Transition Metal Organometallics in Catalysis and Biology

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Lecture – 60
Overall Summary of Transition Metal Organometallics in Catalysis and Biology

Welcome to the course on transition metal organometallics in catalysis and biology, we have come to the 60th lecture or the last lecture of this course and in this lecture, we would be covering the remaining portion of a discussion which were talking about the applications of organometallic compounds in biology and then provide overall summary of the topics that has been covered in this course.

Now, in the last lecture we have looked into the scope of applications of this newly evolving applications of organometallics in biology and which is sort of now defined as the field of bio organometallic chemistry and we have looked in to the scope in terms of applications of these compounds in biology and also, we have started the discussion by the; by looking into molecules; organometallic molecules that are present in nature.

And the discussion started off with 2 molecules; 2 vitamin molecules to be more precise, vitamin B12 and that contains a cobalt carbon bond in terms of methyl cobalamin as well as in terms of another coenzyme B12 which is also derived from vitamin B12. We have looked a given detailed description of the structures showing the presence of organometallic compound, now proceeding further we are going to talk about another interesting enzyme which is called methyl coenzyme M reductase or popularly known as MCR.

Now, these MCR functions via intermediate that is supposedly be proceeding by the formation of a nickel methyl bond, so that is why the organometallic connection.

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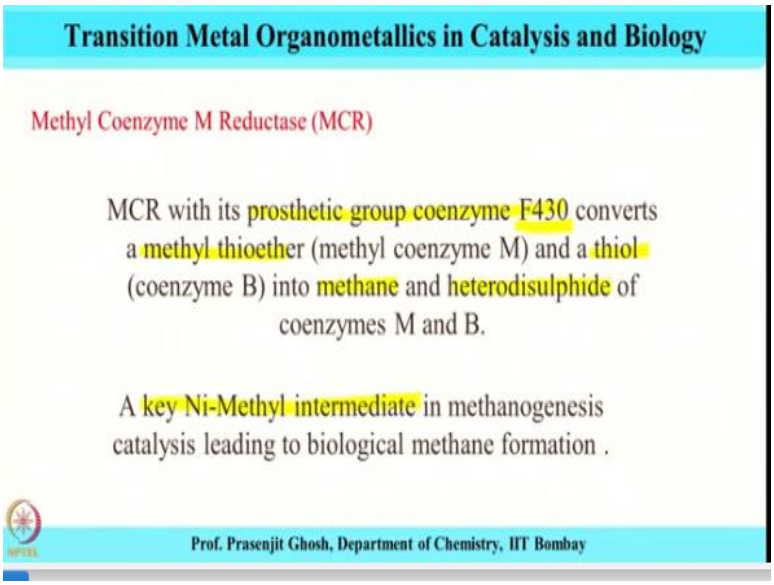

So, MCR has the prosthetic group of coenzyme; MCR with coenzyme converts and the function of the MCR is that it can converts methyl thioether which is coenzyme M and a thiol, the reactants are thioether and the thiol and the product is methane and heterodisulphide of coenzyme M and B and what is important; the bio organometallic connection over here is a key in intermediate continuing a Nickel methyl is supposed to be forming in the methanogenesis or methane production by this enzyme.

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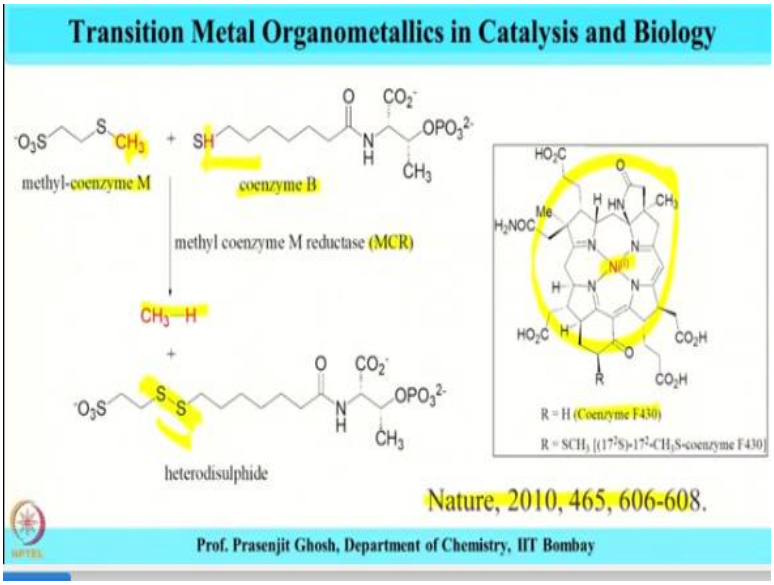

So, let me show it further for example, this is the thiol that has been spoken about, the thiol is of coenzyme B and this is the thioether which is of methyl coenzyme M now, these 2 react in presence of the enzyme called MCR to produce what is called methane and this hetero

disulphide. This MCR uses a cofactor which is called coenzyme 450 and the cofactor contains big organic group as is shown over here.

And inside it is the nickel in +1 oxidation state, so this has been reported very recently in nature 2010 Volume 465, 606 to 608 and request the reader to look up to get more knowledge about this particular enzyme. So, this enzyme converts this thioether and thiol to disulphide along with formation of methane, methane is formed from this methyl and this hydrogen to give this methane.

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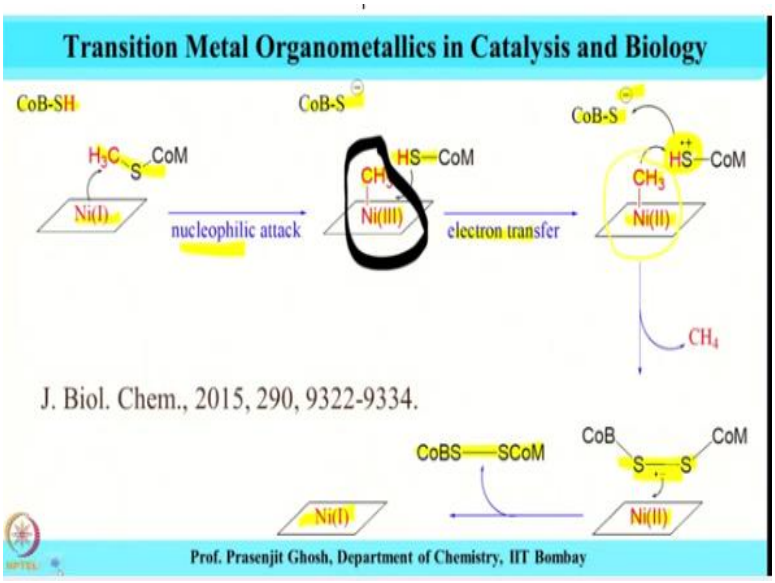

So, this is the methane producing enzyme and it goes through an organometallic intermediate which is shown over here, so for example this is the cofactor which contain nickel 1 and this is the thiol coenzyme B as well as the thioether, so nickel sort of gives electron and gets oxidised to nickel 3 and it forms a nickel methyl bond and this thio; the thiol gets stipulated in the proton is then subsequently observed on the thiol coenzyme M which is shown over here.

And then, there is the electron transfer that occurs from the thiol to nickel 3 and nickel become nickel 2 and what you have over here is a radical cation and the nickel 2 species with the anion in coenzyme B thioether. So, now these methane attacks these hydrogen to eliminate methane and process this radical cation is attacked by the anion which is shown over here and as a result, the formation of a radical anion is observed with nickel 2.

And finally, the electron transfer, reduction of nickel 2 back to nickel 1, happens with the elimination of heterodisulphide, so this is an interesting very nice example and the organometallic connection is the proposed nickel methyl bond which has been suggested to occur, so this nickel methyl species is something which is formed in the production of methane in this enzyme; by this enzyme MCR which contains a cofactor; coenzyme F420.

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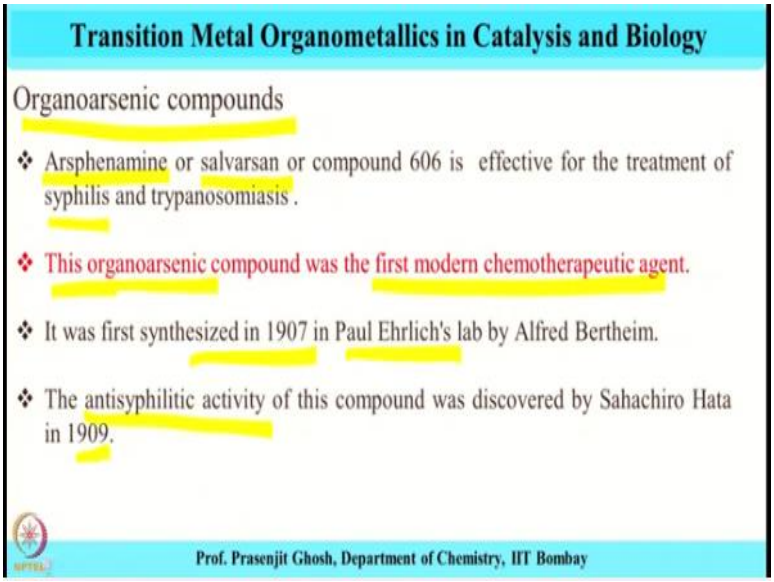

So, this is another enzyme whose intermediate is nickel methyl bond, so we are going to number 1 and moving to another important compounds, these are organo arsenic compounds, there is a drug called Arsphenamine or salvarsan, this is a drug for treatment of syphilis and trypanosomiasis, this is the first; this organosenic is the first modern chemotherapeutic agents, so organometallic being used for pahramceutical property is this is the first example synthesised in 1907 by Paul Ehrlich's lab.

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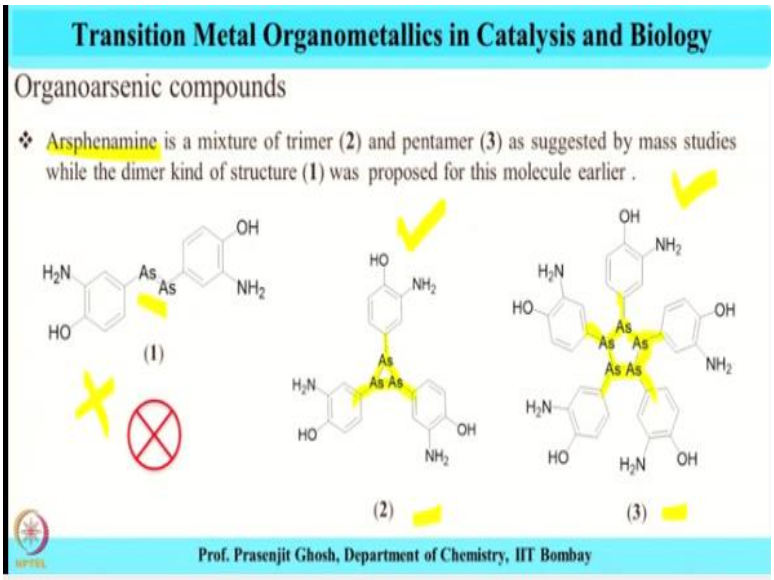

And then antisyphilic activity was discovered in 1909, so now let us take a look at these, molecule initially was thought to have arsenic, arsenic bond but later on this structure was proven to be incorrect and the structure is supposed to be containing arsenic, arsenic single bond in a 3 member or 5 member trimer or pentamer and this arseno phenamine is supposed to be a mixture of these 2 structures; 2 and 3.

So, this is another organometallic compound, which has direct metal carbon bond and being used in medicinal purpose.

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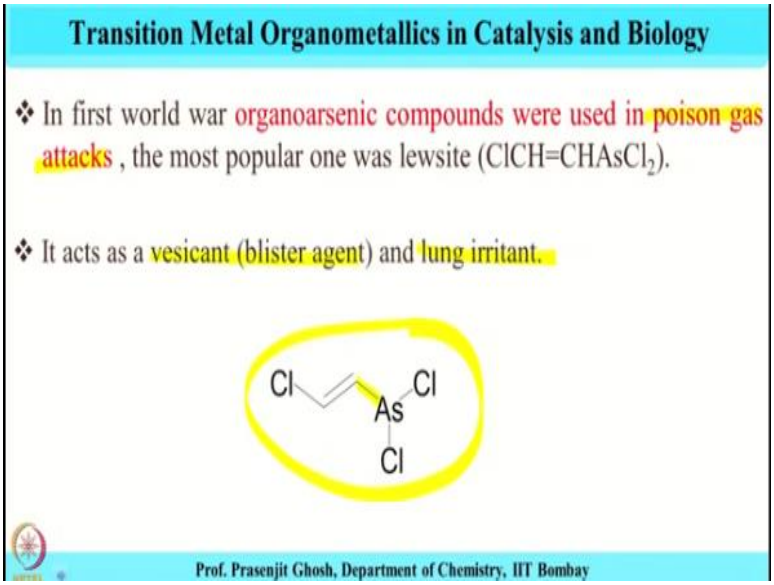

So, we move on to another interesting arsenic compound which is over here, it is a arsenic organometallic compound which contain bond but this was used for negative purposes actually, use as a poison gas in the First World War and these contains; these are lung irritant and contains like you know, leads to blister formation and then but this is also use as a poison, organometallic compound is use as a poison, so this is this arsenic compound.

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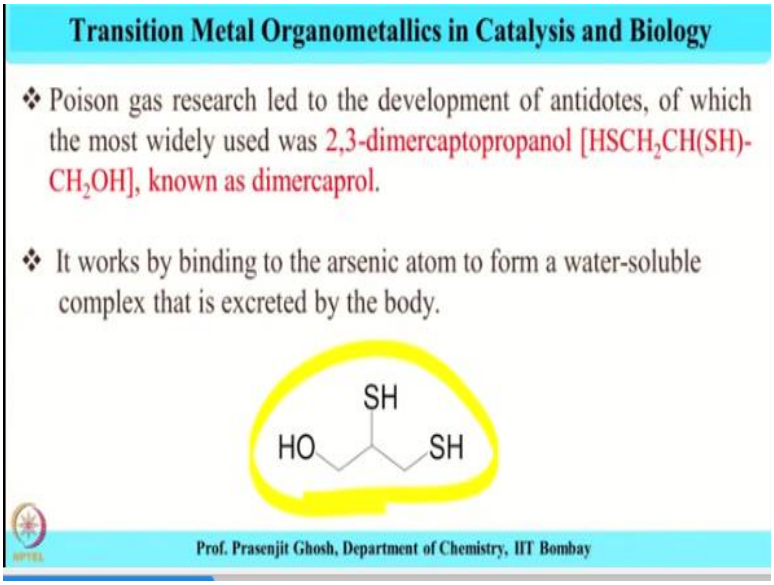

And then as a remedy, an antidote to this ligand, which has this di thiol ligand, were developed as an antidote to get relief from this arsenic poison gas which was done in world war. So, here we see the applications, some of the 9; some good and some bad applications of organometallic compounds.

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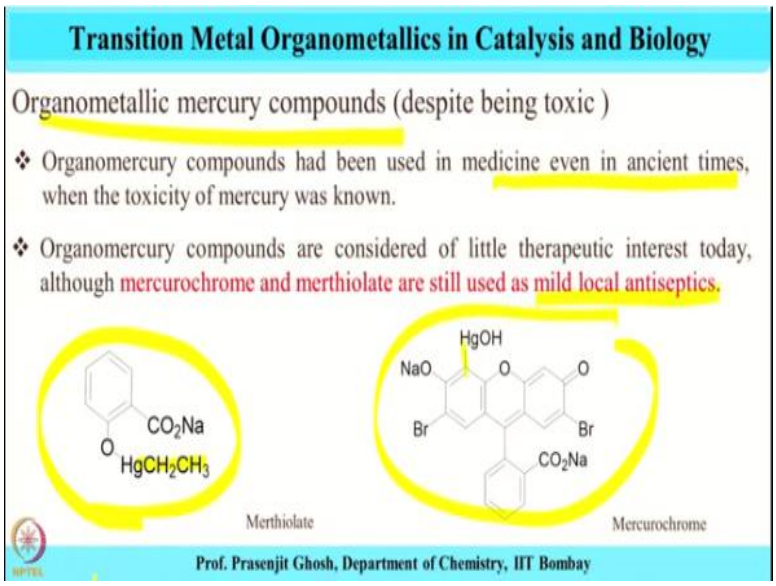

Another use of organometallic compounds is with mercury, so these are organometallic mercury compounds which is despite being toxics, they have been used since in medicines in ancient time and here are 2 mercury compounds which mercurochrome and mercurothiolate, these are organometallic compound which contains metal, carbon bond over here and they are used as local mild antiseptics.

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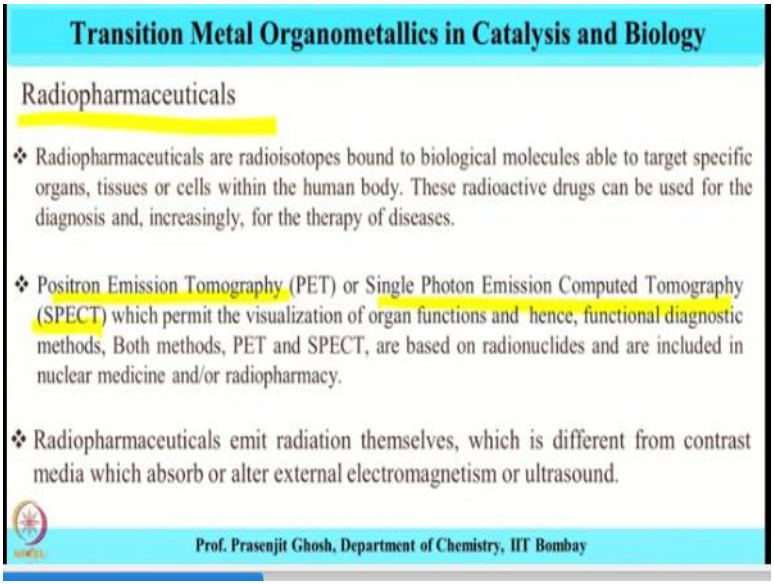

So, here we see a organometallic compounds of mercury being used for antiseptic purpose, so we have talked about the applications in medicines and one important area of organometallic applications is these radiopharmaceuticals, so organometallic compounds are used for radiopharmaceutical, this field is of highly technical and is developing fast with various

technology like positron emission tomography or single photon emission computed tomography and so on and so forth, are taking the front seat.

So, the organometallic connection is about the use of radio organometallic compounds for detection and imaging, purpose for these.

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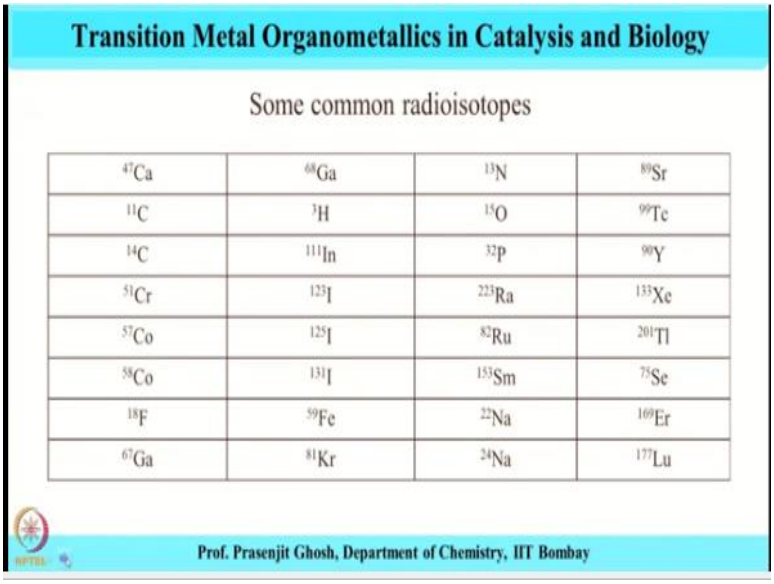

And in these compounds, some common isotopes are shown over here, whose organometallic compounds are often used.

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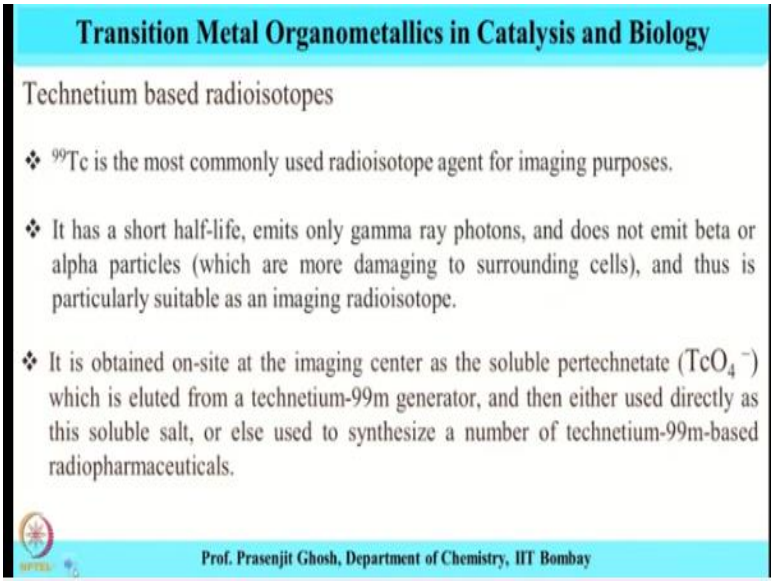

And technetium is one such important radioisotope.

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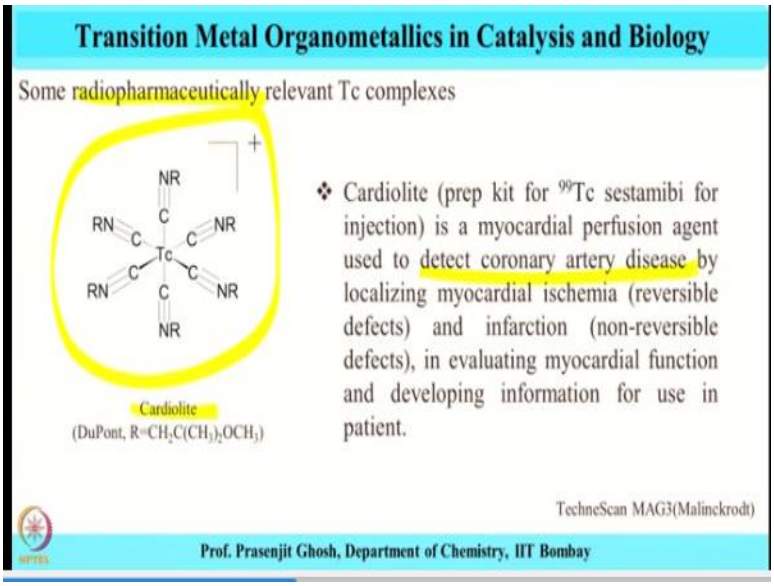

And the compound which has bearing for our discussion at this moment is this isonitrile complex of technetiums which are used for radiopharmaceutical purpose and this is marketed by DuPont with the trade name called cardiolite and this is used to detect coronary artery disease, so heart disease and stuff, has an application from organometallic compound of technetium, so with these we come to the end of our sort of a coverage for the bio organometallic chemistry, so applications of organometallic chemistry and biology.

And let me just summarise that we have started off by looking at the field of bio organometallic chemistry's in how the field has evolved in various directions from the presence of bio orgaometallic compounds in biological nature to the use of bio organometallic compounds for medicinal purpose, the imaging, detection so on and so forth and then we have started our discussion by looking at this vitamin B12, methyl cobalamin at coenzyme B.

Then, we have looked into this nickel enzyme; nickel cofactor for MCR activity and then looked into the organometallic compounds of arsenic and which had use for arsenic and mercury which are used for therapeutic purpose and then we have also looked into the technetium compounds for radio; imaging purpose. So, with these we come to the conclusion of our discussion of bio organometallic chemistry.

And now, I am going to summarise what has been taught, the topics that have been covered in this 60 lecture in this course of transition metal organometallic in catalysis and biology.

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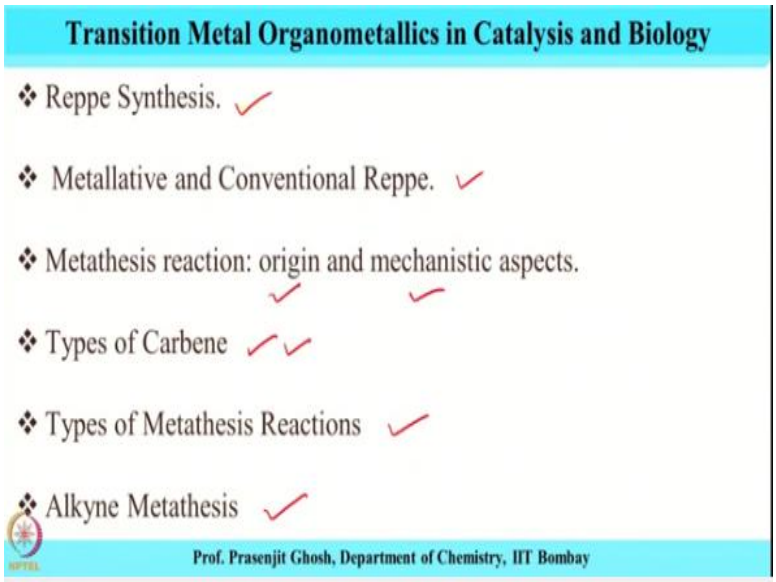

So, we started off in the beginning with Reppe synthesis followed by types of Reppe reactions particularly, metallative and conventional Reppe, the Reppe chemistry sort of revolves around the utility of acetylene, which were obtained for the coal. So, this is sort of like expansion of the coal chemistry or chemistry derived from the coal to other various compounds, bearing functional group, so to make value-added chemicals out of the source obtained from core.

And then, these are of; these processes are of tremendous industrial importance and mainly have been worked out by Reppe, while he was there at BASF, then we have looked into another interesting reaction which is metathesis; olefin metathesis reactions we had looked into their origin as well as mechanistic aspects and we had also noted that metal carbene are the important catalytic intermediates which carry out these catalysis.

And in that context, we have looked into types of carbenes, we have also looked into; we have also discussed that this metathesis is not a singular reaction but actually, engulfs a family of reactions and we have looked into various types of metathesis reactions that have been reported for olefins and their classifications in the topic of types of metathesis reactions. We have also seen that how the knowledge of metathesis reaction gets translated in alkyne metathesis made a

parallel completion of the reactivity of alkyne metathesis kind with the; from the context of alkyne metathesis.

And what we have noted that in alkyne metathesis, the active species again is a metal carbene species which carry out the alkyne metathesis reactions.

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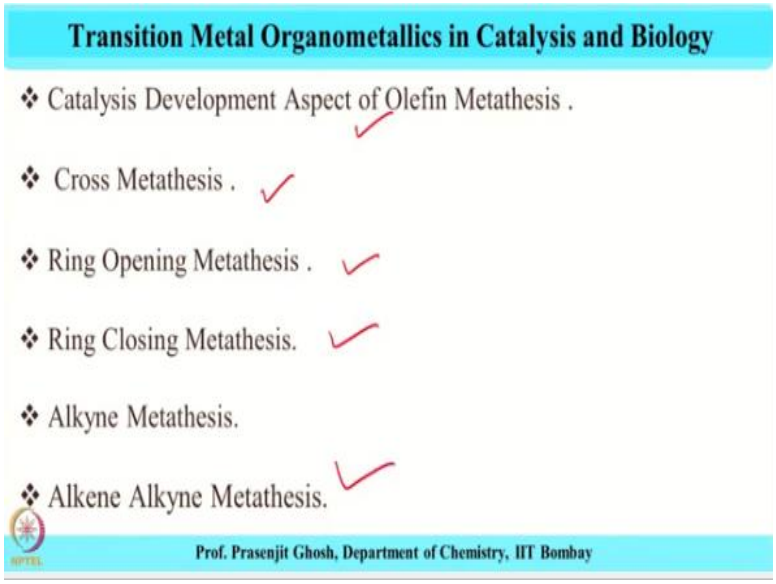

We have further discussed about the catalyst development aspects of olefin metathesis, we have looked into some special applications with regard to cross metathesis, now cross metathesis; these reactions are thermo neutral reactions and then there are conditions required with regard to driving the reaction forward many times it is the evolution of a small molecule olefin for example, ethylene which are formed as a part of cross metathesis that leads to the forward development of the reaction.

We have looked into ring opening metathesis, the version of ring, closing metathesis; we have also looked into alkyne, alkene metathesis as a part of it.

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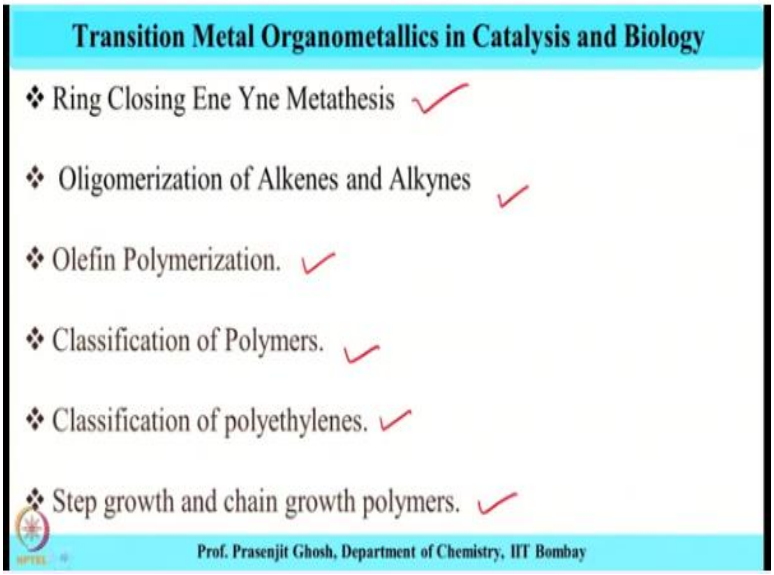

Then, there is this ring closing alkyne in kyne metathesis which in short is called Ene Yne metathesis, we have looked into this. After the metathesis, we looked into another big reactions which are oligomerisations of alkenes and alkynes, in this we have looked into shop catalyses which is shell high olefin polymerisation catalyses, we have seen that how the shop; development of the shop catalyst was an industrial problem which got developed to for a practical need; need based development.

And that was really 3 different reactions which in form olefin oligomerisation, olefin metathesis as well as isomerisation reactions, 3 important organometallic reactions been put together for a singular goal of making some feedstock for detergent, when in form of shop catalyst. We have also seen the development of evolution of olefin polymerisation that started with the heterogeneous Ziegler Natta system.

We also looked at the classification of these poly ethylenes in terms of their texture, their properties, their hardness and their softness, so that is very important criteria and then these properties were ranging from high density polyethylene HDP, linear poly ethylenes, then branched poly ethylenes and each of these structural changes would give different attributes to the overall polymer properties.

And there are catalyst which could exclusively synthesise these type of polymer and we have looked into the development of or catalyst from the basis of organometallic reasoning and organometallic logic that led to the direct achieve; achievement of these individual polymer properties. We have looked into, in this context, we have looked into classification of poly ethylenes also, this we have looked into mechanism by which these polymers are formed like step growth and chain growth.

How does the molecular weight vary as a one changes the polymerisation method from step group to chain growth mechanisms?

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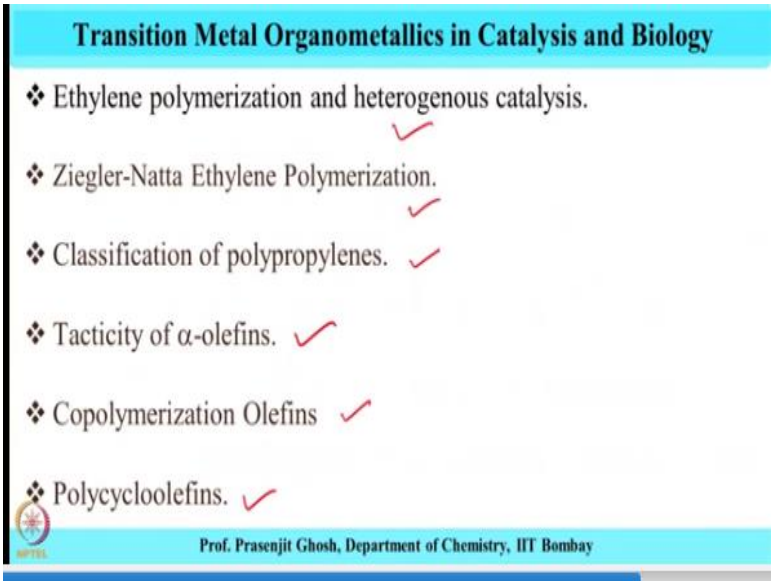

We have also looked at this ethylene polymerisation, polyethylene, the heterogeneous catalysis which is this Ziegler Natta which is this, Ziegler Natta catalyst; Ziegler Natta catalyst is titanium tetrachloride, $TiCl_4$ diethyl aluminium chloride which is this system, we have looked into how these Ziegler Natta system can be moved over from ethylene to propylenes, we have looked into various classifications of propylene depending on the orientation of the methyl groups which sort of leads to the tacticity; a tacticity of propylenes, iso tactic, atactic, syndiotactic.

We have looked into the fallouts of the properties as a result of the tacticity, we have also seen how the catalyst can be changed, geared towards preparing poly propylenes of particular tacticity, so tacticity is important term which we had covered and the importance of tacticity for

subsequent exploitation, the importance of this exploitation was rightfully realised by Natta and he singularly developed this field of poly propylene with Ziegler Natta systems.

Post of that we have also looked into co polymerisation now, co polymerisation can have that we have looked at are of 2 types particularly, the copolymerisation between olefins and alpha olefins, there are 2 types of monomer and also we had looked into the copolymerisation of ethylene with olefins with functional groups. Now, there are a lot of challenges in this area which we had discussed particularly, the one is that of selectivity.

Because, the rates of homo polymerisations of individual olefins are different as well as the functional group on the olefins tend to poison the catalyst that are used for polymerisation so, there are issues of selectivity as well as catalyst poisoning the surface of acutely while designing catalyst for such systems and we had also observed that how organometallic chemistry plays a big role in solving the problem.

What we had seen that this the problem of differential reactivity of olefins versus alpha olefins were more acute for heterogeneous a Ziegler Natta system however, for metallocene based homogeneous system, this differential activity of olefins or alpha olefins were not that acute and hence the catalyst development moved from multi-site heterogeneous Ziegler Natta systems to more well behaved and control metallocene homogeneous system, single site system.

And they were much effective for copolymerisation of olefins as well as for copolymerisation of olefins bearing polar functional monomer. Now, in this case another point to note is that these on developing catalyst for copolymerisation with functional group bearing monomer, the one they moves on from early transition metal to that of the late transition metal which are more electron rich.

And hence they do not get poison by the presence of functional group as to the extent that an early transition metal would do. So, we have looked in great detail that a catalyst development in the copolymerisation of olefins and now, moving beyond, we have looked into the catalyst used

for poly cyclo olefins, synthesis of poly cyclo olefins, we have looked into 2 methods which were used for poly cyclo olefins.

And then the first method which was just addition polymerisation, what we had observed that the catalyst was chosen as such that at the metathesis reaction were suppressed and only the polymerisation were; reaction was utilised and in the second approach, what we had seen; we had seen that addition reaction using intermolecular and intramolecular alternate polymerisation occurred that result in the formation of desired poly cyclo olefins, that too in a highly selective fashion giving a particular type of stereo chemistry.

Another important thing what we discussed is Ziegler Natta polymerisation is that with the advent of Ziegler Natta polymerisation, the focus of catalyst development had been mainly on group 2 metals, as the group 2 metals had been the one which was extremely good for carrying out olefin and alkyne polymerisation however, when the field evolved to develop catalyst for copolymerisation bearing polar functional monomers, the requirements shifted.

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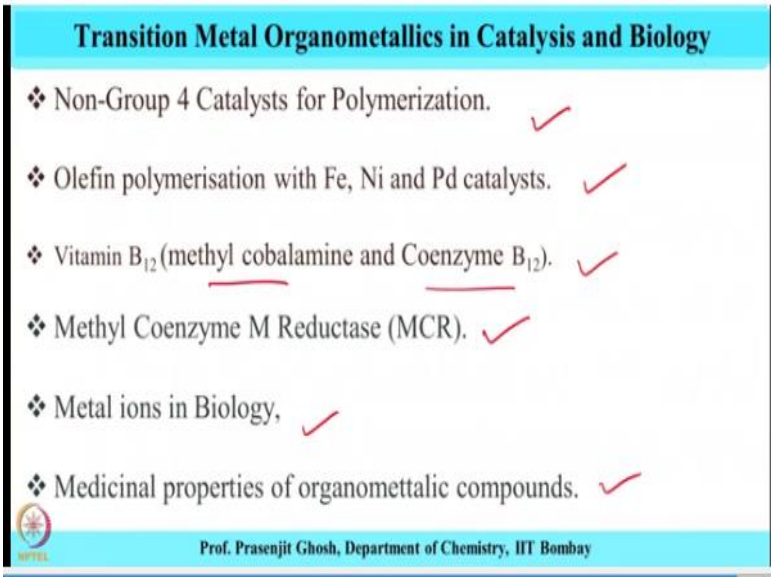

And the focus also shifted to producing catalyst from non-group 4 early transition metal catalyst for polymerisation, in this regard we have looked into lanthanide systems for as well as which for polymerisation as well as nickel and Palladium which are late transition metal for olefin

polymerisation. In this context, we have looked into Iron nickel palladium for the polymerisation.

After that we moved into the bio organometallic aspects of this course where we looked into utility of bio organometallics in biology and in the beginning, we noted the development of the field of bio organometallics which is highly evolving field however, given the fact that it is only emerging, still it had made its footprint in several areas ranging from imaging, radiotherapy applications to sensing and so on and so forth.

And we started off with the naturally occurring bio organometallic compound by looking into vitamin B12 particularly, methyl cobalamin and coenzyme B12, which does contain metal carbon bond in the nature now, this is counterintuitive and very interesting given the fact that organometallic compounds are extremely moist of sensitive and water sensitive and here, we have biology occurring organometallic compound in form of methyl cobalamin and coenzyme B12 which carry out vital functions in biology.

We also looked into another interesting compound called methyl coenzyme M reductase which with its nickel cofactor prosthetic group goes through an (()) (26:13) species containing nickel methyl bond formation which results in methane production, we have looked into utility of various metal ions in biology as well as medicinal property of organometallic compounds.

So, this is how we have spread the topic according to their utility in catalysis and biology and with this, we come to the end of the conclusion of today's lecture as well as the conclusion of these course.

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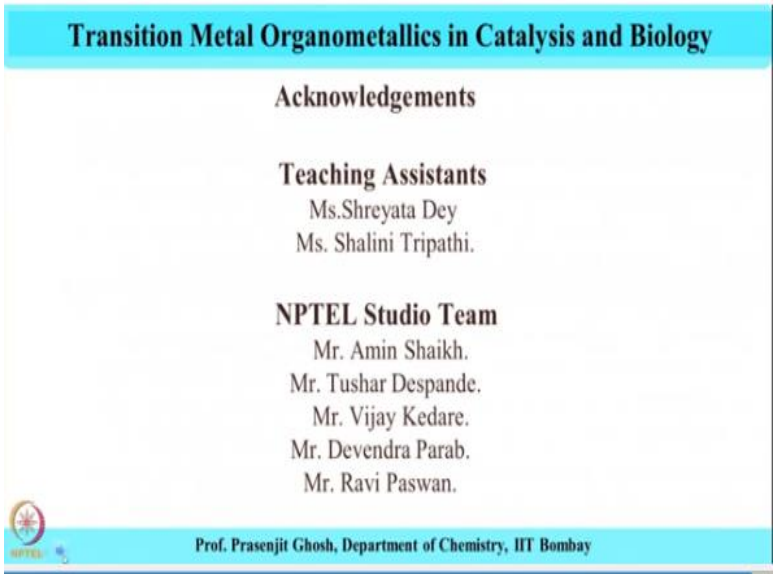

I must be really acknowledge my heartfelt thanks for the teaching assistants, both of them are graduate students here at IIT, Bombay; Ms. Shreyata Dey and Ms. Shalini Tripathi, both are extremely intelligent hard-working graduate students who had helped me tremendously in preparing the material for this course and they had been of great assistance, I must also acknowledge the whole of NPTEL studio team, they have been extremely intelligent, hard-working and supportive in getting this recording done.

I must start with Mr. Amin Shaikh, Mr. Tushar Despande, Mr. Vijay Kedare, Mr. Devendra Parab and Mr. Ravi Paswan. So, with these I thank everybody involved directly or indirectly with the course, I also thank you for taking this course and for being with me in all through the 60 lectures, I hope this course really helps you in getting a better perspective of organometallic chemistry.

Remember in the beginning, I had said that this is an important area where about 9 noble prizes have been conferred in a span of 120 years of history of noble prize, so that sort of highlights, how important is organometallic chemistry in today's world. So, with this again, I once again I thank you for being with me in this course and I hope you had a productive time in taking this course, with best wishes and good luck for your future in the work, I conclude here, thank you.