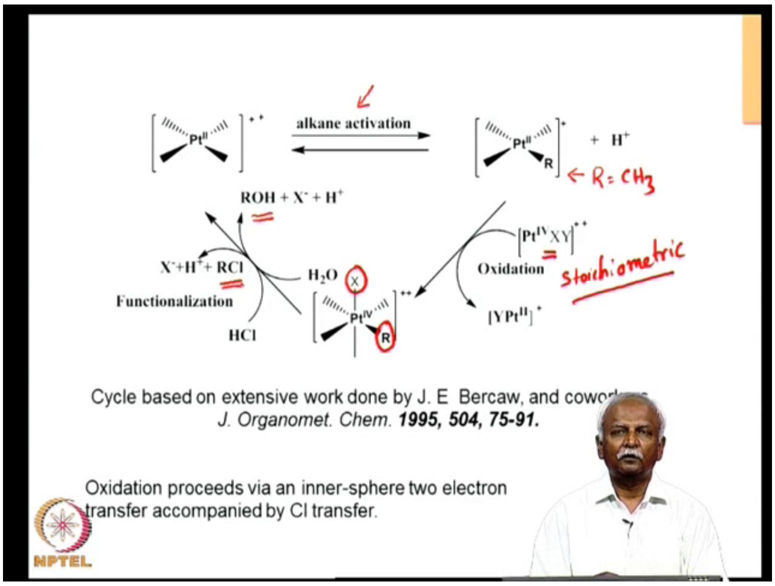

Cycle based on extensive work done by J. E Bercaw, and cowo
J. Organomet. Chem. ***1995, 504, 75-91.***

Oxidation proceeds via an inner-sphere two electron transfer accompanied by Cl transfer.

The mechanism of this reaction was solved much much laterby workers in the west. But it is interesting to see, what is the scheme of things that is going on in this interesting reaction. Platinum two we can ignore the ligands, which are fairly labile, platinum two can react with these alkane apparently, it interacts with the alkane in such a way that you have now formed a platinum carbon bond. Now in this case, if methane is involves R equals CH3 so you form a platinum methyl bond and release a proton into the medium. Now, these reactions are usually carried out in highly solvents and in acidic media.

So, the release of this proton is then followed, by an oxidation of this platinum methyl complex, by platinum 4. This step is the reaction, this, this is a step. Whereas, the platinum two that was used in this in this reaction, is completely regenerated at the end of the cycle. So the platinum four oxidizes this platinum two species, in what might be considered as inner sphere, two electron transfer.

So, two electrons are transferred from the platinum two, to the platinum four and at the same time a ligand which is in x group, which is usually an anionic groupis transferred from the platinum four to the platinum two species. And that we have indicated by this x group here, initially the x was present on the platinum four species,it has now been transferred to the platinum two species. And along with that two electrons have been transferred in a, in a sphere way. This results in a platinum four complex which has got an x group and an r group.

So we can now do a reductive elimination from this platinum four species, by eliminating r x. Now, in case the x is and there is not enough chloride ion concentration, you would end up eliminating. Otherwise, you would get R Cl, as the product. This regenerates the platinum two complex and so the catalytic cycle can continue. Now what you, what you have seen here is a case of electrophilic activation of the C-H bondin methane because you have removed an electron from the methane and released the hydrogen as H plus.

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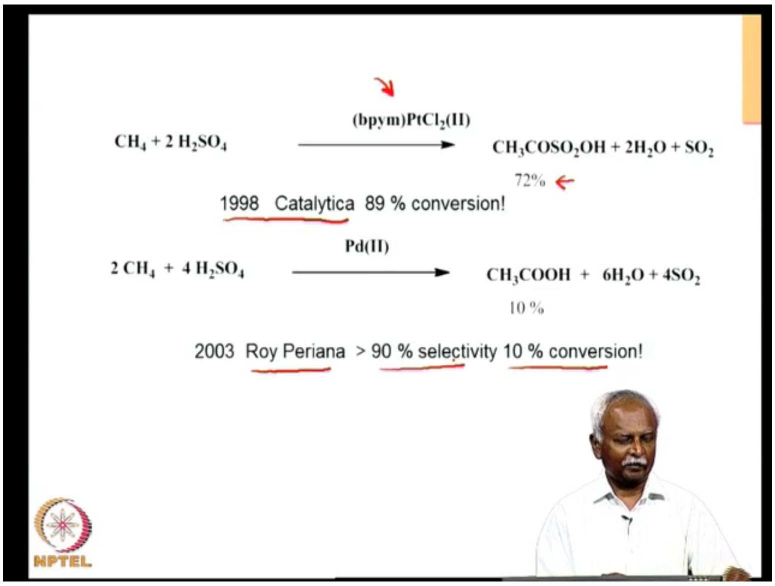

$$CH_4 + 2\,H_2SO_4 \xrightarrow{(bpym)PtCl_2(II)} CH_3COSO_2OH + 2H_2O + SO_2$$

72%

1998 Catalytica 89 % conversion!

$$2\,CH_4 + 4\,H_2SO_4 \xrightarrow{Pd(II)} CH_3COOH + 6H_2O + 4SO_2$$

10 %

2003 Roy Periana > 90 % selectivity 10 % conversion!

So, it was this reaction although it was very important it could not be reproduced by any other catalyst. It was only in 1998 that, alternative system was discovered by this company catalytica which showed that, if you have a ligand which on platinum, nitrogen based ligand on platinum. You could in fact carry out this reaction with extremely high selectivity. And that is methane sulphonic acid could be generated, as high as 72 percent conversion efficiency and the oxidant was in fact sulphuric acid. So, this turns out to be catalytic in platinum and so it is an extremely important discovery. Platinum is still expensive, but you could recover it at the end of the reaction and so this turns out to be a valuable contribution.

Now methane is in fact, one of the most inert compounds and if you can activate it and convert it to methane sulphonic acid, with such high conversion efficiencies, it is a valuable contribution indeed. You could do this reaction with palladium two and that was shown by, in 2003. Unfortunately, palladium is not as efficient as platinum and the reaction only proceeds with 10 percent conversion.

But 90 percent of this 10 percent so that means a total of 9 percent of the product turns out to be only acetic acid. And there are no other side production in this whole reaction. So, conversion of the remaining amount is remaining 90 percent of the methane is recovered unreacted. But it can be recycled in the industrial setup, so both palladium two and platinum two have been shown to be very useful as catalysts for activating methane.

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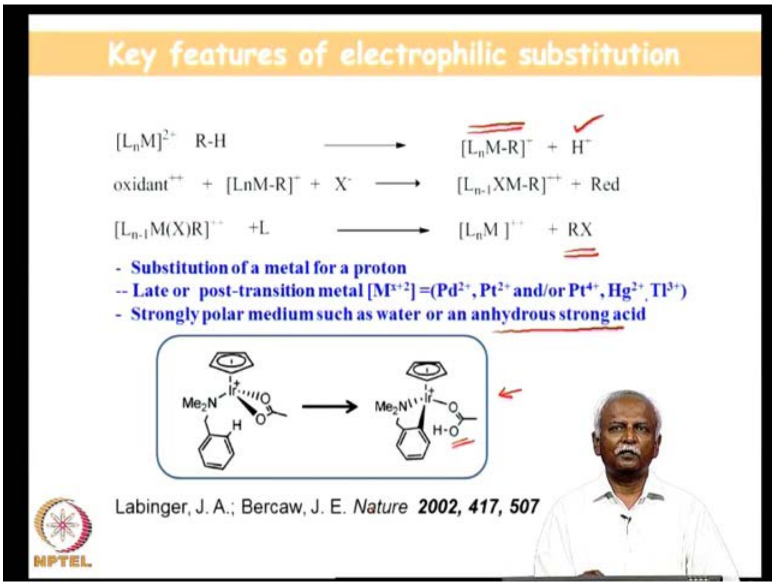

Key features of electrophilic substitution

$[L_nM]^{2+}$ R-H $\longrightarrow$ $[L_nM\text{-}R]^{+}$ + H^{+}

oxidant^{++} + $[LnM\text{-}R]^{+}$ + X^{-} $\longrightarrow$ $[L_{n-1}XM\text{-}R]^{++}$ + Red

$[L_{n-1}M(X)R]^{++}$ +L $\longrightarrow$ $[L_nM\,]^{++}$ + RX

- **Substitution of a metal for a proton**

-- **Late or post-transition metal $[M^{x+2}]$ =(Pd^{2+}, Pt^{2+} and/or Pt^{4+}, Hg^{2+}, Tl^{3+})**

- **Strongly polar medium such as water or an anhydrous strong acid**

Labinger, J. A.; Bercaw, J. E. *Nature* **2002, 417, 507**

Now, let us take a look at the key features of this electrophilic substitution, the key feature I feel is the formation of the metal carbon bond. The metal carbon bond is formed in the very first step and release of H plus is the most important and key step in this whole process. In the second step of course, you need an oxidant and the oxidant could be charged or it could be neutral, but nevertheless it has to remove two electrons.

And probably provide the x minus group so that, r x is generated at the end of the reaction. Now you usually, you can usually do this only with platinum, but there are a few instances, where other heavy transition elements are capable of carrying out this reaction and the medium has to be a very polar and ionic medium. Usually, there is an anhydrous or strong acid that is present. Now, there is a, there is this example that I have shown for you in a box here, which suggests that CH activation can in fact be easier than OH activation. The reaction that you see is an example of inter molecular CH activation, but interestingly you proceed from, only from the left to right, which indicates that the CH bond is activated better than the OH bond. If you were to proceed from right to left, you would have to activate an OH bond. Now, there are a few other examples where this is indeed being shown to, hold water you do have activation of CH bonds in the presence of o h bonds. But nevertheless, this is a good way which or a good example which tells us that, CH bond activation is difficult, but nevertheless it is not impossible.

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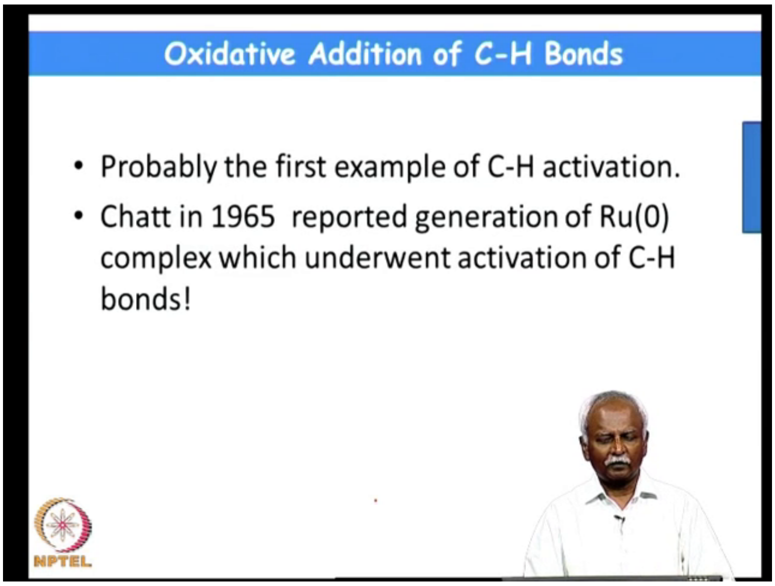

Oxidative Addition of C-H Bonds

- Probably the first example of C-H activation.
- Chatt in 1965 reported generation of Ru(0) complex which underwent activation of C-H bonds!

Now, let us proceed to the next way of CH bond activation and this deals with the oxidative addition of the CH bond. Probably, the first example of CH activation by oxidative addition, was carried out close to Shilov’s work, as early as 1966. This was done by Chatt and he reported the generation of a ruthenium 0 complex, which underwent CH activation.

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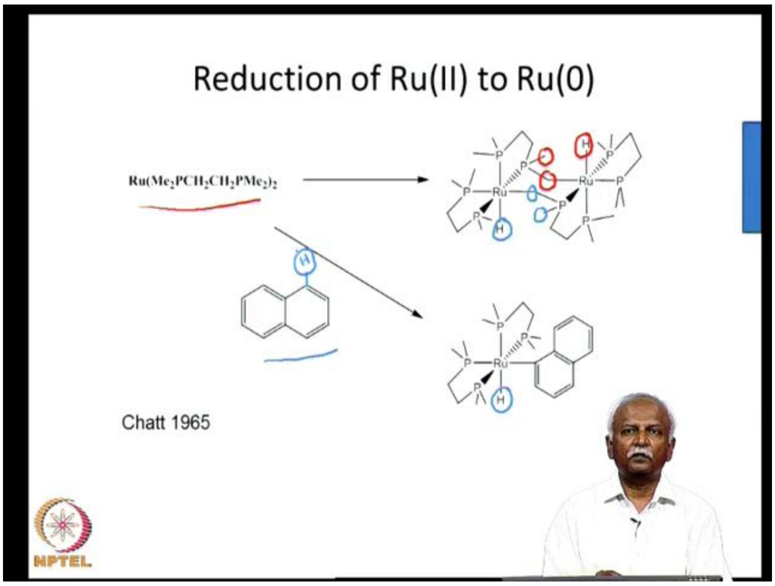

Reduction of Ru(II) to Ru(0)

$Ru(Me_2PCH_2CH_2PMe_2)_2$

Chatt 1965

Interestingly, the initial observation was in fact the case where the ligand was oxidized by or oxidatively added to the ruthenium 0. So here is the ruthenium complex, ruthenium 0 complex which has got 4 phosphorous atoms legated to it, and it carries out activation of the CH bond of another ligand present in the adjacent molecule. So you have a CH3 group becoming, a CH3 group which is present on the metal, the methyl group which is present on the metal, one of the methyl groups. Here is one methyl group, the second methyl group which is present here has oxidatively added and formed a CH2 H group on the ruthenium.

Similarly, the other, the other phosphorous atom which has got two methyl groups, one of them forms a CH2 group and a hydrogen. So, you have a mutual oxidation of the ligand, of the adjacent metal complex. Now, if you do not have, if you have the option of an SP2 CH bond then the molecule seems to prefer the SP2 carbon and it can do this in inter-molecular fashion.

But this time of a molecule that is available in solution and it oxidatively adds the CH bond which is present on the ring. So, this is the hydrogen which has been oxidatively added, but nevertheless this turns out to be the first example of a CH bond being activated in a intermolecular fashion. And the generation of the low oxidation state metal atom, seems to be either key requirement for doing or carrying out such an oxidative addition.

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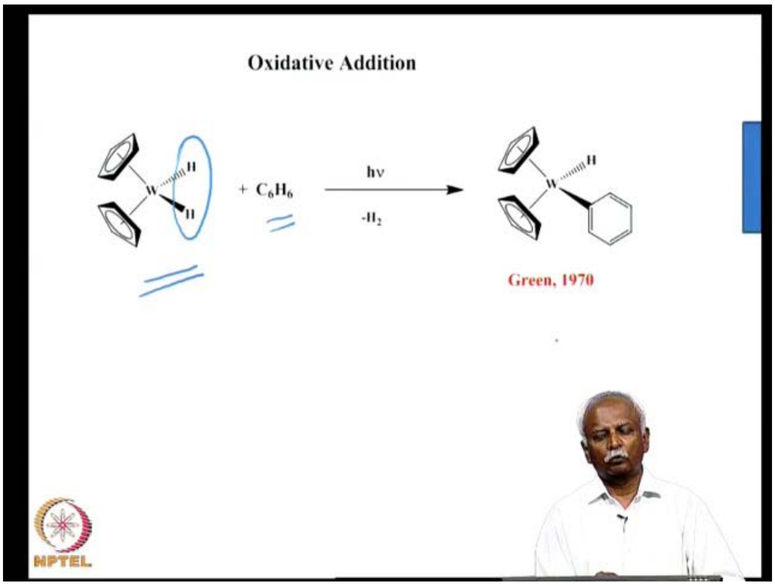

Oxidative Addition

Green, 1970

Now around about the same time or about four or five years later, it was discovered by, who is another pioneer and important contributor in the area of CH bond interactions. He found that, if you took these tungsten dihydride, this is a tungstocene, which has got a two hydrogens attached to it. If you focalize it, in a benzene solution then you would lose these two hydrogens, you would lose these two hydrogens as H2 and that gives you a very reactive tungstocene. Now, this in fact is acoordinatively unsaturated molecule and it reacts with the solvent and forms, a carries out oxidative addition of the CH bond and this is discovered in 1970.

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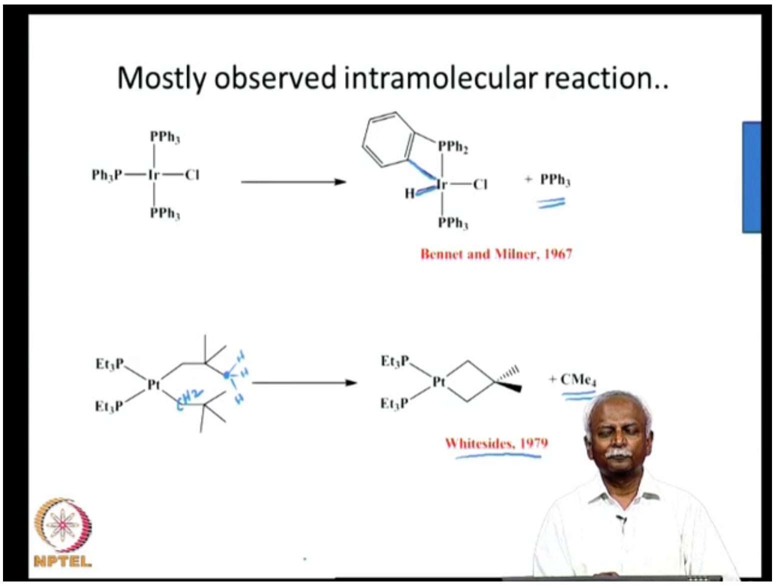

Mostly observed intramolecular reaction..

Bennet and Milner, 1967

Whitesides, 1979

Now, going on further, there were other examples which were accessible, but these are mostly reactions that have been carried out in a intramolecular fashion. The ease with which, an intramolecular CH activation can take place is, in fact tremendously high. They are much much more common than intermolecular CH bond activations. So, here is an example of a CH bond activation, which happens with a PPH3 which is an extremely common ligand. One of the hydrogen's of the phenyl group which is there on the phosphorous, phosphorous has got three phenyl groups. And one of the phenyl groups,the hydrogenin that phenyl group has been oxidatively added in order to generate this molecule.

So, this was discovered along with, this happens with disposition of one of the PPH3 units. But there was another example where found out that you can eliminate a molecule of CME4, tetra methyl methane and that can be done by abstraction of a hydrogen, from a methyl group which is present here, this is a methyl group. And so one of the hydrogens on the methyl group can be abstracted and this CH2 which is present here, can abstract this hydrogen.

And you would end up with, CME4 as a, as a molecule that would be extruded and you form a cyclic molecule. So these are intramolecular fashion, oxidative additions. So this is quite common so when people observed this oxidative addition on a tungsten 0 species, it was in fact a special observation. And so was this observation by Chatt in 1965.

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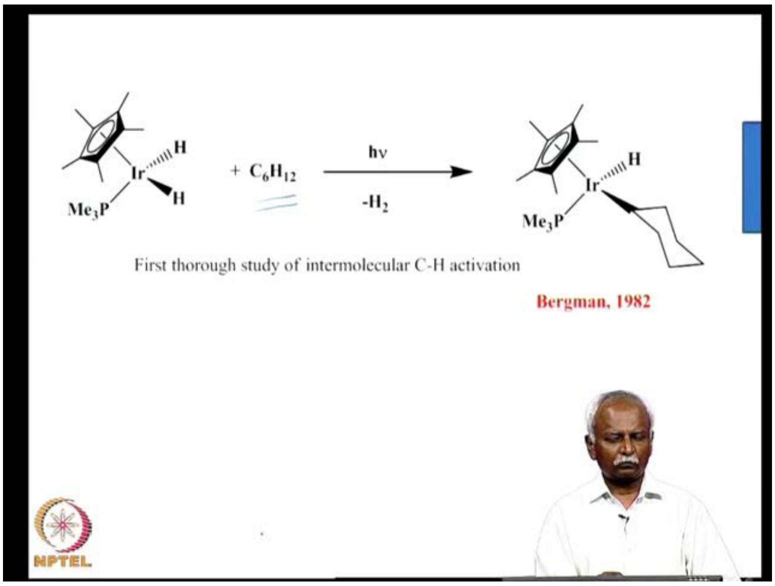

First thorough study of intermolecular C-H activation

Bergman, 1982

So, was the first one to thoroughly study this intermolecular CH activation and he did this using isotopic substitution techniques. And he did extremely thorough job, which allowed one to understand how these reactions are proceeding. So, here is an example where cyclohexane has been used to the solvent. And the same technique of photolysis has been used and cyclohexane has been activated, which is also one of the more unreactive molecules that are, available in the organic milieu. So this was done in 1982.

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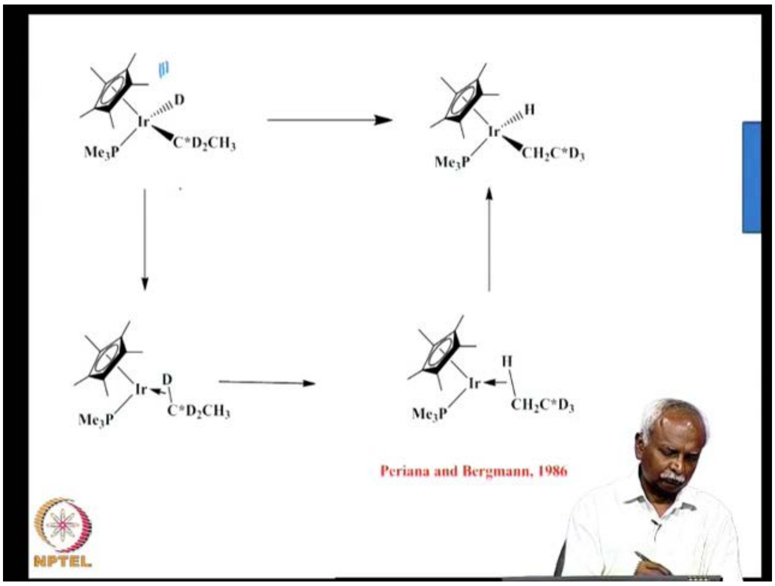

Periana and Bergmann, 1986

And the same system or a similar system was taken by him. And it was shown that the intermediacy of an ethylene was not there and in fact it was completely an intramolecular reaction that was going on. What he did was, he took ethane and now one of the hydrogen’s of the ethane was activated to, in an oxidatively added to the iridium one species and it forms the iridium three compound. So, this is the iridium three compound, which is formed as a result of oxidative addition and after it forms the oxidative addition he showed that, the deuterium atoms do not scramble between the two carbons.

So you always end up with CD3 CH3, if you start with CD3 CH3 you do not get CD2HCH2D in the end of the reaction. So, this would be possible only, if the cycle stuck to this particular reaction cycle, which we have indicated when it oxidatively adds a deuterium. When it oxidatively adds a deuterium, it the interaction is confined to that carbon. It goes back to this same carbon, as a result of a reductive elimination. So, this was shown by Periana and Bergman in 1986.

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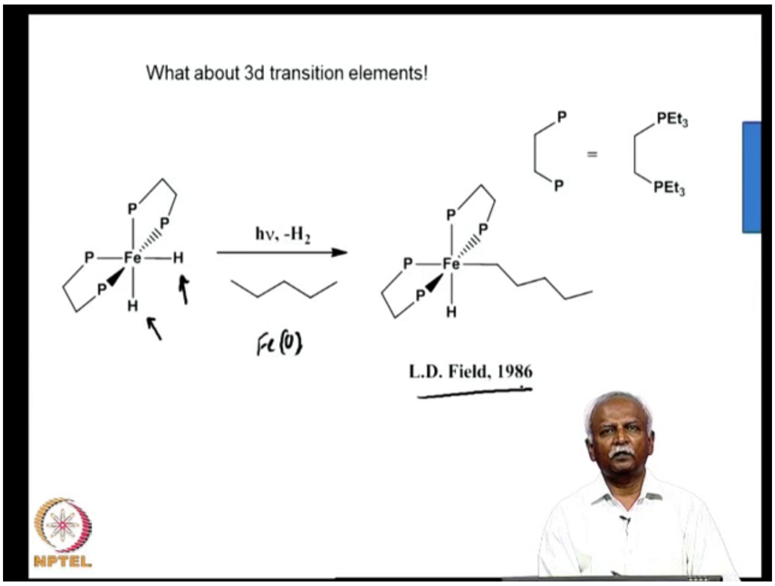

What about 3d transition elements!

L.D. Field, 1986

So, there are very few examples, in the literature about oxidative addition of 3D elements, a notable example is the study by LD field, in 1986. He showed that, you can do this reductive elimination of dihydrogen using iron complex. He the same in hexane. And he showed that you can have oxidative addition of the paraffin to the iron 0 species, which would be generated if you eliminated the two hydrogens which are present.

So the two hydrogens which are present, the two hydrogens are here and these two hydrogens are eliminated as H2. And then you end up with an iron 0 species, which just like the, just like the ruthenium 0 species carries out oxidative addition. But this time it does it with solvent and so you get alkyl hydride as the product. So this was carried out in 1986 and this was the time, when there was lot of excitement about possibility and the reality of CH bond activation.

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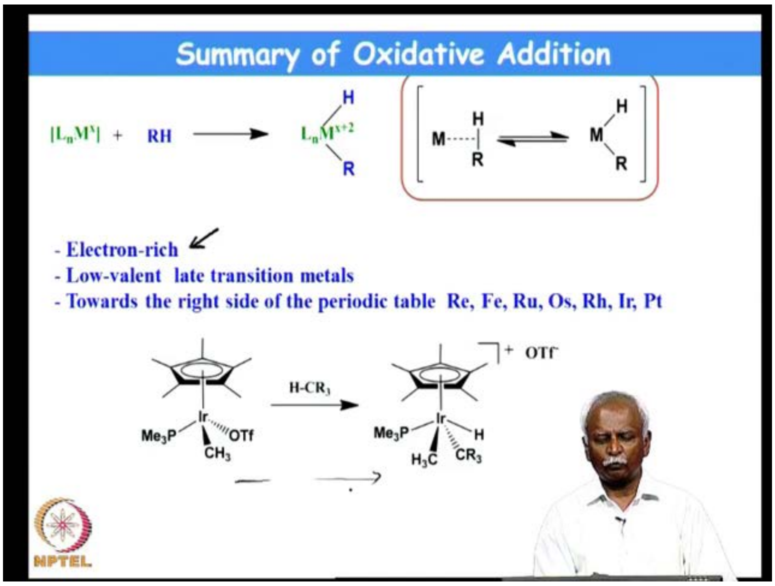

Summary of Oxidative Addition

- Electron-rich
- Low-valent late transition metals
- Towards the right side of the periodic table Re, Fe, Ru, Os, Rh, Ir, Pt

So to summarize oxidative addition, the section on oxidative addition just want to show that the metal has to be generated, either by a drastic reduction step. You usually use photo chemistry or reduction with sodium. And that generates a metal complex in a highly electron rich state. And this happens with late transition metals and the electron rich late transition metal, carries out an oxidative addition of the RH bond.

It up to now mostly it has been the D8 group or the platinum group of elements, which have been observed for oxidative, has been capable of carrying out oxidative addition. And here is an example where, iridium goes from the plus one state, to the plus three state. And or in a, this is an example in fact of a situation where you have iridium three, going to iridium five. But in general it is iridium one going, to iridium three complex.

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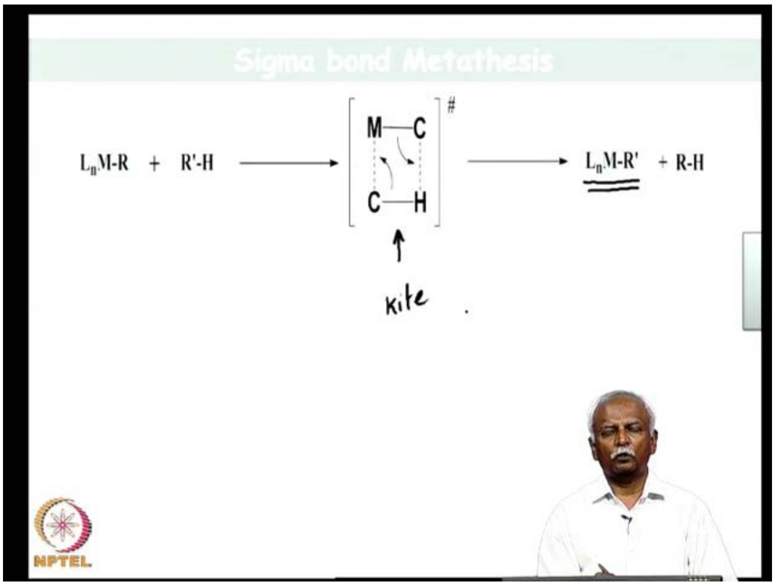

Sigma bond Metathesis

$L_nM\text{-}R + R'\text{-}H \longrightarrow \left[\begin{array}{c} M—C \\ C—H \end{array}\right]^{\#} \longrightarrow L_nM\text{-}R' + R\text{-}H$

So, one other method which has been less commonly observed is the sigma bond metathesis. Technically or at least in principle one can think of a reaction, just like the carbon carbon double bond metathesis. Where, you have a M double bond C reacting with a C double bond C. If one can do that with sigma bonds you could have a transition state where, you have a CMCH cyclic four membered transition state. In which, you would end up with an RH bond and an L M R M R bond. Now, this four membered transition state is very often referred to as a kite like transition state, because you have for four atoms as if in the corners of the kite.

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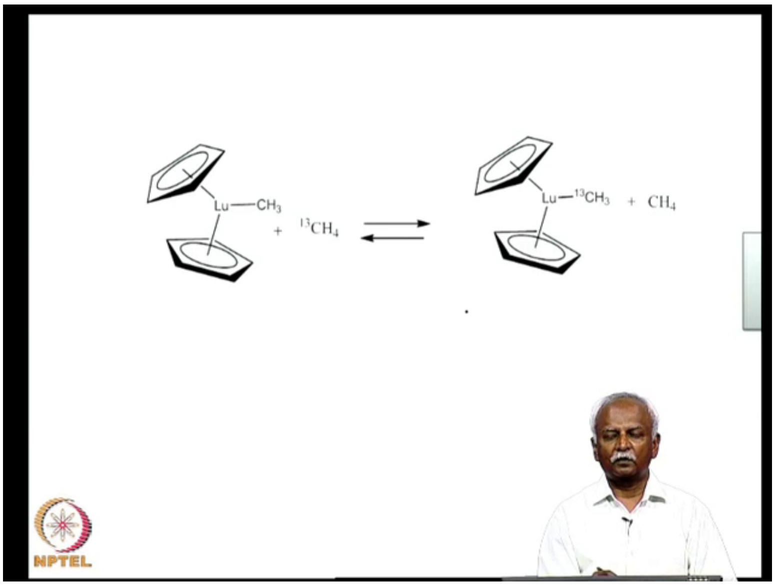

Now, one example of that which has appeared in, is with the actinide elements and the lanthanides, and the actinides high oxidation state do not have the possibility of carrying out an oxidative addition step. So, if you want to have a carbon hydrogen bond activation, it has to be through some other mechanism either a electrophilic activation or a CH bond metathesis. Now, in this case it has been suggested that, this reaction goes through a sigma bond metathesis.

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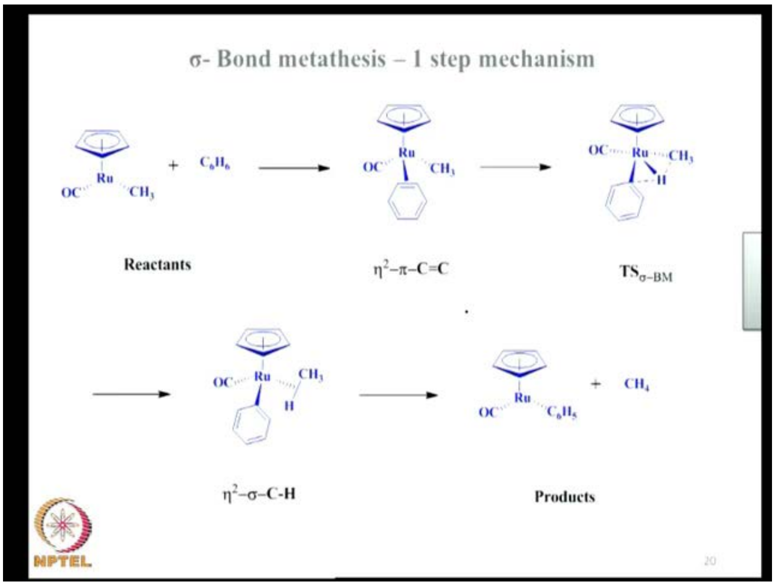

σ- Bond metathesis – 1 step mechanism

In fact the sigma bond metathesis and the electrophilic activation mechanisms are reasonably close together. So, it would be difficult to distinguish these two, but here is a kite like transition state that, we are talking about when you have a carbon ruthenium, a carbon ruthenium, ruthenium, carbon hydrogen intermediate which looks like a kite. So, this looks like a kite and that is why it is called a four membered sigma, a sigma bond metathesis mechanism. Now, we can see that, the hydrogem is transferred directly from the carbon to the other carbon which is leaving.

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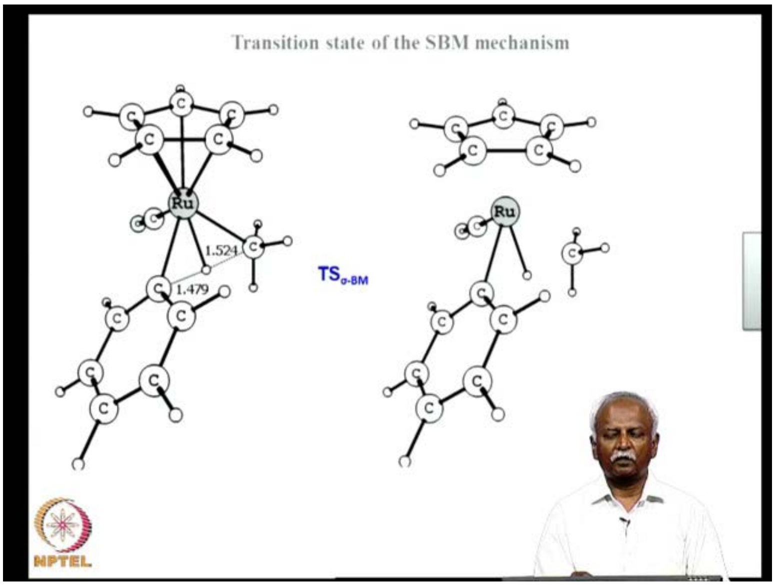

Transition state of the SBM mechanism

And the, for this slide, I have generated a simulated the transition state for you and you can see that the transition state has got this geometry, which I have indicated for you here. The geometry is indicated here and what you have or what do you see on the slide is the hydrogen shuttling between the benzene ring and the methyl group. And the intermediate form as a ruthenium hydrogen, which is almost within the bonding distance.

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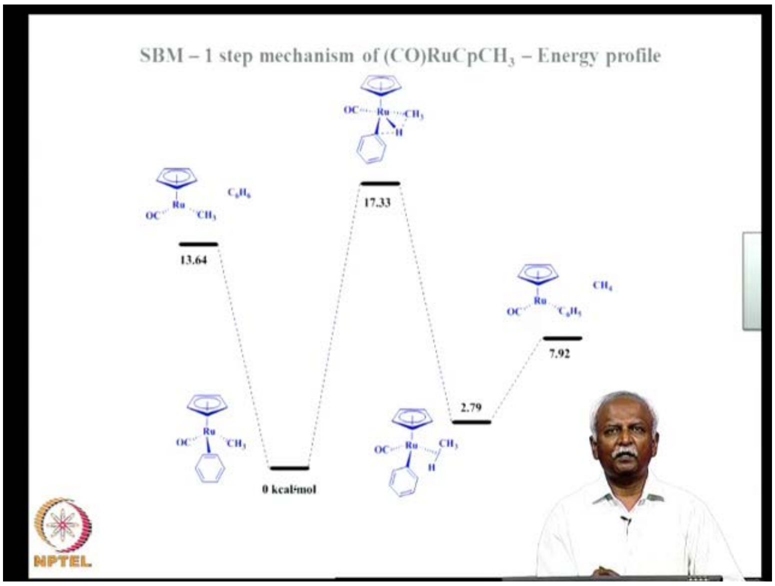

SBM – 1 step mechanism of (CO)RuCpCH$_3$ – Energy profile

So, you can calculate the energetics of such a process and it is clear that the interaction of the ruthenium with the methane and with a benzene ring turn out to be low energy forms. And so you have an oxidation, you have an intermediate where the hydrogen is transferred directly between the benzene, and the methyl group to form the methane complex.

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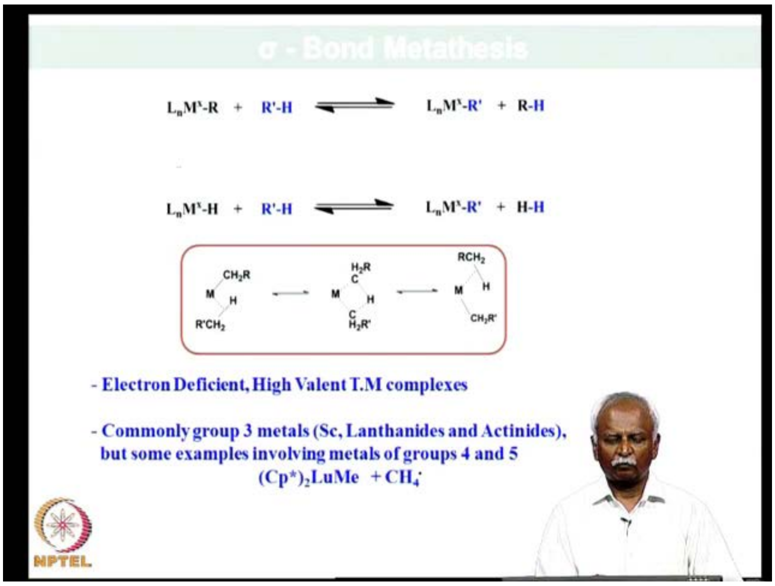

σ - Bond Metathesis

$L_nM^x\text{-}R + R'\text{-}H \rightleftharpoons L_nM^x\text{-}R' + R\text{-}H$

$L_nM^x\text{-}H + R'\text{-}H \rightleftharpoons L_nM^x\text{-}R' + H\text{-}H$

- Electron Deficient, High Valent T.M complexes
- Commonly group 3 metals (Sc, Lanthanides and Actinides), but some examples involving metals of groups 4 and 5
  $(Cp^*)_2LuMe + CH_4$

So, sigma bond metathesis is in fact one of the possible ways, by which you can carry out this reaction. What is different from the electrophilic substitution reaction that, we discussed in the beginning is the simple fact that, these reactions can be carried out in non-polar solvents. And you have a direct transfer of this hydrogen, you do not seem to require the highly polar solvents that, are used in electrophilic activation. But it is commonly done with high valent transition metal complexes and as we saw, in the as we saw for the lutetium complex, that where we seize the metal group.

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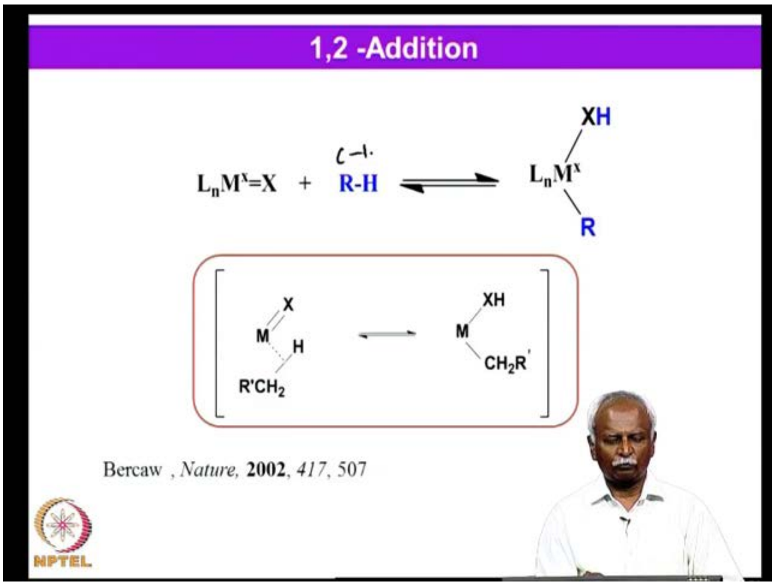

1,2 -Addition

Bercaw , *Nature*, **2002**, *417*, 507

So, yet another possibility is a fact that, you can have a metathesis reaction between two groups which are unequally bonded. Here is a M double bond X group and if that M double bond X group reacts with an R H. This would be similar to the interaction, that we observed when we did a metathesis reaction. When we did the metathesis reaction also we had such types of unequal reactions happening, and I can add the R H or break the carbon hydrogen bond. The carbon hydrogen bond which is present in this case, I could add this, I could add this across the metal, I could add this across the metal X bond and if you do that you would end up with the two groups adding across the M X bond and this was observed by.

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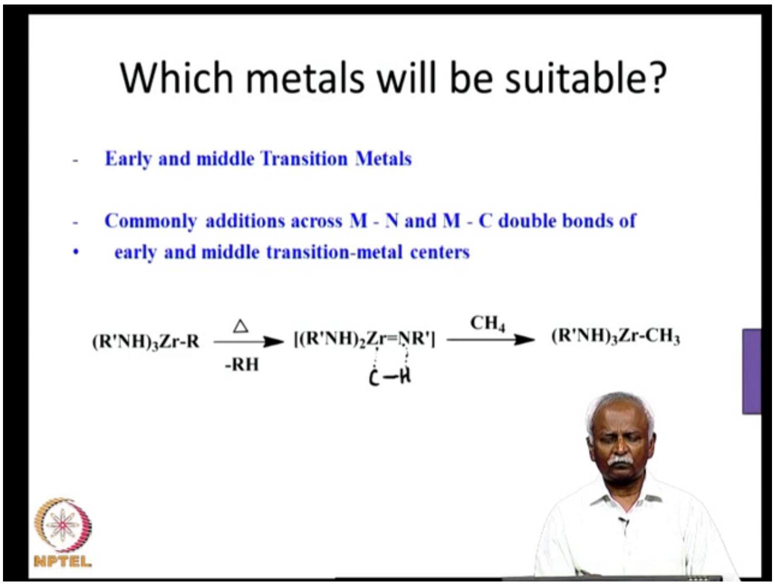

Which metals will be suitable?

- Early and middle Transition Metals
- Commonly additions across M - N and M - C double bonds of
- early and middle transition-metal centers

$$(R'NH)_3Zr\text{-}R \xrightarrow[-RH]{\Delta} [(R'NH)_2Zr{=}NR'] \xrightarrow{CH_4} (R'NH)_3Zr\text{-}CH_3$$

Where X is an, actually a nitrogen group and an complex reacted with methane to form a zirconium methyl group, which is interacting with a, which is now having a third NH group attached to it or coordinated to the zirconium. So, you have the oxidative addition of the carbon hydrogen bond, across the zirconium nitrogen bond. So, you seem to be, directly forming the carbon zirconium bond and the hydrogen nitrogen bond, in order to generate this particular complex. So these are extremely rare example not many of them are known. But nevertheless, in the future we can expect these two areas to develop more, where you have such types of sigma bond metathesis. And metal double bond X groups, doing oxidative addition of the carbon hydrogen bond.

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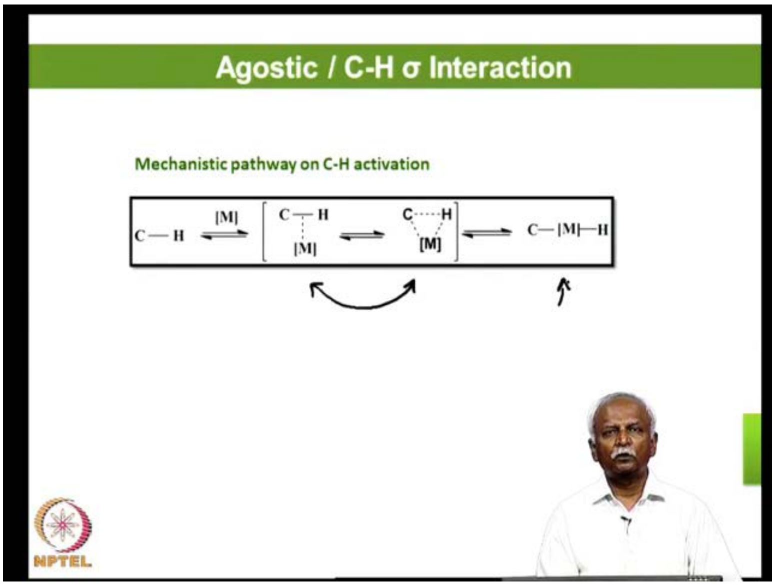

Agostic / C-H σ Interaction

Mechanistic pathway on C-H activation

Now, let us get back to the two common reactions that, we observed. One was the electrophilic substitution and the other was oxidative addition. In both instances, we are removing electron or a pair of electrons from the CH bond. So, the metal must be having an empty orbital, which is interacting with the CH bond. And so you can think of a situation where, you have the C H bond shuttling between these two forms, before separate carbon hydrogen bonds are formed, as in this as shown on the right hand side.

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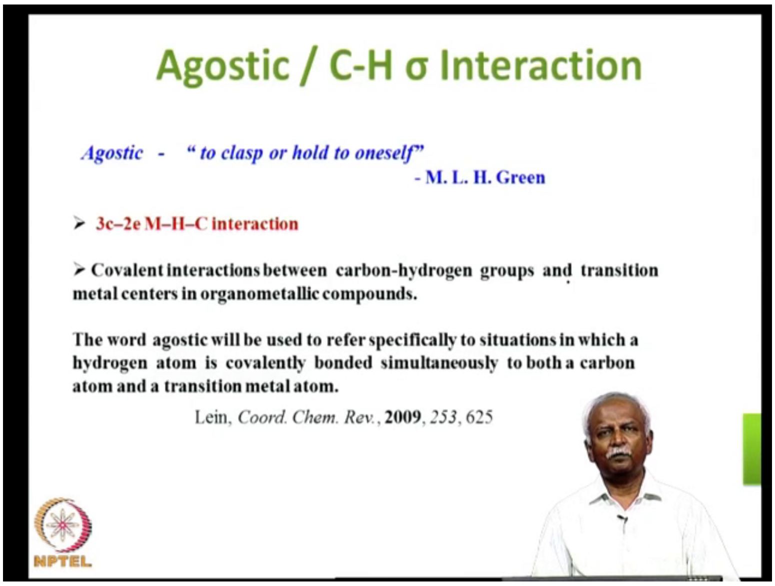

Agostic / C-H σ Interaction

Agostic - *" to clasp or hold to oneself"*

- M. L. H. Green

➢ 3c–2e M–H–C interaction

➢ Covalent interactions between carbon-hydrogen groups and transition metal centers in organometallic compounds.

The word agostic will be used to refer specifically to situations in which a hydrogen atom is covalently bonded simultaneously to both a carbon atom and a transition metal atom.

Lein, *Coord. Chem. Rev.*, **2009**, *253*, 625

So, let us take a look at some of the structures that are being discovered M L H Green, where he showed that it is possible to see the interaction of a C H bond with a metal. He discussed this, a three centered two metal interaction, the two electrons come from the CH bond and the third center is actually the metal center with zero electrons. So, you end up with the three center two electron interaction, where there is an agostic interaction, supposed to be an agostic interaction between the metal and the C H bond.

These covalent interactions between the CH bond and the metal are interesting, because they have been structurally characterized. And a recent review on this whole interaction, is given for you in the slide in coordination chemical reviews. Now, agostic comes from, a term which means to clasp or hold to one self and the metal is holding a ligand close to itself in anagostic fashion.

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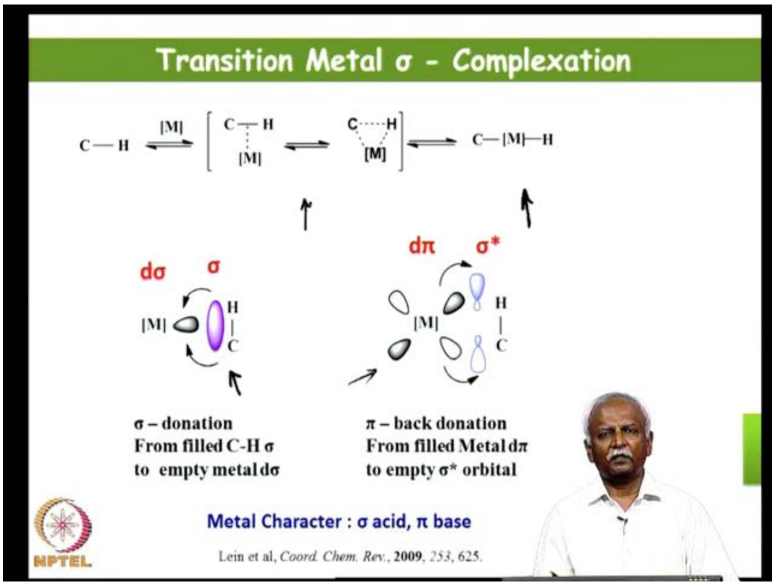

Transition Metal σ - Complexation

σ – donation
From filled C-H σ
to empty metal dσ

π – back donation
From filled Metal dπ
to empty σ* orbital

Metal Character : σ acid, π base

Lein et al, *Coord. Chem. Rev.*, **2009**, *253*, 625.

Many times this is observed only in a intra-molecular fashion and so this CH bond is forced to be close to the metal. If this interaction involves, not just donation of electron density from the CH bond to the metalempty orbitals, as it is shown here. If it involves, pumping of electron density into the anti-bonding orbitals of the CH bond. You would end up with the oxidative addition and you would end up with, the product which will be looking like this. So, this is a spectrum that you would observe, on one hand you would have no interaction between the metal and the CH bond. On the other hand, you can have this agostic interaction between the metal and the CH bond. So you could have all types of interactions.

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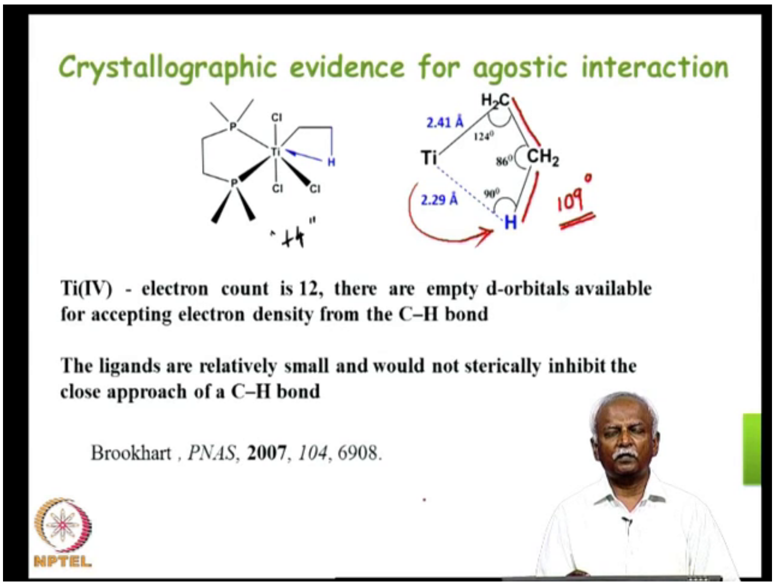

Crystallographic evidence for agostic interaction

Ti(IV) - electron count is 12, there are empty d-orbitals available for accepting electron density from the C–H bond

The ligands are relatively small and would not sterically inhibit the close approach of a C–H bond

Brookhart , *PNAS*, **2007**, *104*, 6908.

And these have been observed in the literature, and we will look at some of these examples. Now, here is an example of a titanium compound, which has got an ethyl group and this titanium is in fact, in the plus four oxidation state and so it is electron deficient, it is electron deficient. And it can, it can, it cannot do an oxidative addition because it does not have two extra electrons to pump into the CH sigma star orbital. But on the other hand, it can interact with the CH sigma bond in an agostic fashion. And that is what you see here, you find that the bond angle between CCH which is, what is listed here. We will mark it with a different color so that, you can visualize it easily.

Here is the angle that, we are talking about CCH, that should have been a 109 degrees. What you expect for an SP3 carbon is 109 degrees, but instead what you observe is very acute angle of 86 degrees. So, that is a significant drop in the bond angle and that is caused by this attractive force that titanium is exerting, on this hydrogen. So one of the hydrogen’s is bent towards the titanium and not only that the bond distance is remarkably short between the hydrogen and titanium.

It is only about 2.3 Angstroms and so this bending is supposed to be arising out of this agostic interaction. So, the ligands which are relatively small and which would allow for this close approach of the CH bond result in agostic interactions. Now, you could seea review of this chemistry againby Brookhart in the proceedings of national academy of sciences, in a 2007 article, which I have given for you here.

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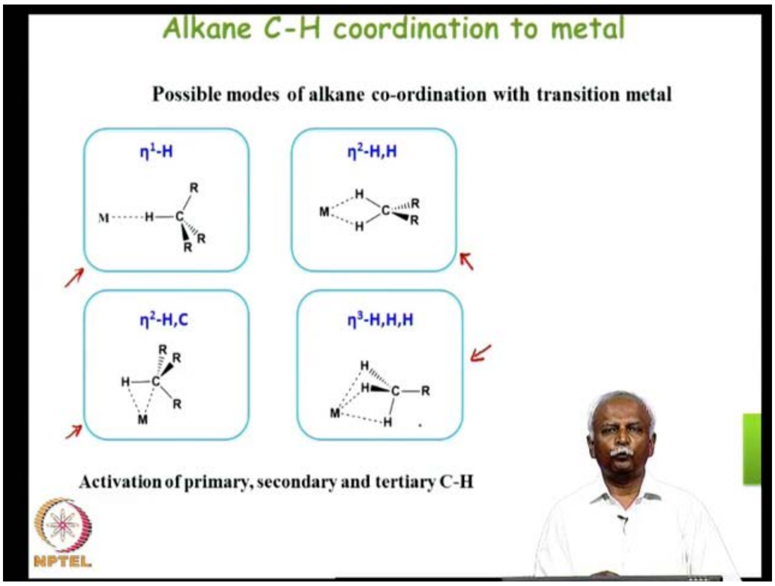

Alkane C-H coordination to metal

Possible modes of alkane co-ordination with transition metal

Activation of primary, secondary and tertiary C-H

Now, alkane CH bonds, alkane CH bonds can coordinate to the metal in a variety of fashions. What we have seen here is, the examples that we have seen here are eta one type of interaction or eta two type of interaction of the CH bond with a metal atom. So these are the two types, that we have seen in the previous examples. But it is also possible for two hydrogen's of this CH a methylene group to interact with a metal in the same agostic fashion. Electron deficient metal accepts, electron density from the CH2 group or even from a CH3 group.

Now, this has been observed for a BH4 minus group for example, a BH4 minus would be analogous to CH4 and that has been shown to interact witha metal like this in this particular fashion also. So, these type of interactions a weak interaction between an alkane group and the metal are generally common. Especially if you look at the crystal structures of these molecules.

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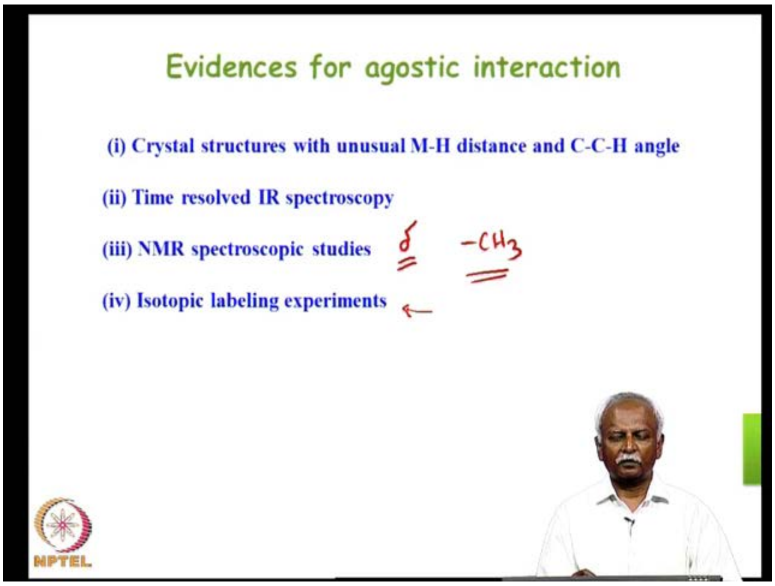

Evidences for agostic interaction

(i) Crystal structures with unusual M-H distance and C-C-H angle

(ii) Time resolved IR spectroscopy

(iii) NMR spectroscopic studies $\underline{\underline{\delta}}$ $\underline{\underline{-CH_3}}$

(iv) Isotopic labeling experiments ←

Now, the other evidences for agostic interaction are as follows not only can we look at crystal structure, anomalous bond angle distances. We could also look at time, resolved infrared spectroscopy where these, intermediates have been noted in the spectrum of molecules generated in a transient way. NMR spectroscopic studies also show, anomalous chemical shifts, the chemical shifts of CH bonds which are interacting with a metal are different from those that do not. And restricted rotation of a methyl group is possible when, one of the hydrogen’s is interacting with the metal. So, finally isotopic labeling studies have also been made all of them, point to the fact that there can be weak interaction between the metal and the CH bond. And these interactions are presumably or probably the intermediates, which are available for us before the electrophilic substitution is going to happen.

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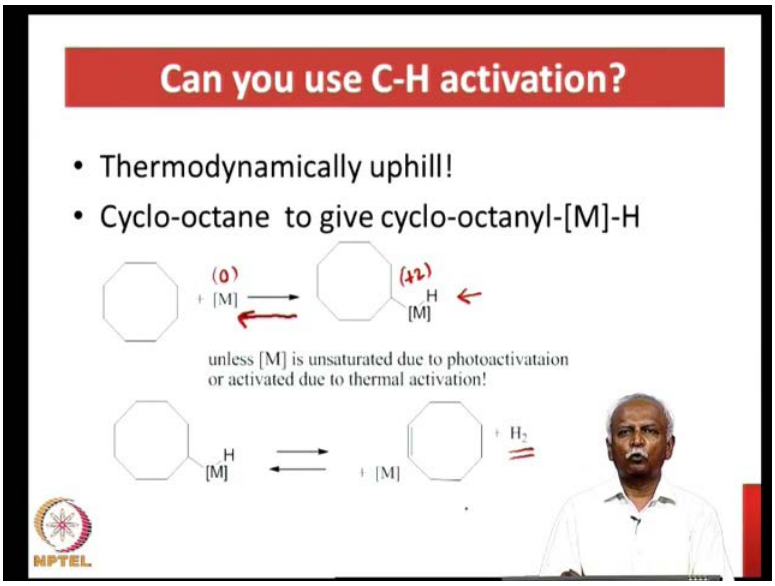

Can you use C-H activation?

- Thermodynamically uphill!
- Cyclo-octane to give cyclo-octanyl-[M]-H

unless [M] is unsaturated due to photoactivataion
or activated due to thermal activation!

Now, can we use CH activation for carrying out any useful reaction. This is in fact a question that would plague you. We have seen several examples, where CH activation has happened. But, many of these intermediates have been generated at, a lot of cost in terms of energy pumped in through light or energy pumped in through a strong reducing agent or for that matter by extreme heating. So, is it possible to use these reactions and the reason for this difficulty is because we are going thermodynamically up hill. This reaction which I have shown for you, here with cyclo-octane as an example and a generic metal has undergone oxidative addition in, as it has gone from left to right.

This is the oxidatively added species, where the metal has undergone an oxidation state change of plus two. So, it is usually true that thermodynamically speaking, it is easier for the reaction to go in this direction. In other words energy, delta g is negative when you go from left to right rather than, from right to left, so how will we solve this puzzle, how can we utilize this reaction effectively.

Similarly, we have seen several hydrogenation reactions activation of dihydrogen was one of the topics that we have covered. And in those cases we have noted that, if the possible to go from the right side of this equation to the left side rather easily, but not vice versa. So, if we have to push this reaction from left to right, one has to somehow remove this hydrogen from this equation, remove this hydrogen from this particular scheme.

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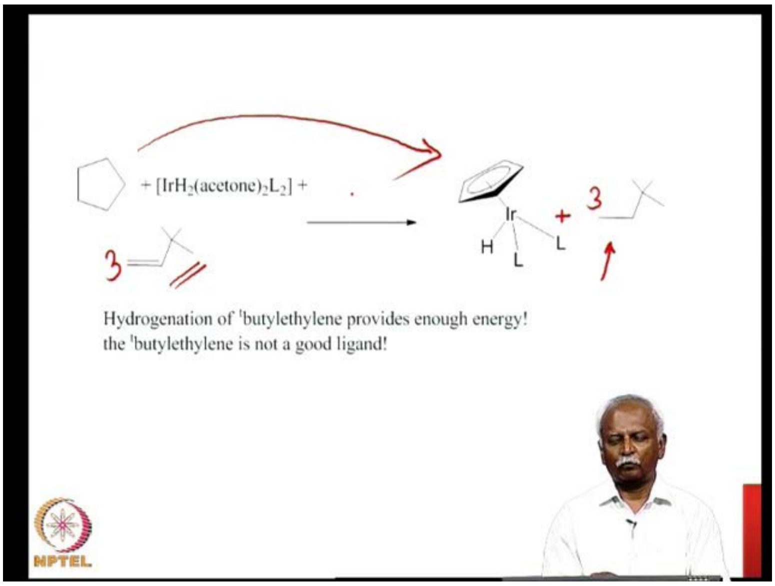

+ [IrH$_2$(acetone)$_2$L$_2$] +

Hydrogenation of ^{t}butylethylene provides enough energy!
the ^{t}butylethylene is not a good ligand!

So, this was done by several workers who found out that if you have a good acceptor for the hydrogen. Now, the good acceptor for hydrogen could be a variety of different ligands, but what they found was tertiary butyl ethylene was a very good acceptor. Not only does it mop up the hydrogen, during the hydrogenation process, but it also it is not a ligand that would poison the catalyst. In these reactions, if the ligand which is liberated or ligand which is available, if that blocks the coordination site then the reaction will not proceed.

So, we found out that, tertiary butyl ethylene because of its bulky, tertiary butyl group is not a good ligand and so is capable of taking up the hydrogen. And being removed from the, from the reaction as this molecule, which I have marked with an arrow. So, a catalyst which is capable of carrying out activation of dihydrogen, hydrogenation and dehydrogenation is shown here. It is a iridium three plus catalyst and it carries out hydrogenation of tertiary butyl.

And provides enough energy and pushes this reaction from left to right. In this particular example, that in have shown for you, you would need three equivalents of tertiary butyl to give you three equivalents of the saturated molecule. Because you have removed, several hydrogen’s from the cyclo-pentane, which has got converted into the cyclo-pentadiene molecule which is present on the iridium.

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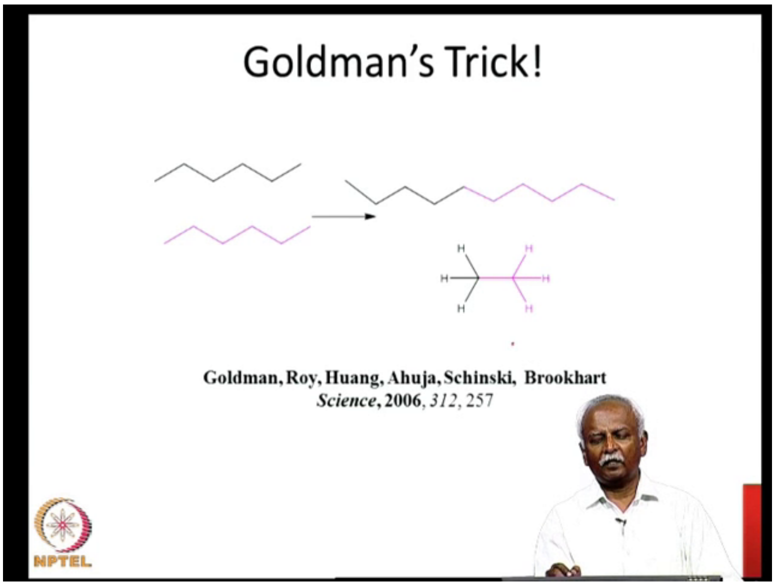

Goldman's Trick!

Goldman, Roy, Huang, Ahuja, Schinski, Brookhart
Science, 2006, *312*, 257

So, it was a it is to the credit of Goldman and Brookhart, who have now used this reaction very effectively and the way they have done it, is by, is as follows. They have carried out what is called alkane metathesis, which involves CH bond activation. Alkanes are paraffin's, so in essence they are unreactive, but if you carry out a CH bond activation and convert it to an alkene. They become more reactive and in fact they can now carry out a metathesis reaction.

After it carries out a metathesis reaction, it can be hydrogenated by the same set of catalysts and this amazing reaction was published in science in 2006. And it really is a landmark paper, which tells you that CH bond activation has come off age and can now be used in a useful fashion. Now, here is a reaction which took cyclo-hex, we took hexene, we took hexene and converted it into decane and ethane.

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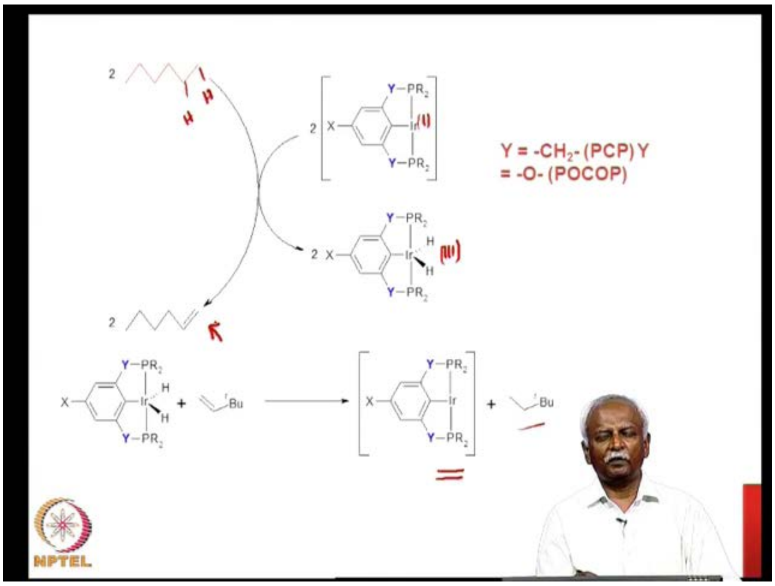

So, here you have a six plus six carbon alkane getting converted into a ten carbon chain and a two carbon or a ethane molecule. So, let us take a look now at, the type of reaction that they are proposing, they have carried out, here is a catalyst which can hydrogenatethis, tertiary butyl ethylene and ethyl tertiary butyl methane is what you have here. And you end up with this molecule, which has got no hydrogen’s which is the reactive form of the catalyst. This catalyst can remove two hydrogens, from another molecule which is hexane molecule and generate one hexene.

It will coordinate to the least sterically hindered carbon and that would be terminal carbon of the hexane. So, we have a hexane molecule reacting with the iridium center and the iridium center now, becomes airidium three center, iridium one center which is present here. This is the iridium one centre,that becomes iridium three center with abstraction of two hydrogens, which have come from the two terminals points of the hexane. And so you generated an unsaturated form of the hexene, one hexene will generated one hexene and the dihydrido complex. Now, let us see how we can utilize this hexene in a reaction that would allow us to carry out some interesting chemistry.

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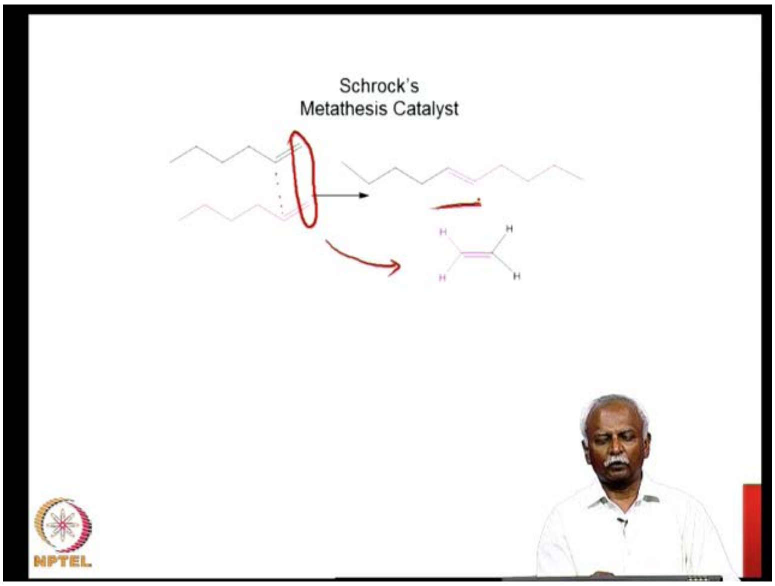

Schrock's
Metathesis Catalyst

They Goldman and Brookhart did a metathesis reaction now, with a, with the hexene one hexene. So, you would end up with combining these two carbons together and generating ethylene. And if these two carbons come together, you would form a decane, so that is a ten carbon alkene which has got the carbon double bond, carbon in the center of the molecule.

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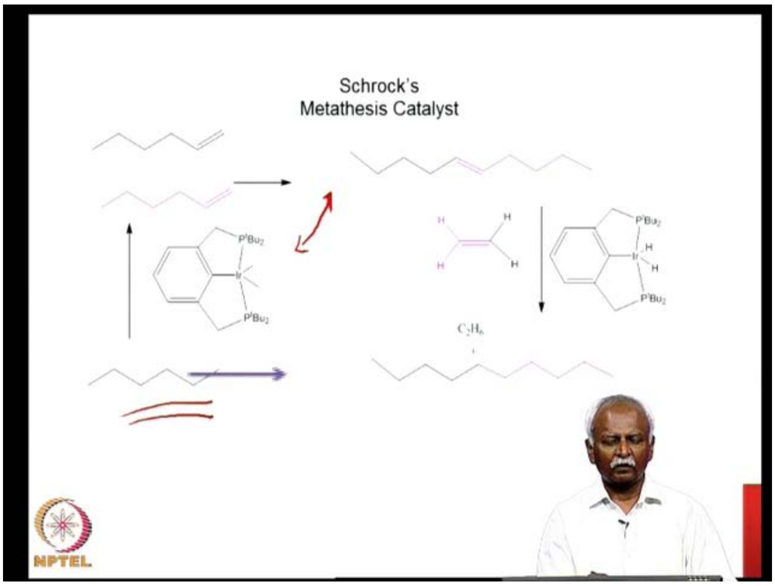

Schrock's
Metathesis Catalyst

Now, let us carry out this same reaction, which is the dihydride, addition of the dihydride to this alekene, so that they will give us the saturated variety of the C2H4. So, the ethylene would get converted to ethane and the decene, would get converted to the decane. So, you have converted the molecule which was simple C6H14, you took the C6H14 and converted into a decene and ethane by combination, combining two different catalysts. One catalyst, which will do CH bond activation, another catalyst which would do the metathesis reaction.

Now, not all catalysts are capable of being combined together like this. Very often when, you do tandem catalysis, as this is called tandem catalysis, results in complications because the reactants or the intermediates would sometimes poison one of the catalysts. Or the two catalysts themselves would interact with one another and cause complications. So this is the unique example and if you read the paper you will realize that, they had to try out many different catalysts metathesis, catalysts before they could arrive at the successful combination of ligands for the alkane meta alkene dehydrogenation and for the metathesis reaction. So, let us proceed further now.

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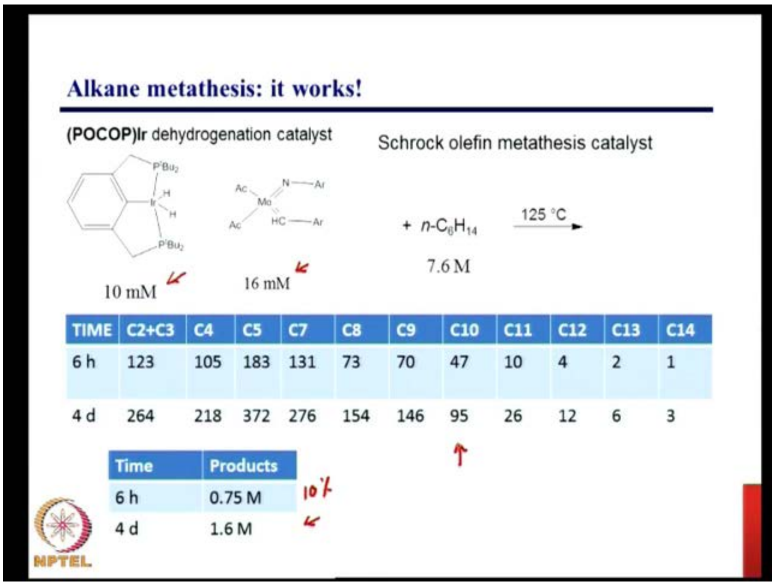

Alkane metathesis: it works!

(POCOP)Ir dehydrogenation catalyst

Schrock olefin metathesis catalyst

$+ \; n\text{-}C_6H_{14} \xrightarrow{125\ ^\circ C}$

10 mM

16 mM

7.6 M

TIME	C2+C3	C4	C5	C7	C8	C9	C10	C11	C12	C13	C14
6 h	123	105	183	131	73	70	47	10	4	2	1
4 d	264	218	372	276	154	146	95	26	12	6	3

Time	Products
6 h	0.75 M
4 d	1.6 M

10%

And the here I have shown for you, what happens when you have this metathes is, alkane metathesis carried out with the metathesis catalyst, which is has 16 milli moles andthe total of 7.6. In this example about 7 moles of hexene were used and this reaction mixture was in fact cooked together at 125 degrees in a sealed tube. What they have shown is that, after 6 hours of reaction you get close to 123 orclosed to 0.75 moles.

It is about 10 percent reaction at the end of the reaction, at the end of a 6 hours. And at the end of four days, you get only 1.6 moles of the product, which means, which means about 5 percent of the reactants have been converted after four days. So, this is in fact a very slow catalytic process, you would not be having a fast catalysis, as a result of these two reactions. And at the same time, another fact is that you have to carry out it at high temperatures in a batch process and also notice that you just do not get just decane, that it is decane is one of the products.

You get a variety of alkenes and alkanes in the reaction mixture and this is a, this is, this table gives you a combinations of all the alkenes and the alkanes that have been formed as the result of this reaction. And you also have C3 products being formed, because you have ethane, ethene reacting with other molecules. And so you end up with, the very complex mixture of products, it is not necessarily extremely useful chemistry. But nevertheless it is illustrated a key principle that CH bond activation can be used in a very useful fashion for carrying out reaction with paraffins.

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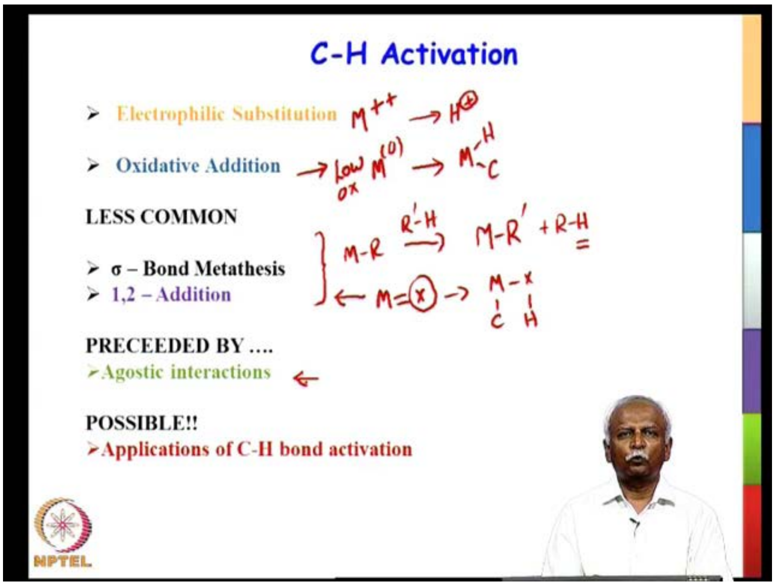

C-H Activation

- Electrophilic Substitution
- Oxidative Addition

LESS COMMON

- σ – Bond Metathesis
- 1,2 – Addition

PRECEEDED BY ….
- Agostic interactions

POSSIBLE!!
- Applications of C-H bond activation

So, what we have seen today is the fact that electrophilic substitution reactions, electrophilic substitution reactions can be used with alkanes and you need a metal in a high oxidation state. The metal has to be in a very high oxidation state so we will indicate that with the plus plus. Metal has to be in the high oxidation state and usually it generates H plus. So you have a reaction medium which is very polar, which will allow for this stabilization of H plus. Usually it is water and it is an acidic medium, that is present. You can also have on the other hand, with a low oxidation state metal.

So, the low oxidation state metals are can be denoted by M0 and that can also end up with an oxidation of metal to MH and MC bonds. Where, oxidative addition of the CH bond, this is also been observed fairly readily. So, these two are two examples of CH bond activation, which is commonly observed. The intermolecular variety is very common, but intermolecular species have also been observed in recent times. What is less common though, is a fact that you can have sigma bond metathesis. Although, the result is the conversion of one MR bond is converted into, by reacting with an R dash H, it gets converted into an MR dashed with an RH being released.

This hydrogen is coming from the reactant, that was added into the reaction mixture, a direct transfer of a hydrogen has happened. This is a less common although, it is been observed in several systems now, but these are again carried out with electrophilic metals where, you cannot carry out oxidative additions. The last example, the 1, 2 addition is again an example which is less common, not as common as the electrophilic substitution or activation of the oxidative addition. But 1, 2 additions are being observed with M double bond X systems, M double X systems where the C and the H add on to MC and XH. Usually, the X group is basic.

And so it is, it is like a system where you have an external base, you have an internal base. In this case, which interacts with the proton and mops out the proton that is being liberated. So, in all these cases, you the reaction could be preceded by agostic interactions. These agostic interactions are systems where, you have a small or weak interaction between the hydrogen CH bond and the metal atom. And if you want to have an agostic interaction, you would have to have metal.

And if you want to observe the agostic interaction you should have the metal in a high oxidation state where it is co-ordinatively unsaturated. Finally, we conclude with the positive note that, there are possible applications of the CH bond, the CH bond can be productively used for doing for example, a metathesis reaction as illustrated by Goldman and his group.