Reagents in Organic Synthesis
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Ag and Rh BASED REAGENTS IN ORGANIC SYNTHESIS

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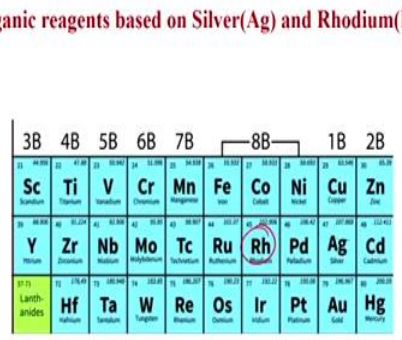

Welcome again, today we will discuss organic reagents based on silver and rhodium. So you can see rhodium and silver they are in the same row ,say fifth row and rhodium is in the group of cobalt and silver is in the group of copper.

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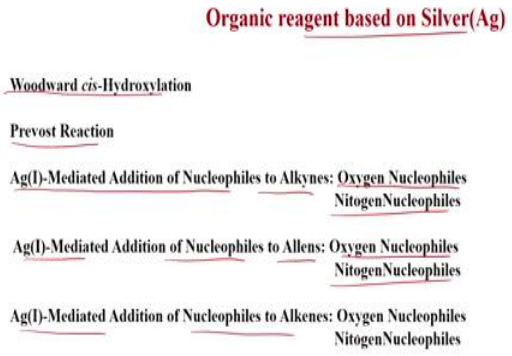

So we will see first the silver, organic reagents based on silver. And here we will discuss first Woodward cis-hydroxylation, then Prevost reaction, then silver mediated addition of nucleophiles to alkynes oxygen nucleophiles nitrogen nucleophiles, then silver one mediated

addition of nucleophiles to allens, oxygen nucleophiles, nitrogen nucleophiles. Also silver mediated addition of nucleophiles to alkenes, oxygen nucleophiles, nitrogen nucleophiles. And silver 1 mediated cyclo-addition reaction.

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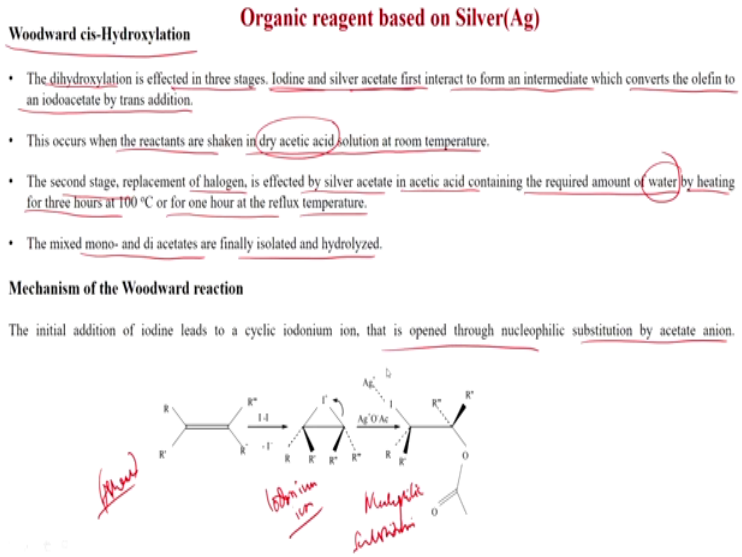

So first we will feel Woodward cis-hydroxylation, this is an important reaction developed by Nobel Laureate Woodward. So the dihydroxylation is affected in 3 stages; iodine and silver acetate first interact to form an intermediate which converts the olefin to an iodoacetate by trans addition. This occurs when reactants are shaken in dry acetic acid solution at room temperature.

So first you have to shake with dry acetic acid in iodine and silver acetate, the second stage replacement of halogen is effected by silver acetate in acetic acid containing the required amount of water, this is also important the water you have to present by heating for 3 hours at 100 degree centigrade for 1 hour at the reflux temperature. And the mono and di acetates are finally isolated and hydrolysed, so this is the mechanism. This is the alkene and the iodonium ion is formed first, iodonium ion like bromine reaction, iodine also reacts in a similar way and here this iodonium ion is formed.

Now silver acetate reacts with this iodonium ion as you can see it is reacting here so here the groups are inverted. And now you get this intermediate that is open through nucleophilic substitution by acetate anions, so this is nucleophilic substitution and now iodine will coordinate with silver plus so that we will see.

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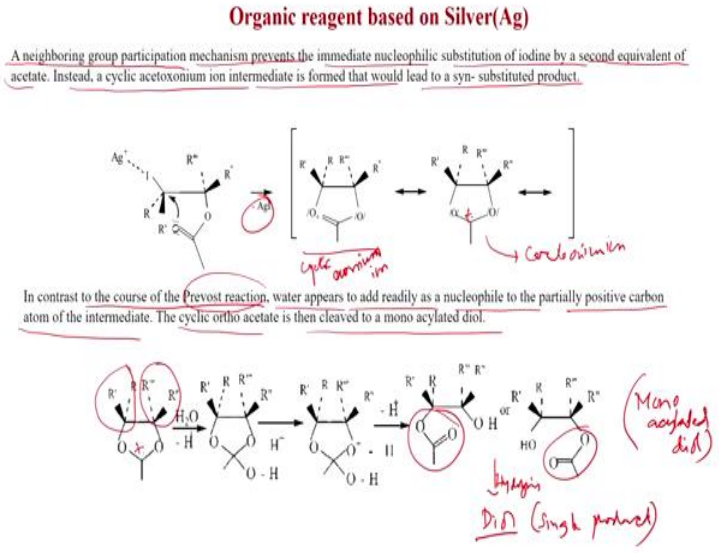

So in the second stage in neighbouring group participation this is important. In neighbouring group participation mechanism prevents the intermediate nucleophilic substitution of iodine by second equivalent of acetate. Instead, a cyclic acetoxonium ion intermediate is formed that would lead to a syn-substituted product. So this is very important, whenever a neighbouring group is present, then the neighbouring group can react with the electrophile so the substitution can reaction happen with the neighbouring group because it is a intramolecular process that is quite fast.

So here the acetate anion is present in such a way that it can do a nucleophilic substitution and with elimination of silver iodide you get this cycling oxonium ion, so this is the cyclic oxonium ion and this can be in resonating structure with this carbonium ion, there is a positive charge here carbonium ion.

In contrast to the course of the Prevost reaction that we will see that in Prevost reaction we cannot use water, but here we have to use water. Water appears to add readily as a nucleophile to the partially positive carbon atom of the intermediate. The cyclic orthoacetate is then cleaved to a mono acylated diol.

So this is the carbonium ion and now water attacks to generate this, so see this stereo chemistry this is actually syn, so we will see that when this water attacks to the carbonium ion, you generate this and then it is opening actually so either the acetate will form this carbon atom or this carbon atom whatever, so this is actually mono acylated diol, you get a

mixture of mono acylated diol but after hydrolysis you get the diol, so after hydrolysis you get diol, single product.

So this is the reaction happening with iodine, silver acetate, acetic acid and followed by acetic acid water reflux that cyclic oxonium ion is reacting with water and then the mono acylated diol is formed and so like this mono acylated diol is formed that after hydrolysis will give the diol.

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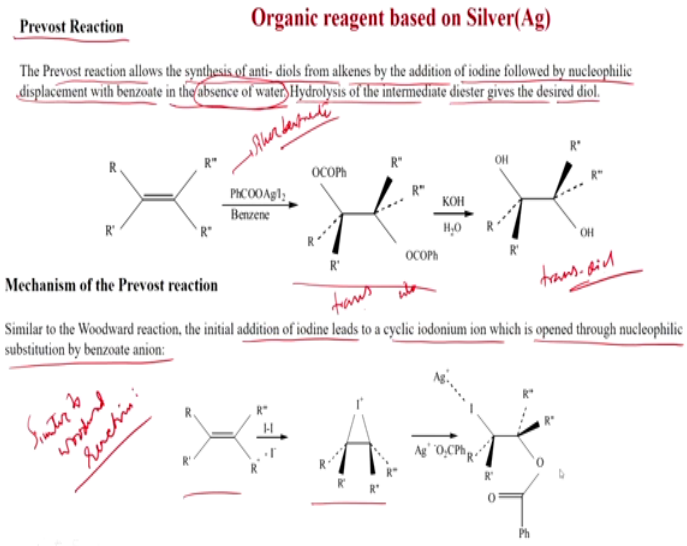

So now we will see the Prevost reaction, so in the Woodward reaction it is the syn addition, but Prevost reaction we will see this is trans addition and the Prevost reaction allows the synthesis of anti-diols from alkenes by the addition of iodine followed by nucleophilic displacement with benzoate in the absence of water so this is very important in the absence of water. Hydrolysis of intermediate diester gives the desired diol.

So this is the overall reaction with silver benzoate, so this is silver benzoate and iodine benzene you get this so this you can see this is the trans so trans di-benzoate and after KOH H2O treatment you get the trans diol. So, what could be the mechanism here? Similar to the Woodward reaction, the initial addition of iodine leads to cyclic iodonium ion which is open through nucleophilic substitution by benzoate anions.

So this step is similar like Woodward reaction, so similar to Woodward reaction like alkene reacting with iodine generating the iodonium iron, and earlier we had seen the silver acetate here the silver benzoate is reacting so you get this opening of the iodonium ion by the silver benzoate and you get this species like this.

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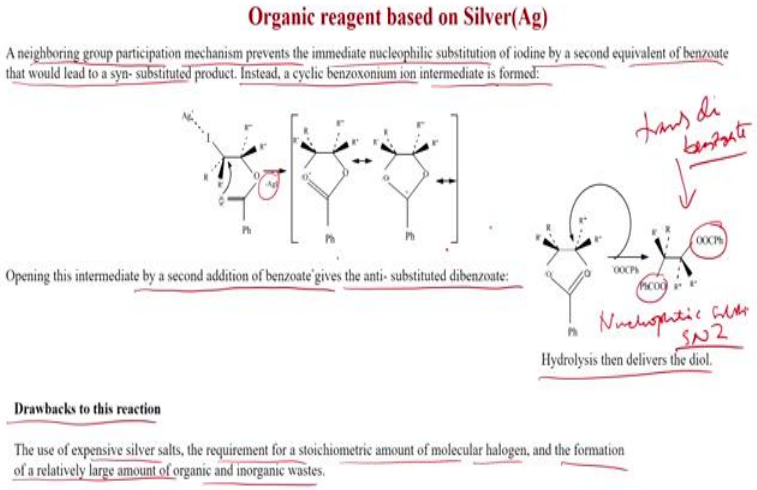

And a neighbouring group participation also happens here, neighbouring group participation mechanism prevents the intermediate nucleophilic substitution of iodine by a second equivalent of benzoate that would lead to a syn-substituted product. Instead, cyclic benzoxonium ion intermediate is formed. So here also the neighbouring group participation happens because the neighbouring group is within the molecule so the reaction will be always faster when there is a neighbouring group.

And after silver iodide elimination you get this oxonium ions so similar like Woodward reaction you get the oxonium ion and this will be equilibrium with the carbonium ion. So up to this it is similar, and now here only the difference because if you do not add water then opening this intermediate by second addition of benzoate gives the anti-substituted di-benzoate.

So instead of water if you have excess benzoate then this benzoate will open, so benzoate will give an inversion here so ultimately you get the trans di-benzoate so you get trans di-benzoate, so this is very important. Earlier when water added then the stereochemistry did not change, but now benzoate is attacking here so there will be inversion in this centres nucleophilic substitution SN2 and hydrolysis then delivers the diol.

So what are the drawbacks of this reaction, the use of expensive silver salts, the requirement for a stoichiometric amount of molecular halogen, and the formation of a relatively large amount of organic and inorganic wastes that are the drawbacks like silver iodide will form.

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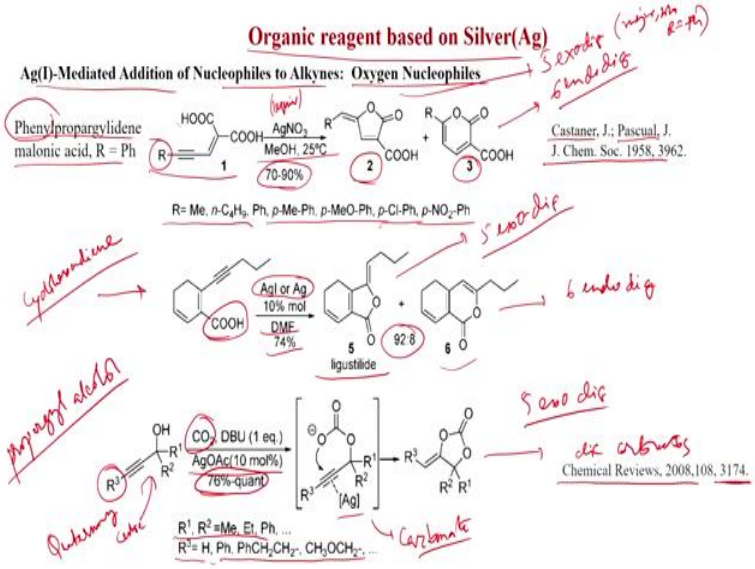

Now, we will discuss organic reagents based on silver some cyclisation reaction so silver mediated addition of nucleophiles to alkynes, oxygen nucleophiles. And phenyl propargylidene malonic acid. So in the gold catalyst we have seen that gold complexes with alkynes very well, similarly silver also complexes with alkynes very well and different addition reaction can be done.

Like with phenylpropargylidene malonic acid so this is the phenylpropargylidene malonic acid when R is equal to PH so with this triple bond, double bond is there and with silver nitrate one equivalent so this is the first report actually in 1958 by Castaner and Pascual. So they first developed this that the alkyne can co-ordinate with silver and after alkyne coordinates with silver from silver nitrate, the carboxylic can do a reaction here. So here you can see this is 5 exo dig and this is formed by 6 endo dig. And 5 exo dig is major when R is equal to Ph, so when R is equal to alkyl then you get mixture of 2 and 3.

So with silver nitrate 1 equivalent methanol 25 degree centigrade, just starting with methanol at room temperature you get these products 70 to 90 percent yield. And not only phenyl, other aromatic groups can also be tolerated, after this development many other groups try to explore this chemistry and many defined cyclisations have been reported. Like here this is actually cyclohexadiene system cyclohexadiene and carboxylic acid there and alkyne is present with end propyl group. Now they develop the silver iodide or silver 10 mole percent only.

And when DMF solvent you get 74 percent yield of this 5 exo dig, so 5 exo dig is the major here. The 5 membered ring is formed and this triple bond becomes double bond of course and this is an important molecule, it is called ligustilide, you get this product in 92 is to 8 ratio so this product is from 8 percent, this is from 92 percent. This is from 6 endo dig. Now, if you treat this propargylic alcohol so propargylic alcohol and this is a quaternary centre.

So, first you have to generate a carbonate with CO2 DBU 1 equivalent you generate this carbonate so this is carbonate and after that you treat with silver acetate 10 mole percent and then the activation of the alkyne by Silver will happen and the desired cyclisation will happen so this is also, so 5 exo dig then you get the cyclic carbonate in 76 to quantitative yield, so this method is very useful to generate cyclic carbonate with an exocyclic double bond and you can see R1, R2 can be methyl, ethyl, phenyl, etc, R3 can be hydrogen with terminal alkyne also then internal alkynes Ph, Ph CH2 CH2, CH3 OCH2 etc groups can be incorporated.

So this method is quite general that alkyne can be activated with silver and then defined oxygen nucleophile can react and define cyclic products, so this is in Chemical Reviews 2008, 3174 is the page number, there you can get this defined heterocyclic synthesis by silver.

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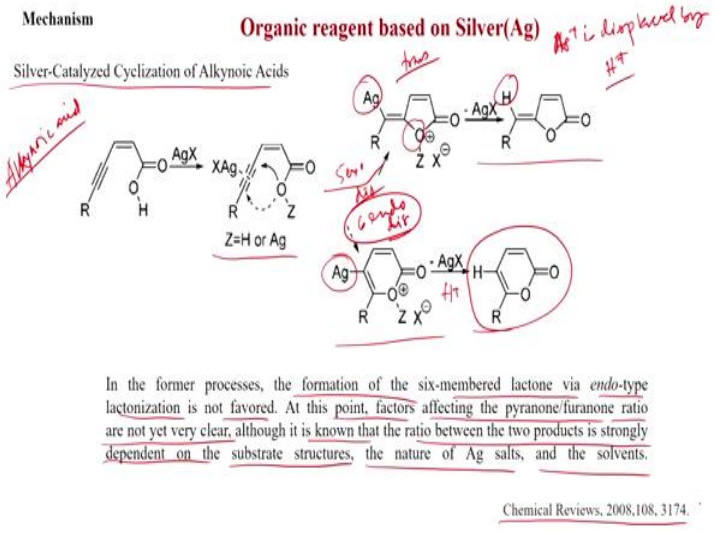

So now we will discuss the mechanism for silver catalysed cyclisation, so this is alkynoic acid, alkynoic acid, here triple bond, double bond and this is acid. So with silver as always silver will coordinate with the triple bond and now there is this is the exo, this is endo

possiblity with Z is equal to hydrogen or silver so when 5 exo dig will happen 5 exo dig then you get this after addition silver will be always in the trans so this is very important trans orientation, in coming nucleophile and silver will be in the trans orientation of the double bond. And after Silver X elimination and this is actually H plus is coming so silver plus is displaced by H plus either from solvent or workup with water you get it.

So this is the five-member cyclic products, this is butyrolactone with double bond actually two double bonds are present; one internal and other external. And with 6 endo dig you get this so here you can see this attack happens here and you get silver here and again silver X elimination and H plus of course you get this 6 membered ring. So this is very important that always the Silver will coordinate with alkyne and then 5 exo dig or 6 endo dig will operate depending on the substitution.

So the formation of the six membered lactone via endo-type lactonization is not favoured. At this point, factors affecting the pyranone, furanone ratio are not yet very clear, although it is known that the ratio between the two products is strongly dependent on the substrate structures, the nature of silver salt and the solvent. So depending on the substrate structure and silver salts and the solvents you can get different ratio of these two products, this was also reviewed in the Chemical Reviews 2008, page number 3174.

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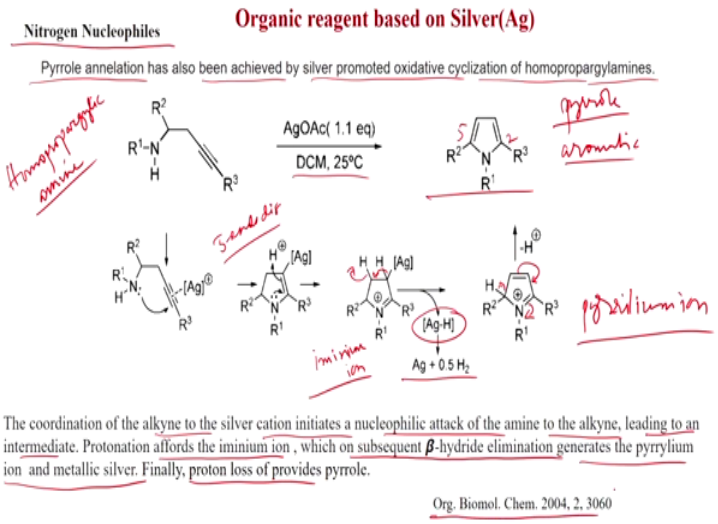

So, now we will see nitrogen nucleophiles, so not only oxygen, nitrogen nuclophiles can also be used and here also you can deferent aza product. So pyrrole annelation has also been achieved by silver promoted oxidative cyclisation of homopropargyl amine like this one

homopropargylic amine, here with silver acetate 1.1 equivalent DCM you get this pyrrole. So this is important, this is his aromatic, so not only the addition there are also dehydrogenation is happening that we will see. So this hydrogen is attacking and then after aromatisation you get this product pyrrole. So what could be the mechanism? So here also silver coordinates with the triple bond and here the 5 endo dig will happen 5 endo dig, 5 endo dig will happen and you get this intermediate.

So the coordination of alkyne to the silver cation initiates a nucleophilic attack of the amine to the alkyne leading to an intermediate. Protonation affords the iminium ions, so this is iminium ion. And this is very important, now this iminium ion will undergo the beta hydride elimination that will generate pyrrylium ion and metallic silver. So you can see, after beta hydride elimination, so, what will happen? This silver hydride will eliminate that is ultimately will go to silver plus 0.5 hydrogen. So after beta hydride elimination you get this pyrrylium ion so this is pyrrylium ion.

And now H plus will eliminate for the aromatisation so like this H plus eliminates and generates the pyrrole. So this is very important when you put homopropargylic amine with silver acetate you can get the pyrrole, substituted pyrrole actually. This is 2,5 di-substituted pyrrole you can get very easily. This was published in Organic Biomolecular Chemistry, 2004.

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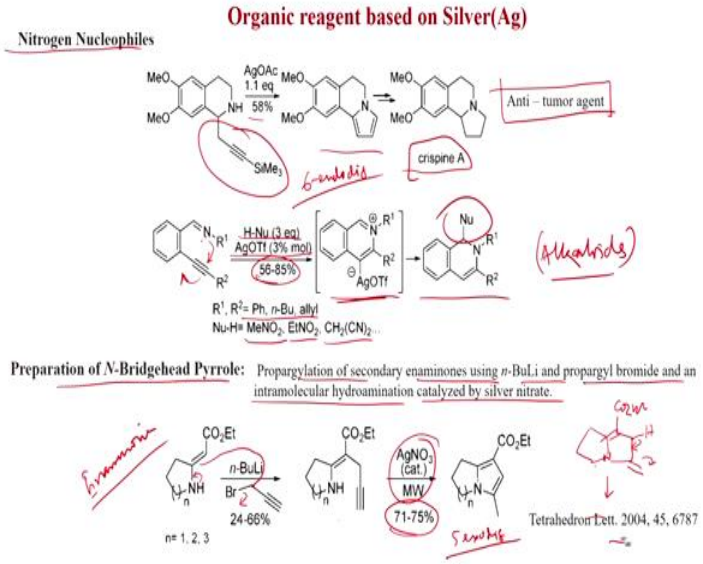

More examples of nitrogen nucleophiles here you can see the tetrahydro isoquinoline derivative like this group is there, the triple bond has trimethylsilyl group. Here also with

silver acetate 1.1 equivalent you get this pyrrole formation. So here also similar mechanism and beta hydride elimination and when then proton loss will give this aromatic product and this can be hydrogenated to make this compound which is called crispine A and this is an anti-tumour agent so this is very important you can get easily this pyrrolidine fused tetrahydro isoquinoline by this strategy. Also if you have an amine here and a triple bond here then with H nucleophile, H nucleophiles is this nitro methane, nitro ethane, malononitrile and with silver sulphate only 3 mole percent then you get this intermediate because this nitrogen will first attack here then this will happen so this is 6 endo dig.

6 endo dig will happen and now this is iminium ion, here the nucleophile will attack and you can get this product in 56 to 85 percent yield. So R1, R2 can be phenyl, n-butyl, allyl and nuclophiles. I already told nitro methane, nitro ethane and malononitrile can be used. So this is very important, you can get this compound, alkaloids very efficiently with the incoming nucleophiles is present here. Also N-bridge pyrrole can be formed by this strategy, propargylation of the secondary enaminones using n-butyl lithium and propargyl bromide a intramolecular hydroamination catalysed by silver nitrate.

So with butyl lithium and propargyl bromide you can get first this, so here butyl lithium will take and now this, this will attack here and this will happen and after the isomerisation of course you get this because iminium ions will form that will isomerise to this, this is much more almost stable. And now after silver nitrate so what will happen? Silver nitrate so after silver nitrate addition so nitrogen will add here and you get this after proton loss and this will isomerise to give this, so for isomerisation you get this is the aromatic part this part. So silver nitrate microwave condition you can get 71 to 75 percent yield. So this is two-step process, first n-butyl lithium reacts with this enaminones so this will be enaminone with propargyl bromide you get this.

Now you put silver nitrate catalytic amount in microwave condition, this is 5 exo dig is happening. And after isomerisation you get the aromatisation, this was published in Tetrahedron Lett 2004, page number is 6787.

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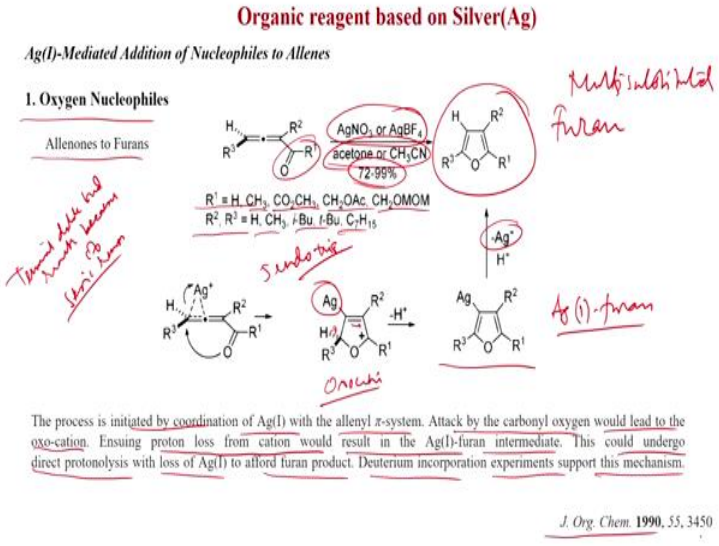

So far we have seen alkynes, now we will discuss allenes. So allenes can also be used in this cyclisation strategy. So first we will see oxygen nucleophiles and allenones to furans. So this is allenones, you can see this is carbonyl group present with the allene and with silver nitrate or silver tetrafluoroborate acetone or acetonitrile solvents you can get these products which are furan, multi-substituted furan actually multi-substituted furan.

You get this product in 70 to 99 percent yield, here R1 can be hydrogen, this is R1, hydrogen means the aldehyde, CH3 means ketone CO2CH3, CH2OA3, CH2OMOM, R2 R3 can be hydrogen, CH3 isobutyl tert butyl so different groups are possible, this is a very general method and you can get this furan.

So, what will be the mechanism? So here in the allene, generally the terminal double bond reacts so terminal double bond reacts because of steric region, so in the allene there are two double bonds and now silver will coordinate with the terminal one and now this is only possible here so 5 endo trig is happening. And so the process is initiated by coordination of silver ions with allenyl Pi system. Attack by the carbonyl oxygen will lead to the oxo-cation, so this is the oxo cation, oxo cation and here the reaction is happening and silver goes here. And after elimination of protons, proton loss from cation would result in the Silver (I) furan intermediate. So after proton loss so this proton will loss and you get this silver containing furan so this is silver (I) furan.

And now of course H plus will come and silver plus will eliminate, you get the furan. This could undergo direct protonolysis with loss of silver (I) to afford furan product, deuterium

incorporation experiment supports this mechanism. So, if you put deuterium then here we can get deuterium. So this is very important method to generate furan from allenones. If you put the allenones with silver nitrate or silver tetrafluoride with acetonitrile solvent, you can get very good products, this was published in JOC 1990.

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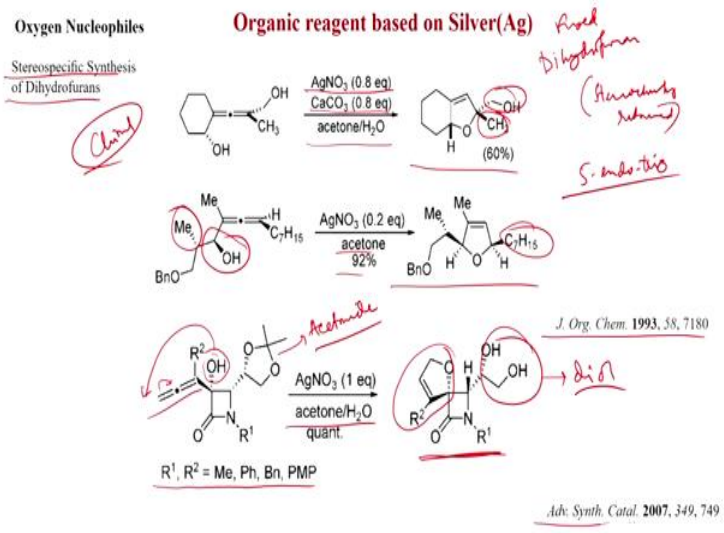

Now we will see stereospecific synthesis of di-hydro furans, this allene and also this is secondary alcohol, this is chiral, these are stereo centres. And with silver nitrate 0.8 equivalent, calcium carbonate 0.8 equivalent in acetone water solvent you get this this is di-hydro furan, fused di-hydro furan you get 60 percent yield and this stereo chemistry is retained this is very important, stereochemistry retained. Also you see this is chiral allene, this is chiral alcohol, there is another chiral centre with silver nitrate 0.2 equivalent acetone you get this, so all these cases 5 endo trig cyclisation is happening.

Here also the stereo centres are retained, here you see this group is there in the starting material also, this was published in Journal of Organic Chemistry 1993. Now, if you have this one, this one you can see the lactam is present, also tertiary alcohol with a quaternary centre, this is the allene and now this will add here and you get this di-hydro furan and the stereochemistry is intact.

Also in this condition this is acetonide so acetonide because the reaction happened with acetone, water you get the hydrolysis, so this goes to diol. And here the cyclisation happen selectively and this motif is undisturbed in this reaction. So different groups can be tolerated;

R1, R2 can be methyl, Phenyl, benzyl, PMP group, this work was published in Advanced Synthesis & Catalysis 2007.

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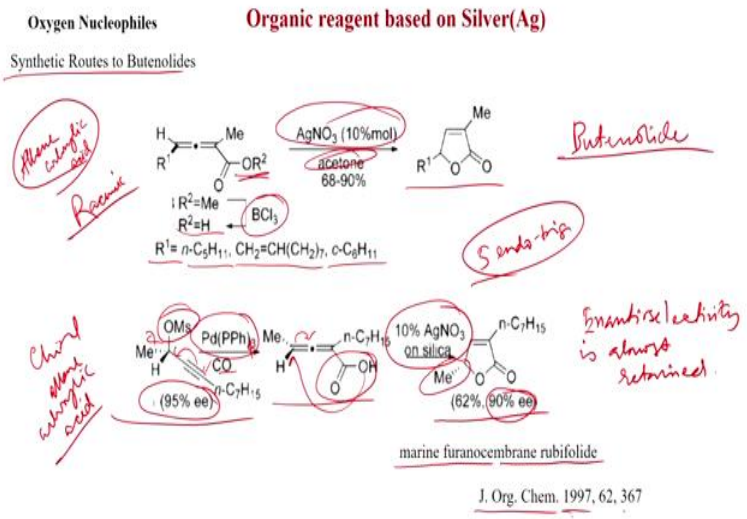

Now we will discuss synthetic routes to butenolides. So you see the allene group and carboxylic acid, so allene carboxylic acid so here what will happen, this if you get the ester, ester can be converted to the acid by treatment with boron trichloride then you can get the acid. And that acid if you treat with 10 mole percent silver nitrate in acetone solvent, you can get this butenolide, so this is butenolide. So this butenolide compound you can get very easily by reacting allene carboxylic acid with silver nitrate 10 mole percent. And you can see R1 can be n C5 H11, this is the allyl group and this is the cyclohexyl group.

And this is of course racemic, so this is racemic and now a chiral synthesis is possible, chiral allene carboxylic acid. So, if you have chiral allene carboxylic acid like this way, this is the propargylic alcohol, you have to put a mesyl protection, and this product you can get in 95 percent ee. And then this one PdPPh3 whole 4 and carbon monoxide you get this. So here the allene is formed, this methyl group eliminates so carbon monoxide ultimately will go to CO2H group, here it is attacking like this and you get the allene and as well as the carboxylic acid group.

Now this substrate is very much suitable for our reaction that is the 5 endo trig cyclisation, so 5 membered ring will form like this so silver will coordinate here and this hydroxyl will attack here, you get this. So here the stereochemistry also is retained the methyl group and

you get this product after treating with 10 mole percent silver nitrate, you get this product in 62 percent yield and 90 percent ee.

So you start with the product with 95 percent ee and you get 90 percent ee. So enantioselectivity is almost retained, so this is very important during the cyclisation the enantioselectivity did not do lose so much. So enantioselectivity is almost retained, starting material was 95 percent and the product you get 90 percent in enantiomeric excess. And this is very important product, this is marine furanocembrane rabifolide and this work was published in Journal of Organic Chemistry 1997, page number is 367.

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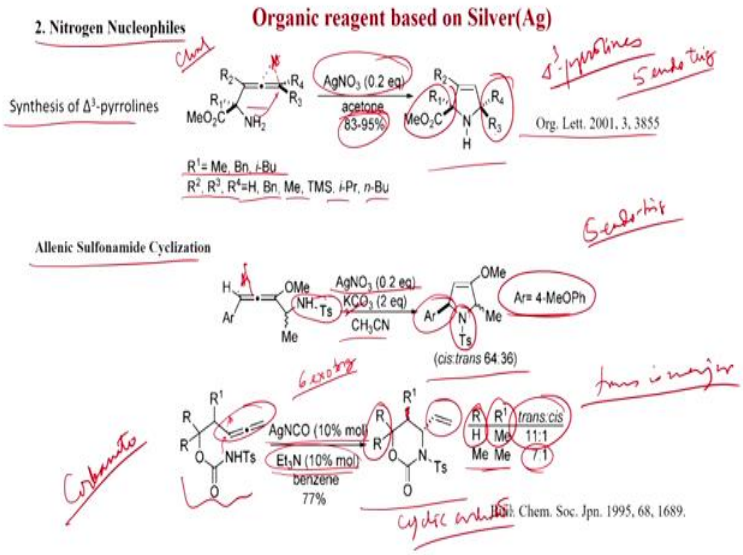

So now we will discuss nitrogen nucleophiles. So wherever oxygen nucleophiles will work, nitrogen nucleophiles also work so nitrogen nucleophiles to allenes we will see and synthesis of Delta 3 pyrrolines. Like here, this is also you can see this is chiral chiral allene system as well as extra chiral centre is present here. This is the amine ester motif and with silver nitrate 0.2 equivalent acetone solvent you get this product in 83 to 95 percent yield, so these are Delta 3 pyrrolines. And R1 can be methyl, benzyl, isobutyl, R2, R3, R4 can be hydrogen, benzyl, ethyl, TMS, isopropyl, n-butyl different groups can be screened. And this work was published in Organic Letters 2001.

So here also this similar reaction is happening 5 endo trig so 5 endo trig is happening, the silver coordinates with this terminal double bond and then this attack happens and here this stereochemistry is retained like oxygen nucleophiles also. This stereochemistry is also retained and you get this cis-geometry here CO2 Me and R3 will be cis. So now we will

discuss allenic sulphonamide cyclisation so this is sulphonamide and this is allene. And here also you can get this same 5 endo trig cyclisation and this N-tosyl group as here so here silver coordinates and here the attack happens and after proton comes of course, the silver will eliminate and you get this centre.

So here when Ar is equal to 4 methoxy Ph then you can get cis is major, cis is trans 64 is to 36. And this is the condition, silver nitrate 0.2 equivalent this will be potassium carbonate 2 equivalent and acetonitrile solvent you get this product. So here this base is required, this is the acidic proton NH-tosyl so after deprotonation only this becomes active nucleophiles. And now this you can see this is carbamate motif, carbamate. And this one there is a carbamate motif, there is a allene motif and with Ag NCO 10 mole percent.

Tri ethyl amine here also we have to use a base like tri ethyl amine 10 mole percent benzene you get this cyclic product, so this is cyclic carbamate is forming and you see here because this ring is only possible six exo because six or five membered ring you will form in general so here 6 exo trig cyclisation is happening, so silver is coordinating here and this nitrogen is attacking here and you get this double bond vinyl group.

When R is equal to hydrogen, these are hydrogen R1 is equal to methyl, then trans-cis ratio is equal to 11 is to 1 so this is the trans one so this will be, and when methyl both is methyl, R is equal to methyl, R1 also methyl then 7 is to 1 so trans is major, and this was published in Bulletin of Chemical Society Japan 1995, page number is 1689.

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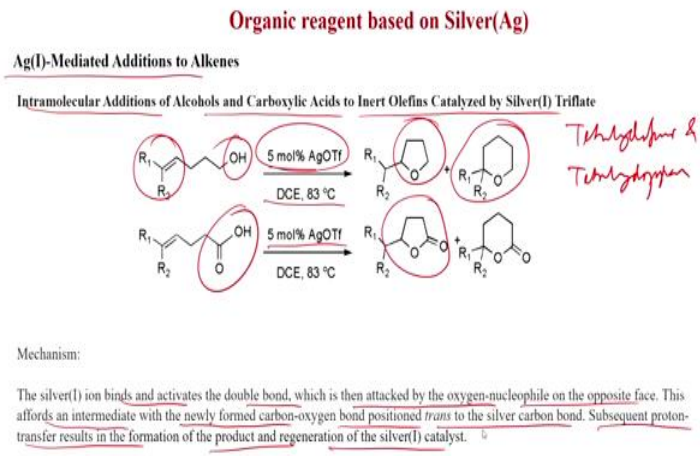

Now, we will discuss silver mediated additions to alkenes, so alkenes can also be used in this reaction, intramolecular addition of alcohols and carboxylic acids to inert olefins catalysed by silver 1 triflate, like here there is a double bond and alcohol with 5 mole percent, silver triflate, DCE 83 degree centigrade you get tetrahydrofuran and tetrahydropyran, so tetrahydrofuran and tetrahydropyran. With carboxylic acid also you get cyclisation, you get the lactone five membered or six-membered. And we will see depending upon R1, R2 you get this ratio, the silver ion binds and activates the double bond which is then attacked by the oxygen nucleophiles on the opposite phase.

This affords an intermediate with the newly formed carbon-oxygen bond positioned trans to the silver carbon bond. Subsequent proton transfer results in the formation of the product and regeneration of the silver 1 catalyst.

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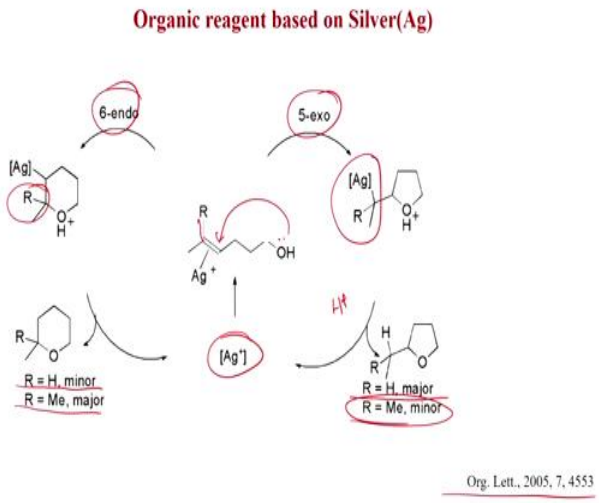

So this is the mechanism, so silver coordinates with the double bond so like it coordinates with triple bond allene, it can coordinate with double bond also and then there is R when the 5 exo addition will take place so this will attack here and then you get this and after H plus comes you get this one and silver plus you regenerate. So when R is equal to H then this is major, when R is equal to methyl then this is minor so this is very important. Now 6 endo will give this product so 6 endo gets the here it will attack R so when R is equal to methyl then this will be major because the attack will take place the more substituted carbon and there the carbonium ion of course will be stable so R is equal to H this is minor, R is equal to methyl this is major and this is the paper Organic Lett 2005.

So this is very important, when there is di-substituted olefin that is the olefin the terminal carbon it is di-substituted then the six-member ring tetrahydropyran will form. On the other hand, if it is mono-substituted olefin then you get the tetrahydrofuran.

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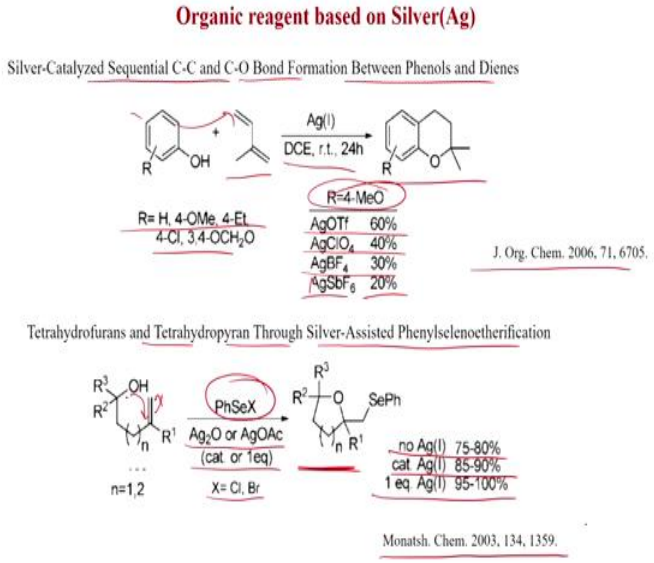

So silver catalysed sequential C-C and C-O bond formation between phenols and dienes also is possible here. This is phenol, this is diene so here this attack will take place followed by silver mediated cyclisation will give this. And different groups can be tolerated here and with 4 methoxy groups R is equal to 4 methoxy here the methoxy group then silver triflate gives 60 percent, silver chlorate 40 percent, silver tetrafluoroborate 30 percent and AgSbF6 only 20 percent yield, this was published in JOC. So here the silver is acting as a Lewis acid, Friedel-Crafts reaction is happening followed by the oxo cyclisation.

Tetrahydrofuran and tetrahydropyran through silver assisted phenylselenoetherification also is possible. Here you see PhSeX, silver oxide, silver acetate catalytic or 1 equivalent, X is equal to chlorine, bromine, phenyl selenium chloride or phenyl selenium bromide, you get this cyclisation that is ether formation like this and of course, selenium ion is formed here and without silver also this reaction occurs and you get 75 to 80 yield. Now catalytic amount of silver will increase the yield to 85 to 90 and 1 equivalent silver (I) give 95 to 100 percent yield, this work was published in this Journal in 2003.

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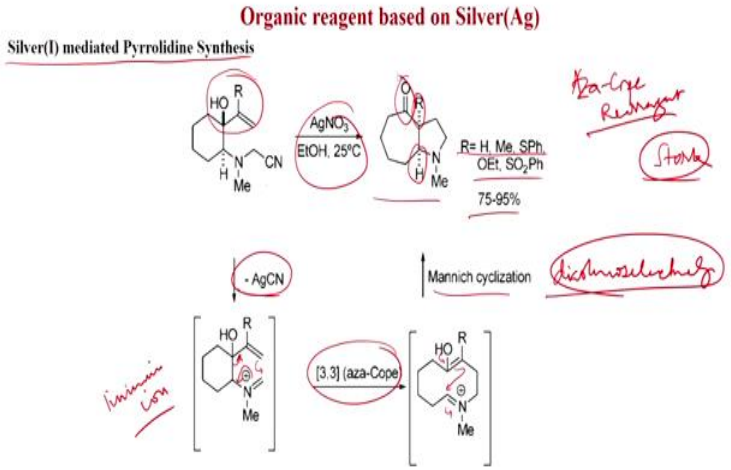

Now again we will discuss pyrrolidine synthesis, so this is aza-cope rearrangement, so aza-cope rearrangement will happen, this reaction developed by Stork, he is famous organic chemist. So if you have this one CH2CN group with anaemic group and this is the allelic alcohol then with silver nitrate treatment you get this, so this ring expansion happens and pyrrolidine is formed and they are also same orientation, and different groups can be tolerated, you get 75 to 95 percent yield.

So what could be the mechanism? So first silver cyanide elimination so this iminium ion will form so this is the iminium ion and then the 3,3 aza-cope rearrangement will happen, so this we will add here, now this will go here and this will go here. So here this enol is formed, after that the Mannich cyclisation will happen, so this will be like this so this is here it is connecting R and this so you get the Mannich cyclisation seven membered ring is formed and this reaction happened very diastereoselectivity so diastereoselectivity because of the ring requirement this is syn always when there is Sp2 centre, it likes to take syn orientation, this was published in JACS 1988.

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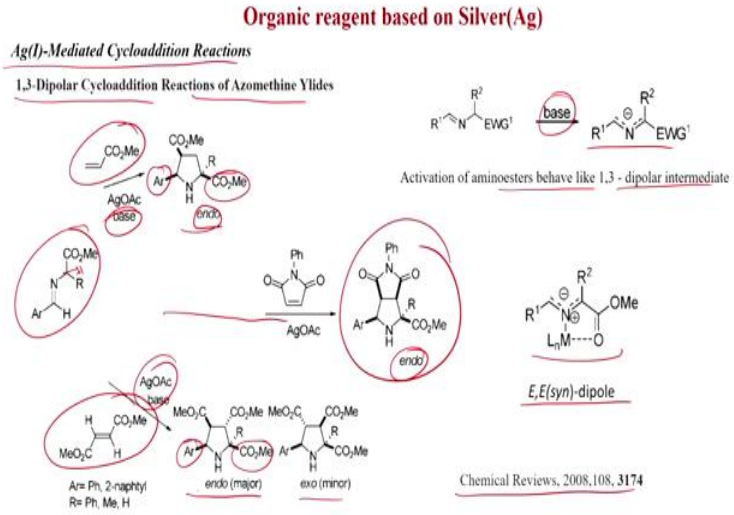

Now silver mediated cycloaddition reactions are also possible, 1,3 dipolar cycloaddition reactions of azomethine ylides, here there is a hydrogen and that review with a base and then you can get the azomethine ylides. And now different electrophiles can be treated like here methyl acrylate will give this so this is the endo product CO2Me and R, they are in the same side. Also maleimide can give this product bycyclic product this is also endo. And dimethyl fumarate also silver acetate base will give this pyrrolidine, tetra-substituted pyrrolidine very important and this is the major product here also CO2Me and Ar on the same side so this is the Endo and this is Exo isomer.

And activation of amino esters behaves like 1,3 dipole if you put base then this dipole will form and this dipole impact with the silver and this E, E syn dipole will form and this syn dipole then react with this different dipolarophile and to give this cycloaddition, this is also reviewed in the Chemical Reviews 2008.

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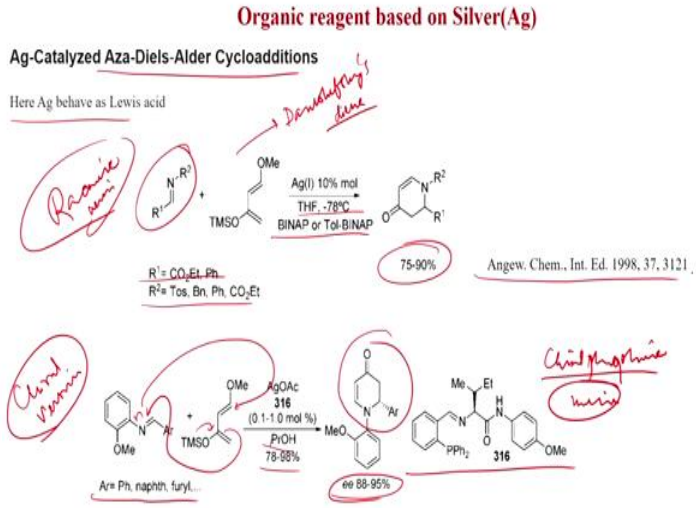

So silver catalysed Aza-Diels-Alder reaction is possible here, silver behaves as Lewis acid like here amine and this is Danishefsky diene with silver 1 10 mole percent, THF minus 78 degree centigrade BINAP or tolyl BINAP, you get this product in 75 to 90 percent yield and different groups are tolerated, R1 CO2 E2 Phenyl, R2 is equal to tosyl, benzyl, phenyl COO2Et etc.

So this is racemic version and this is chiral version, the same reaction Danishefsky diene and the imine you get this, so what happens like this way reaction happens, this will react here and this nitrogen will react here and after methanol elimination we get this double bond again. Silver acetate 0.1 to 1 mole percent isopropanol solvent you get 78 to 90 percent yield.

And enantiomeric excess is 88 to 95 percent with this chiral phosphine so chiral phosphine and amine is present. So they of course bind with silver, and silver of course coordinates with the amine nitrogen so the chiral environment is formed and that is why you get the enantiomeric excess and air can be phenyl, methyl, furyl, etc this work was published in Angew Chem 1998.

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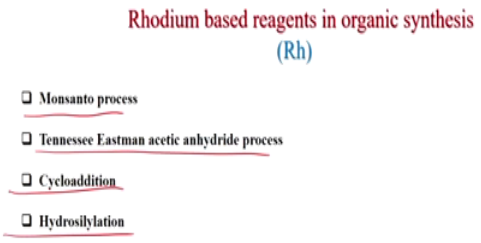

So far we have seen the silver mediated synthesis, now we will see rhodium based reagents in organic synthesis, so first we will discuss Monsanto process then Tanessee Eastman acetic anhydride process, then we will discuss cycloaddition reaction and then we will discuss hydrosilylation reaction.

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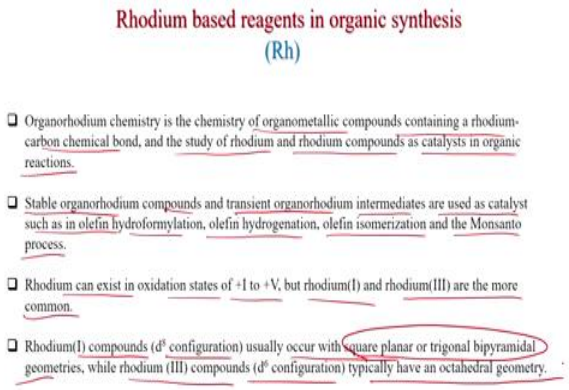

So organorhodium chemistry is the chemistry of organometallic compounds containing rhodium carbon chemical bond and the study of rhodium and rhodium compounds as catalysts in organic reactions. Stable organorhodium compounds and transient organorhodium intermediates are used as catalysts such as olefin hydroformylation, olefin hydrogenation, olefin isomerisation and the Monsanto process. Rhodium can exist in

oxidation states of plus 1 to plus 5, rhodium 1 and rhodium 3 are the more common. Rhodium 1 compound d8 configuration usually occur with square planar or trigonal bipyramidal geometry. While rhodium 3 compounds d6 configuration typically have an octahedral geometry.

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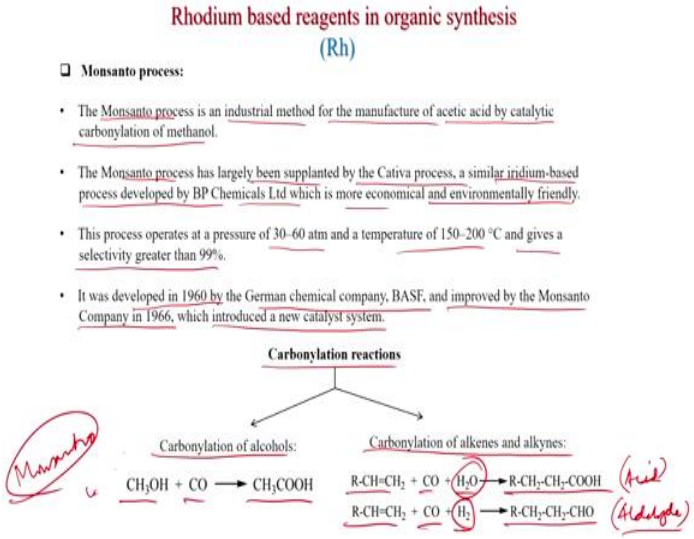

So first we will discuss Monsanto process, the Monsanto process is an industrial method for the manufacture of acetic acid by catalytic carbonylation of methanol. So this is the process for the manufacture of acetic acid for methanol, the Monsanto process has largely been supplanted by the Cativa process, a similar indium-based process developed by BP chemicals Ltd which is more economical and environmentally friendly.

This process operates at a pressure of 30 to 60 atmosphere and temperature of 150 to 200 degree centigrade and gives a selectivity greater than 99 percent. It was developed in 1960 by the German chemical company BASF and improved by the Monsanto company in 1966, which introduced a new catalyst system.

So this is the carbonylation reaction, so carbonylation of alcohol, this is the Monsanto process, methanol plus carbon monoxide you get the acetic acid. Also, olefins and alkynes can be carbonylated like here olefin used H2O you get the acid and with alkyne carbon monoxide, H2 you get the aldehyde. So when additionally, H2 is given then the aldehyde and H2O is given then you get the acid so we will discuss this reaction.

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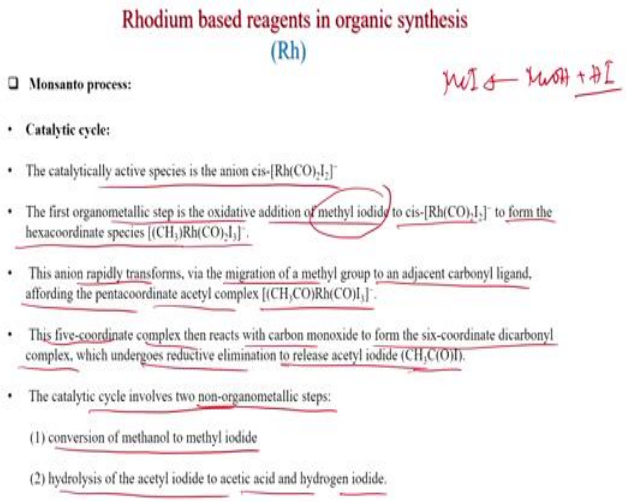

Monsanto process, catalytic cycle, the catalytically active species is the anion cis-Rh CO2I2 minus. The first organometallic step is the oxidative addition of methyl iodide that we will see. Methyl iodide this is formed from methanol plus HI, so that we will see how HI is coming. Addition of methyl iodide to cis-Rh CO2I2 minus to form the hexa coordinate species CH3 Rh CO2I3 minus.

And the anions rapidly transform via the migration of methyl group to an adjacent carbonyl group affording the pentacoordinate acetyl complex like always happens, the methyl group inserts into the metal carbon monoxide bond. This five coordinate complex then reacts with carbon monoxide to form the six coordinate di-carbonyl complex, which undergoes reductive elimination to release acetyl iodide.

And this acetyl iodide only will generate the HI, so the catalytic cycle involves two non-organometallic steps; conversion of methanol to methyl iodide, hydrolysis of the acetyl iodide to acetic acid and hydrogen iodide.

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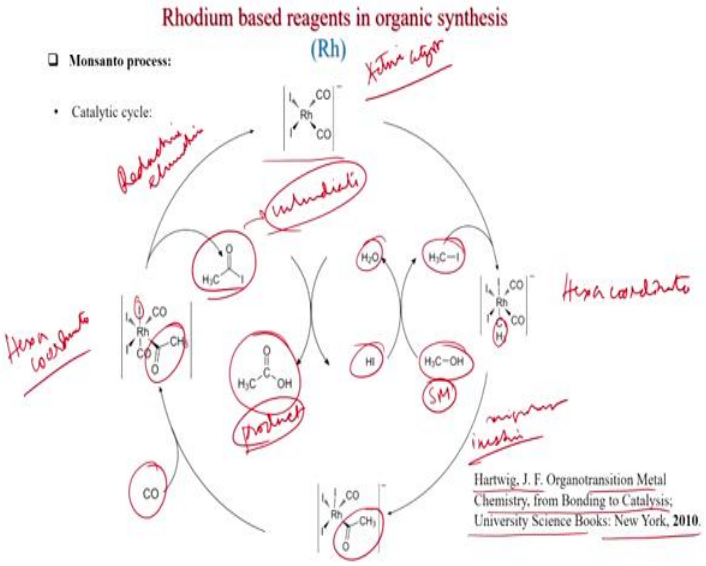

So this is the catalytic cycle, this is the active catalyst here, active catalyst (Rh Co)2 I2 minus. Here this methyl iodide will react so methyl iodide will form from methanol, HI will react to give water and methyl iodide, this methyl iodide will add here so this is CH3 group and this is I so now this is hexa-coordinate.

Now the insertion will happen, so this is the migratory insertion will happen this CH3 group inserts in this metal CO bond and you get this COCH3 group. Now again another carbon monoxide will come so again it will be hexa-coordinate so this will be again hexa-coordinate after additional carbon monoxide. And now reductive elimination will give this acetyl iodide one iodide and this acetyl group will generate acetyl iodide and this catalyst is regenerated.

Now this acetyl iodide reacts with water, so this is very important this reaction happens in presence of water so the acetyl iodide gets hydrolysed with water to generate acetic acid so this is the product and HI so this HI will generate methyl iodide after reaction with methanol. So methanol means the starting material and this is the product so you see this is reviewed by Hartwig in Organotransition Metal Chemistry from Bonding to Catalyst University Science Book New York 2010.

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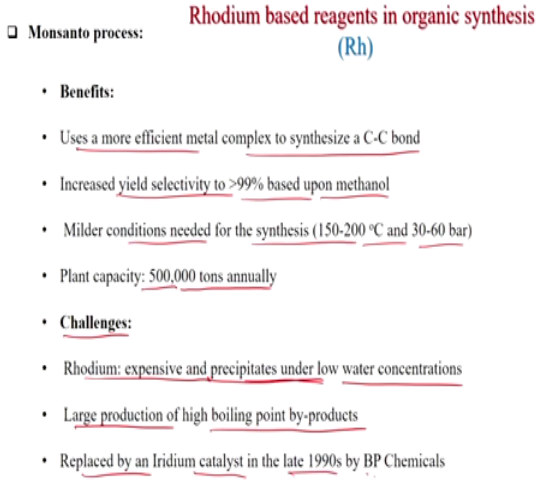

So there are some benefits of Monsanto process, uses a more efficient metal complex to synthesise a carbon-carbon bond. Increased yield is selectivity greater than 99 percent based upon methanol. Milder conditions needed for the synthesis 150 to 200 degree centigrade and 30 to 60 bar. Plant capacity 5 lakh tonnes annually. Challenges; rhodium expensive and precipitates under low water concentrations. Large production of high boiling point by-products like HI will form. Replaced by an iridium catalyst in the late 1990s by BP chemicals.

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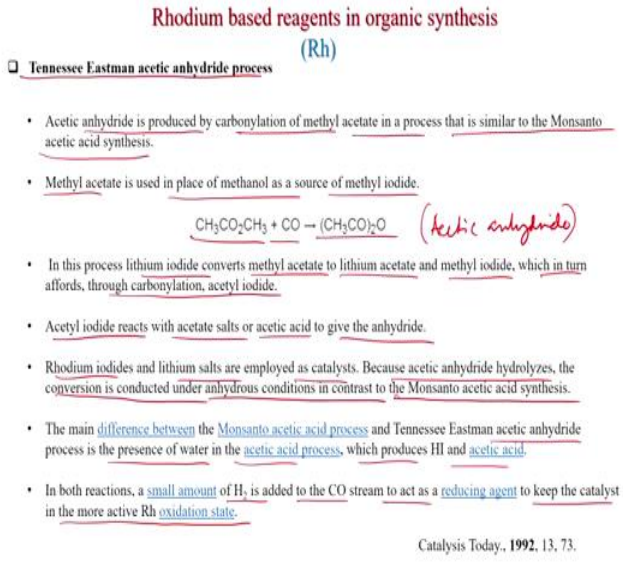

So now we will discuss Tennessee Eastman acetic anhydride process, so this process as you see this is generating acetic anhydride so this process should be done in the anhydrous

condition. So acetic anhydride is produced by carbonylation of methyl acetate in a process that is similar to the Monsanto acetic acid synthesis. Methyl acetate is used in place of methanol as a source of methyl iodide. So this is the reaction so this is methyl acetate, carbon monoxide will generate the acetic anhydride. In this process, lithium iodide converts methyl acetate to lithium acetate and methyl iodide which in turn affords through carbonylation acetyl iodide. So you are also acetyl iodide is formed, acetyl iodide reacts with acetate salt or acetic acid to give the anhydride, this is important.

Rhodium iodides and lithium salts are employed as catalyst because acetic anhydride hydrolyzes the conversion is conducted under anhydrous condition in contrast to the Monsanto acetic synthesis. The main difference between the Monsanto acetic acid process and Tennessee Eastman acetic anhydride process in the presence of water in the acetic acid process which produces HI and acetic acid.

In both reactions, small amount of H2 is added to the CO stream to act as a reducing agent to keep the catalyst in the more active rhodium oxidation state. So one difference in the Monsanto process is you have to use the water that will generate the hydrolysis of acetyl iodide to acetic acid and in this case you cannot use the water, here the acetate anion will react with acetyl iodide to generate the acetic anhydride. So this was reviewed in Catalysis Today 1992.

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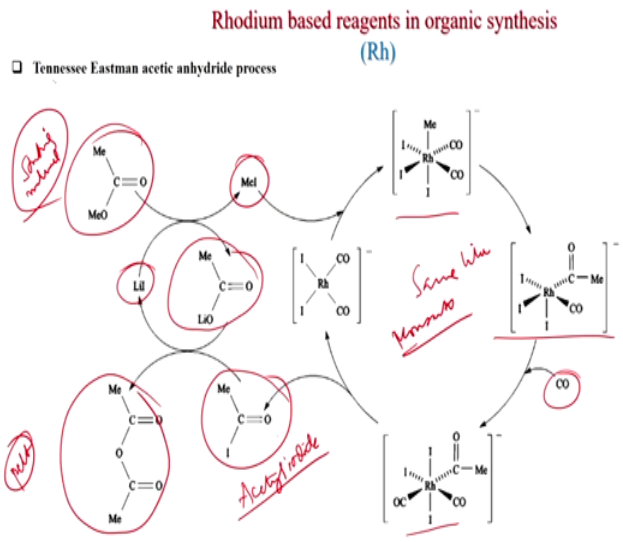

And this is the catalytic cycle if you see clearly, then this cycle is same, this is same like Monsanto. Here this is intermediate methyl hydride is coming this is happening then the

migrator insertion carbon monoxide is happening and this is also same acetyl iodide. So this is same, now here the methyl acetate will generate methyl iodide by reacting with lithium iodide. And in this way it is generate this acetic acid lithium, lithium salt and that is reacting with the acetyl iodide to generate acetic anhydride so this is the product and this is the starting material.

So earlier in the Monsanto this was getting hydrolysed to acetic acid, here it is reacting with this anion of acetic acid to generate this so that lithium iodide is forming, that lithium iodide is reacting with the methyl acetate to generate methyl iodide. So this is the Tennessee Eastman acetic anhydride process.

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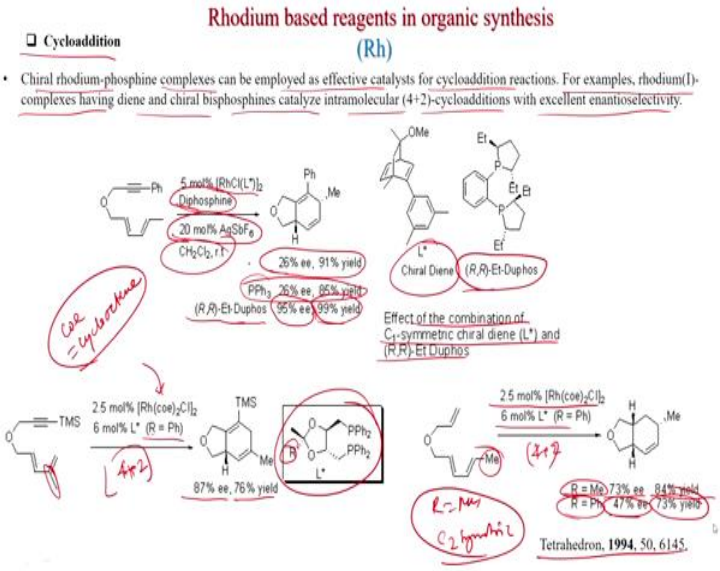

Now we will discuss cycloaddition reaction. Chiral rhodium phosphine complexes can be employed as efficient catalyst for cycloaddition reactions. For example, rhodium (I) complexes having diene and chiral biphosphine catalyse intramolecular 4+2 cycloadditions with excellent enantioselectivity. Like here this you can see this is nicely suited for 4 plus 2, there is a triple bond, there is a diene and with 5 mole percent rhodium Cl L star so L star is this chiral diene at diphosphine, this is the diphosphine like duphos this is also chiral and 20 mole percent AgSbF6, dichloromethane room temperature you get this product 26 percent in 91 percent yield without phosphine and when PPh3 is added then also same yield 26 percent ee, 85 percent yield.

So this tells that not only diene here, they use a chiral diphosphine that is why when R R Et Duphos is used this enantiomeric excess increase to 95 percent ee and you get product also

high yield 99 percent yield so both are important. COE is cyclooctene so diene is not present so phosphine is important here with 6 mole percent L L star that is R is equal to Ph so R is equal to Ph so this is almost two phosphine groups are present and this product is formed, this is also 4 plus 2 and this bicyclic compound is formed in 87 percent ee, 76 percent yield so with phoshphine ligand here is enough to give the enantiomeric excess. Here also the same catalyst so 2.5 mole percent rhodium cyclo octene whole 2 Cl whole 2, 6 mole percent L star L star R is equal to Ph that case you get the cyclisation product 4 plus 2.

And when R is equal to methyl then you get 73 percent ee, 84 percent yield, on the other hand R is equal to Ph that case you get 47 percent ee, 73 percent yield. So, what does it mean? So R is equal to methyl case R is equal to methyl then the catalyst C2 symmetric. So then C2 symmetric catalyst is giving good ee for this kind of cyclisation when there is a methyl group, this is the terminal double bond each methyl group here the internal carbon as the methyl group, so this was published in Tetrahedron 1994.

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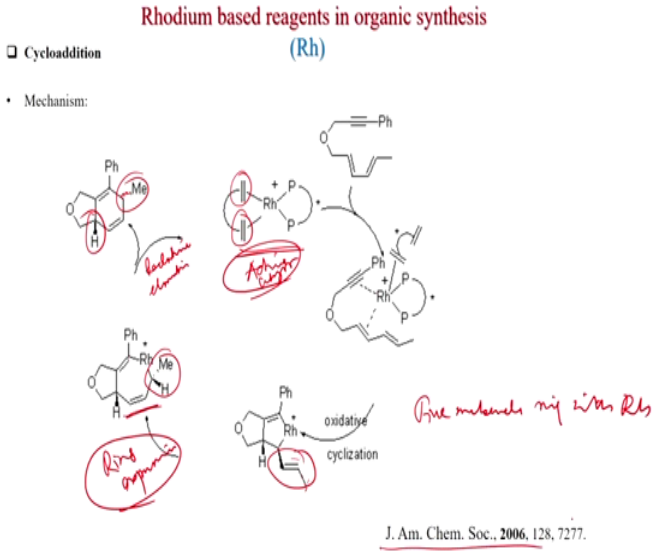

So, what is the mechanism? So here this phosphine coordinate, also this diene will coordinate with rhodium so this is the active catalyst. Now this triple bond and one double bond will coordinate with rhodium to generate this species, and now oxidative cyclisation will happen. So after oxidative cyclisation this bond will form carbon rhodium here, here also carbon rhodium so five-membered ring is formed. First five-membered ring with rhodium like this and another double bond is there of course.

And now the ring expansion will happen, here what happens, now this carbon rhodium bond breaks and it attacks here and you get this double bond is here and this is methyl group so it attacks here so generate the methyl group hydrogen selectively and now the reductive elimination will happen. So then raductive elimination you get this, this, rhodium gets eliminated and this chiral centre you get methyl is down so chiral centre is retained there and this is of course trans geometry, hydrogen and methyl are in the trans, this was published in JACS 2006.

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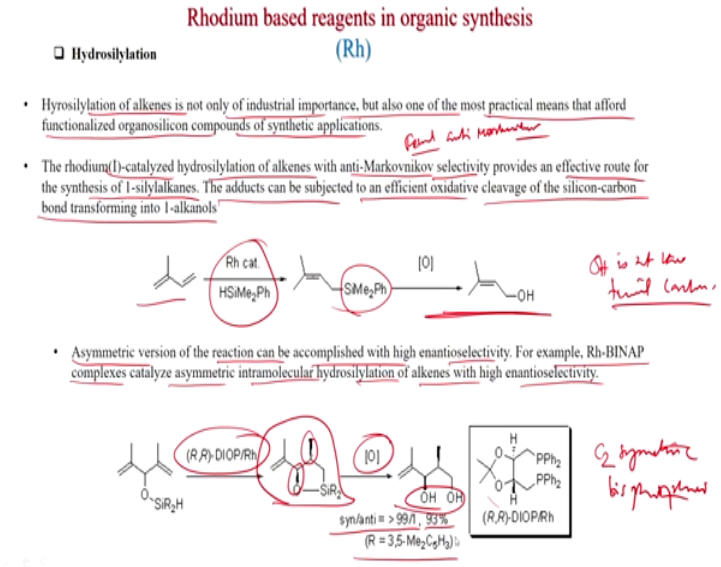

Now last reaction we will discuss hydrosilylation, hydrosilylation of alkenes is not only an of industrial importance, but also one of the most popular means that afford functionalised organosilicon compounds of synthetic applications. The rhodium (I) catalysed hydrosilylation of alkenes with anti-Markovnikov selectivity, so this is formal anti-Markovnikov like boron addition and effective route for the synthesis of 1-silylalkanes, the adducts can be subjected to an efficient oxidative cleavage of the silicon carbon bond transforming into 1 alkalnol.

So this is diene rhodium catalyst HSIMe2Ph dimethyl phenyl silyl then this SIMe2Ph group goes to terminal and this double bond we rearrange this here and after oxidation you get this. So OH is at the terminal carbon so that is the formal anti-Markovnikov additional. Asymmetric version of the reaction can be accomplished with high enantioselectivity for example, Rhodium-BINAP complexes catalyse asymmetric intramolecular hydrosilylation of alkenes with high enantioselectivity.

Like here if you use this C2 symmetric phosphine C2 symmetric bis phosphine and rhodium then this is formed intermediate. So here these two are same so this is a newly generated chiral centre and silyl takes the terminal carbon and after oxidation you get this diol. Syn anti greater than 99 is to 1, 93 percent yield and R is equal to 3,5 Me2C6H5 CH3 this R group silyl R is equal to C5Me2CH3.

So today's reaction first we have seen silver mediated cyclisation reaction, so we have seen the addition to alkenes by oxygen as well as nitrogen nuclophiles and different cyclic products have formed then we have seen the addition to allene so allene case we have seen in general the allenes in coordinates with silver at the terminal double bond and then you can get the endo-cyclisation product. Also you can get exo-cyclisation like when OCONH tosyl group is present, carbon bond motif in that case we have seen the six exo dig is forming.

Then we have seen the double bond, double bond also can be coordinated with silver and you can generate formation of tetrahydrofuran, tetrahydropyran, also pyrrolidine formation we have seen pyrrolidine, pyrroline formation with the addition of nitrogen nucleophiles to double bond. And before that we have seen the Woodward cis-hydroxylation, in the cis-hydroxylation you have to use the water acetic acid and the Prevost method that trans diol is formed that case you cannot use water, so that case the benzoate will externally do the substitution on the intermediate cyclic oxonium ion and that is why you get the trans product.

And also you have seen the silver can catalyze many cyclo addition reaction 3 plus 2 this is we have seen azomethine ylide and different dichlorophile. And also 4 plus 2 cyclo addition also we have seen that is the aza-Diels Alder reaction with Danishefsky's diene we have seen. And with rhodium catalyst we have seen the Monsanto process, this is the acetic acid preparation from methanol and carbon monoxide with rhodium catalyst. We have seen the active intermediate is acetyl iodide which is hydrolysed to acetic acid and this HI forming, HI is converting methanol to methyl iodide and methyl iodide is adding to the rhodium system. On the other hand, Tennessee system you generate the acetic anhydride form methyl acetate carbon monoxide.

Here also acetate iodide is formed but you cannot use water, here what happens the acetate, the lithium acetate that is adding to the acetyl iodide and you get this acetic anhydride and lithium iodide that lithium iodide is converting methyl acetate to methyl iodide. And then we have seen rhodium catalyse cycloaddition reaction, we have seen if there is a triple bond and

double bond also with chiral diene and chiral phosphine, you can generate the product in a symmetric way, thank you.