Reagents in Organic Synthesis
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Lecture 26 - Au Based Reagents in Organic Synthesis

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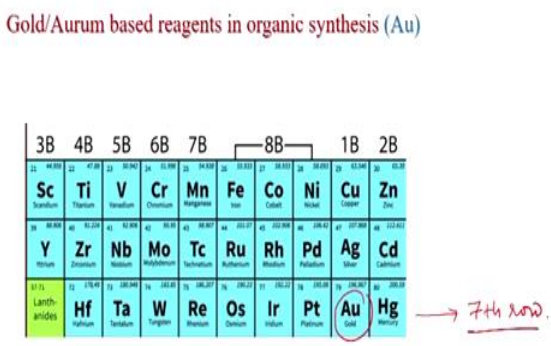

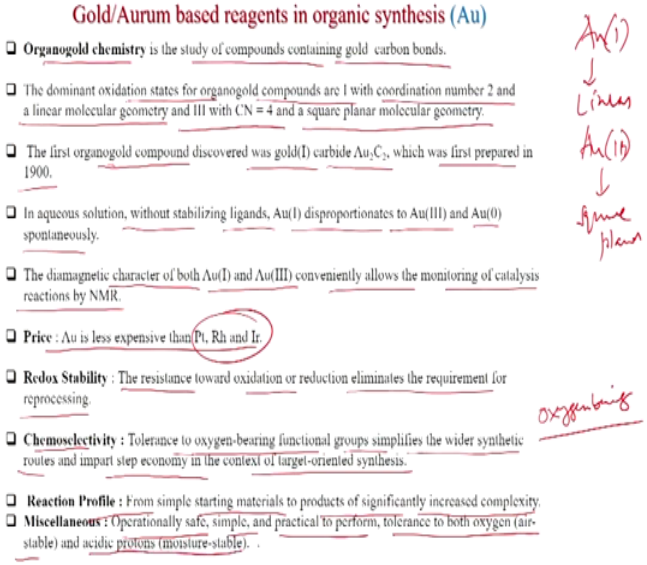

Welcome again, today we will discuss organic reagents based on gold. So as you can see, this gold is in here, it is in the same group with copper and it is in the 7th row element. So first we will discuss basic about gold chemistry. So organogold chemistry is the study of compounds containing gold carbon bonds, the dominant oxidation states for organogold compounds are one with coordination number 2 and a linear molecular geometry. So gold 1 has linear geometry, on the other hand gold 3 with coordination number 4 and square planar molecular geometry.

So gold 3 has square planar geometry. The first organogold compound discovered was gold 1 carbide Au2C2 which was first prepared in 1900 and in aqueous solution, without stabilizing ligands gold 1 disproportionate to gold 3 and gold 0spontaneously. So gold 1 will disproportionate to go 3 and gold 0 in aqueous solution. The diamagnetic character of both gold 1 and gold 3 conveniently allows the monitoring of catalysis reactions by NMR. So this is very important, gold 1 and gold 3 are diamagnetic, so you can get their study by NMR. And gold is less expensive than platinum, rhodium, iridium this is very important. Though we think that gold is expensive but it is less expensive than platinum, rhodium and iridium.

Redox stability, the resistance toward oxidation or reduction eliminates the requirement for reprocessing. Chemo selectivity, tolerance to oxygen bearing functional group simplifies the wider synthetic routes and impact step economy in the context of target oriented synthesis. So this is very important the oxygen bearing, we will see, oxygen bearing functional group it can tolerate and reaction profile from simple starting material of two products of significantly increased complexity. So this is very important, we will see that gold catalyze many tandem reaction and you can get compounds of higher complexity.

Miscellaneous; operationally safe, simple and practical to perform tolerance to both oxygen, air stable and acidic protons, that is the moisture stable. This is also very important, it is air stable as well as the acidic condition you can use.

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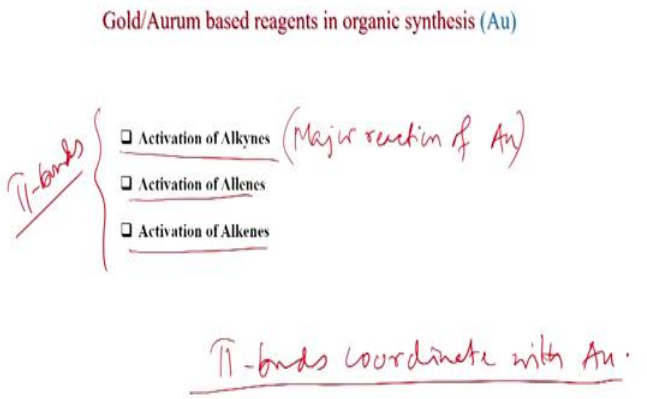

So first, we will study activation of alkynes because this is the major reactions of gold and then we will discuss activation of allenes and then we will discuss activation of alkenes. So all have, these all have pi bonds. So, what does it mean? Pi bond coordinate with gold, so that

is the major chemistry of gold that the pi bonds will coordinate with gold and that will make an electrophilic species and then defined nucleophile can react to alkanes, allenes and alkynes.

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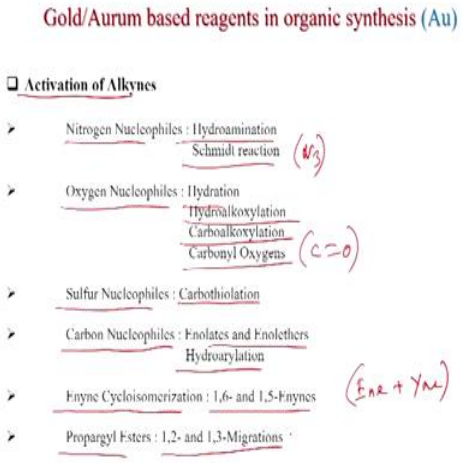

So first we will discuss activation of alkynes and here we will discuss nitrogen nuceophiles, hydroamination, then we will discuss Schmidt reaction and this is with azide. Then we will discuss oxygen nucleophiles, hydration we will discuss; hydro alkoxylation we will discuss, carboalkoxylation then carbonyl oxygen that is the CO group also participates and sulpur nucleophiles, carbothiolation we will discuss. Carbon nucleophiles also we will see, enolates and enol ethers then hydroarylation we will discuss. Enyne cycloisomerization 1, 6 and 1, 5 enynes; ene plus yne, so double bond plus triple bond is present. Then we will discuss propargyl esters and we will see 1, 2and 1, 3 migrations.

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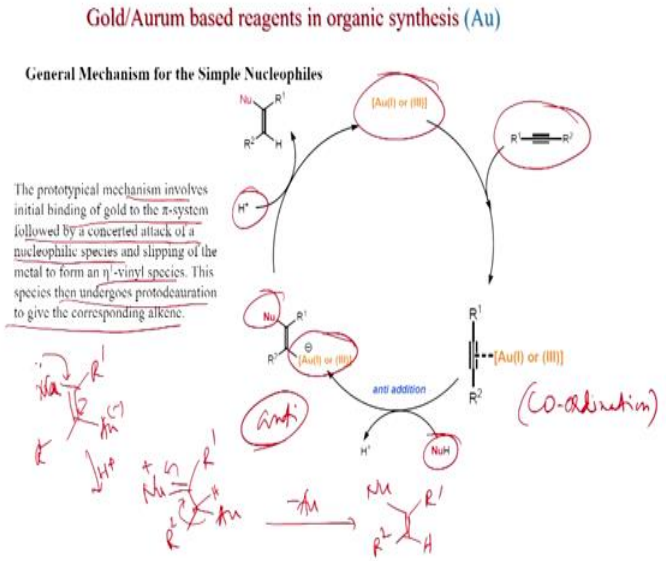

So general, what is the general mechanism for simple nucleophiles? So the prototypical mechanism involves initial binding of gold to the pi system followed by a concerted attack of a nucleophilic species. So whatever we told that gold will coordinate with the pi system and then a nucleophilic attack will happen and so like this this is gold 1 or gold 3, then here it as an alkyne and now the coordination, so this is the coordination. So, coordination of the gold to the triple bonds happens and now a nucleophillic species will attack.

So this is the nucleophillic species is attacking to the gold and this is very important, they are Anti. So nucleophile and gold will be in the anti-orientation. So that will be the selectivity also we will see and after that so it will give a pi Eta 1 vinyl species. This species then undergoes protodeauration to give the corresponding alkene. So this is the one acidic proton has to come here. So this can be thought that this nucleophile if it is oxygen or nitrogen then what happens, it can also with its lone pair, with its lone pair it make like this and here a H plus comes. So, this plus R1 R2 gold, so here this hydrogen comes and now what will happen?

This gold will eliminate, so minus gold, then you get R1 nucleophiles R2 and hydrogen, of course, the double bond is present here, so this is the mechanism that the nucleophile attacks in the are anti-orientation with the gold and after that protodeauration happens. So an acidic proton has to come and this gold eliminate.

So this is very important in the gold chemistry that gold can add and can eliminate without disturbing, so it can facilitate the reaction and then it can eliminate so easily, so you do not need any oxidant that is the fancy of the gold chemistry.

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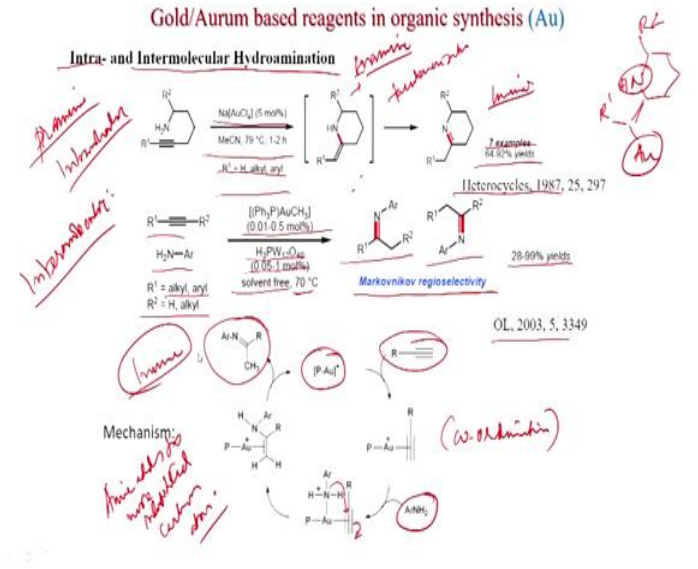

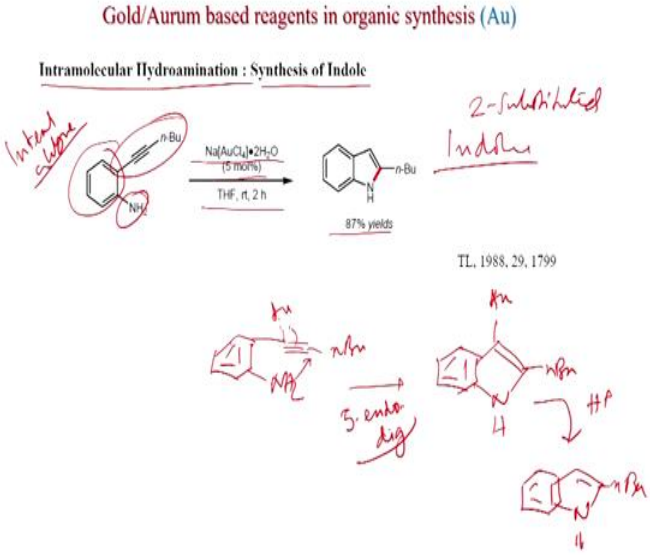

So we will see different reactions. First, we will see intra and inter molecular hydroamination, like this primary amine, so this is primary amine, an alkyne is here. Now with NaAuCl4 5 mole percent, acetonitrile solvent, 79 degrees centigrade, 1 to 2 hours and R1 can be terminal or internal alkyne, R2 is equal to hydrogen methyl alkyl.

So this can be substitution or hydrogen is possible and then you get this intermediate. So what is this? So if you see the number 1, 2, 3, 4, 5, 6, so this is 6-exo dig cyclization is happening and as I told that gold will be here, so this it would draw the intermediate with the gold, then it will be like this. So gold will be here because this is the nucleophile NaH. NaH is a nucleophile, gold will be here and after proton from the solvent this gold will eliminate and will give this enamine.

So this is enamine and after tautomerization, so this is tautomerization you get the imine. So, after tautomerization you get the imine and this reaction is quite general and you have seven examples and 64 to 92 percent yield, this was published in Heterocycles, in 1987. So this is intramolecular, this is intramolecular.

Now we will see intermolecular. So in the intermolecular there is a separate alkyne and here they have used aromatic amine R1 can be alkyl aryl R2 can be hydrogen alkyl, so with terminal alkyne also will work and with Ph3P AuCH3, 0.1 to 0.5 mole percent and H3P this is another co-catalystH3PW2O40, 0.5 to 1 mole percent. This is solvent reactions, 70 degree centigrade, you gave this imine.

2 imines can be possible but the Markwonikov's Regioselectivity will happen. So the addition will take place at the more substituted center, that we will see and this product is obtained 28 to 99 percent, research published in Organic Letters. So we will see the mechanism now. So, this is the active catalyst and now if it is terminal alkyne is there then this coordination happens first, coordination and now this amine can add to the gold first and will make a species like this and now the addition will take place.

So as you can see this addition takes place selectively higher at the more substituted. So amine adds to more substituted carbon atom because that is the Markwonikov's Rule because here the carbocationic character was denied at this carbon. So amine reacts here and gold actual gold can coordinate and gold ultimately comes here and then after this proton the elimination of gold will happen, so gold also is eliminating here. This is the active catalyst and you get this imine product.

So this is very important, the imine formation from alkynes and amine, primary amine you can with the gold you can generate the imine and the amine addition takes place at the more substituted carbon atom. Intermolecular hydroamination, synthesis of indole also is possible, like here if you see this, this is aromatic group, this is the alkyne, this is internal alkyne, internal alkyne and this is the amine with NaAuCl4 2H2O, 5 mole percent, THF room temperature 2 hours. So, you get this indole.

So this is very important product, 2-substituted indole, indole is formed in the 87 percent yield. If you see the mechanism here also, the gold will coordinate to the triple bond and now addition will take place. So, this addition will take place and gold will come of course here and you get this intermediate gold. So here you can see this is 1, 2 ,3, 4, 5; so this is 5 endo

dig-cyclisation and this process will be very facile because indole you know this is aromatic, so this process will be very facile, so you get the indole after gold elimination. This is the tertiary butyl, n-butyl, so this way you can get easily indole products.

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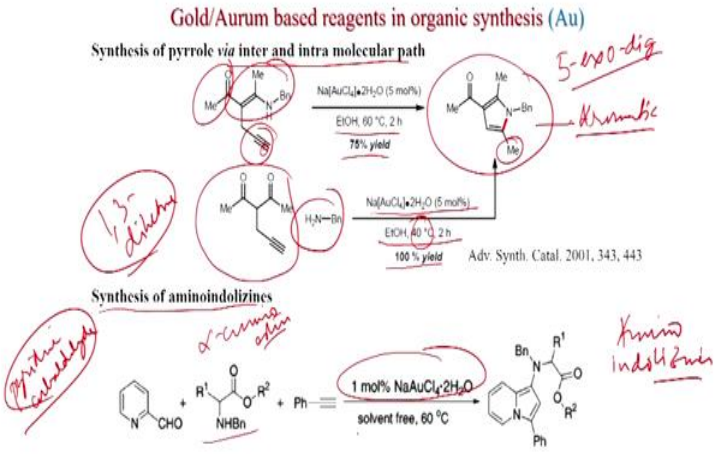

Now we will discuss synthesis of pyrrole via inter and intra molecular path, so you can see here a carbonyl group is here and this is enamine and a triple bond is present and this carbonyl group does not participate but this enamine participates. So, this nitrogen adds to this triple bond and so 1, 2, 3, 4, 5, so this is 5-exo dig cyclisation happens and you get an aromatic product. So this is aromatic, so whenever an aromatic product forms, this process would be very facile and you can see it is quite substituted, 3-substituted pyrrole is formed and ethanol solvent 75 percent yield.

Now this reaction you can also do with 1, 2 diketone. So this is 1, 3 diketone because if you mix 1, 3 diketone and benzylamine then also you get this intermediate. So this is the you do not have to preform this one, in situ we can generate this form mixing this 1, 3 diketone and benzylamine under the same condition NaAuCl4 2H2O, 5 mole percent. Here just temperature you have to decrease to 40 degree centigrade, 2 hours and you get a 100 percent yield. So this is very efficient reaction for this indole synthesis, mechanism will be similar that the gold will coordinate and as I told that the gold and the nucleophile will be in the trans-orientation and that will give the methyl group here. So this methyl is forming here actually.

So this carbon is going to a methyl group and synthesis of aminoindolizines, here also you can see this is pyridine, pyridine carbaldehyde. Similar reaction, pyridine carbaldehyde, this

is alpha-amino ester, alpha-amino ester and phenyl acetylene, you get this amino indolizines. Similar reaction and only 1 mole percent NaAuCl4 2H2O is enough to give this product. Here also solvent free condition can be used and 60 degree centigrade you will get very good yields.

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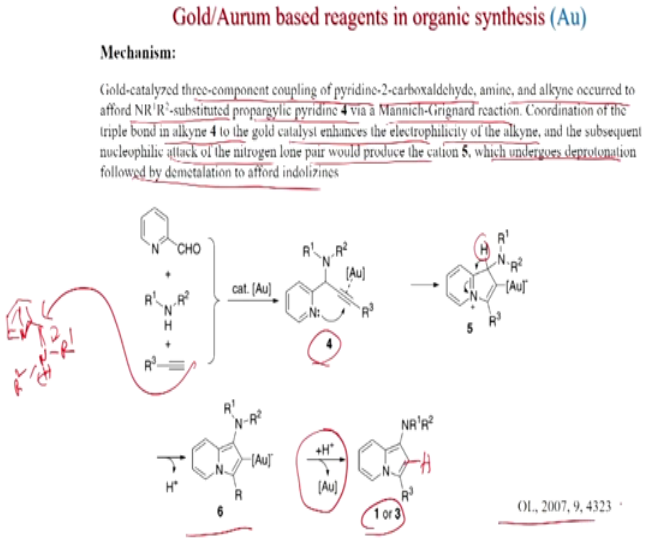

So we will see the mechanism of this reaction. So pyridine a gold-catalyzed 3 component coupling of pyridine-2-carboxaldehyde, amine and alkyne occurred to afford NR1R2 substituted propopargylic pyridine 4 via a Mannich-Grignard reaction.

So iminium is formed, so this is the iminium, CHR1R2 and you get iminium ion. So this is the iminium ion in-situ form and then the triple one ends here and after the addition you get this 4. Coordination of this triple bond in alkyne 4 to the gold catalyst enhance the electrophllicity of the alkyne and the subsequent nucleophilic attack of the nitrogen lone pair would produce the cation 5. So this anti addition takes place, after that this gets a positive charge and gold is here, R3 is here and now a deprotonation will happen which undergoes deprotonation followed by demetalation to afford indolizines.

So this proton will eliminate to generate this species and now again an H plus, so this is the removal of gold always like this. So if you have a proton then the gold will eliminate and you get this hydrogen here and these indolizines are obtained in this way, very efficient way you can get indolizines, this was published in Organic Letters, 2007.

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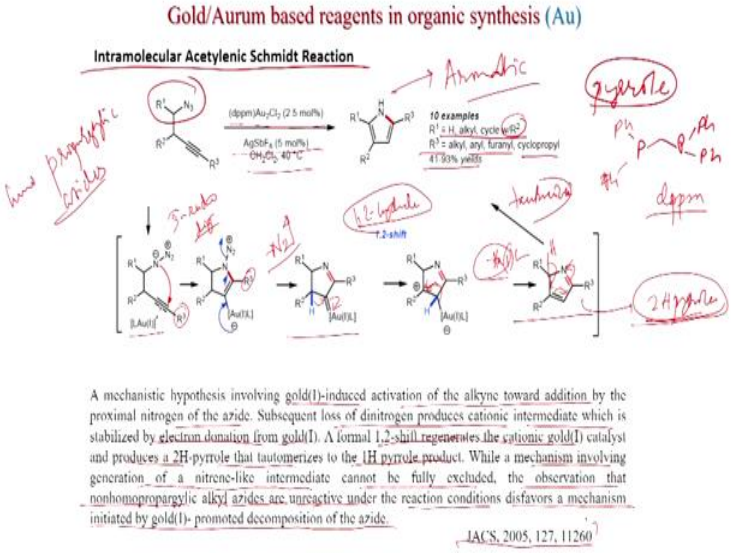

Now we will see intramolecular acetylenic Schmidt reaction. So, in the Schmidt reaction azides are used, so you can see this azide is there and alkyne is present and similarly here also you get pyrrole. So pyrroles you get here also, here also substitute pyrroles and defines functional groups, R1 can be hydrogen alkyl cyclic, R2 can be also like this a cyclic, R3 is equal to alkene and funaryl cyclopropyl, you get 41 to 93 percent yield under this condition dppm. So this is the structure of dppm.

Di-phenyl phosphinomethane and we will see the mechanism of this reaction now. This reaction is quite efficient with dppm Au2Cl2 2.5 mole percent, and AgSbF6 5 mole percent, dichloromethane 40 degrees centigrade, you can get good yields.

So what could be the mechanism? As always the triple bond will coordinate with the gold and now this N minus will attack here, so this is also 5-endo dig, so 5-endo dig cyclization will happen and so this is the newly this red is the newly generated bond and R3, and now nitrogen eliminate and this gold will, this gold lone pair will circulate like this with the elimination of nitrogen. So this process will be very fast because nitrogen gas will eliminate and you get this intermediate.

A mechanistic hypothesis, involving gold 1 induced activation of the alkyne toward addition by the proximal nitrogen of the azide subsequent loss of dinitrogen produces cationic intermediate which is stabilized by electron donation from gold. A formal 1-2 shift regenerates the cationic gold 1 catalyst and produces a 2H pyrrole, that tautomerize to the 1H pyrrole product.

So 1-2 hydrogen shift will happen, so this one will shift here. So this is 1-2 hydride shift, hydride shift and here carbocation will generate here and then this is double bond will generate, gold will eliminate, so that is the facile that the gold can eliminate so easily. After that gold will eliminate and you get this first 2H pyrrole because this is not aromatic and then the tautomerization, so this way the tautomerization will happen and you get the aromatic, this is aromatic, This was published in JACS 2005, 127, 11260.

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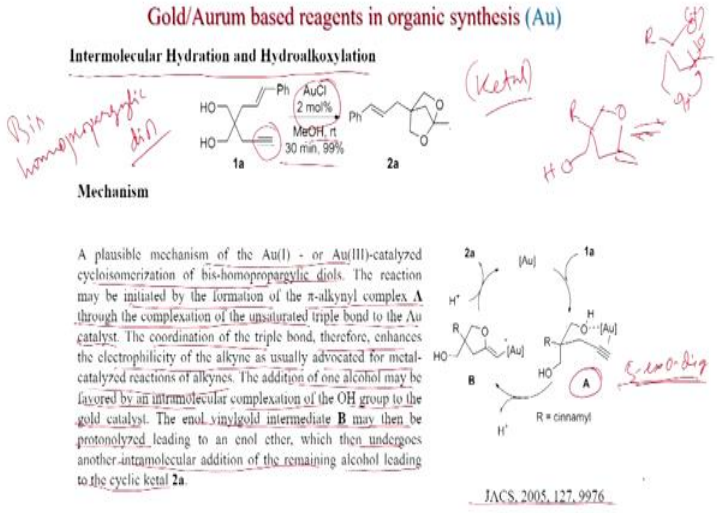

Now we will see intermolecular hydration and hydroalkoxylation. This is also important reaction because you can get ketal. So here a ketal is formed and of course these two oxygen coming from the alcohol and if you see this triple bond is reacting here and this carbon is actually here this methyl group and this double bond of course did not participate in this cyclization and with gold chloride 2 mole percent in methyl on room temperature 30 minutes you get 99 percent yield of this product.

So what would be the mechanism of this reaction? A plausible mechanism of the gold 1 or gold 3 catalyzed cycloisomerization of bis-homopropargylic diols. So this is bis-homopropargylic diol, so this is 1, 2, 3; so this is bis-homopropargylic diols. The reaction may be initiated by the formation of the pi alkynyl complex A through the complexation of the unsaturated triple bond to the gold catalyst. So this could be the intermediate, as always the triple bond coordinates to the gold and here also this alcohol can be activated by the gold. The coordinates of the triple bond therefore enhance the electrophilicity of the alkyne as usually advocate for metal catalyzed reaction of alkynes.

The addition of one alcohol may be favored by an intermolecular complexes and of the OH group to the gold catalyst. The enol vinyl gold intermediate B then be protonolyzed. So after the addition, so here you can see also 1, 2, 3, 4, 5, 5 exo dig-cyclization will happen and this intermediate will form and which then undergoes another intramolecular addition of the remaining alcohol leading to the cyclic ketal 2a.

So after this you can think that this will form R-O like this, but this will be equilibrium with the oxonium because if some acid is there then and this alcohol will add to the oxonium ion to generate the ketal. So this is very important if homopropazyllic diol is there and then the cyclic ketal formation can be done with simple gold catalyst, gold will activate the alkyne as well as the one alcohol and then the 5 exo dig-cyclization first will happen and then an oxonium of course will generate so that further the another alcohol will add to generate the ketal. This was published in JACS, 2005.

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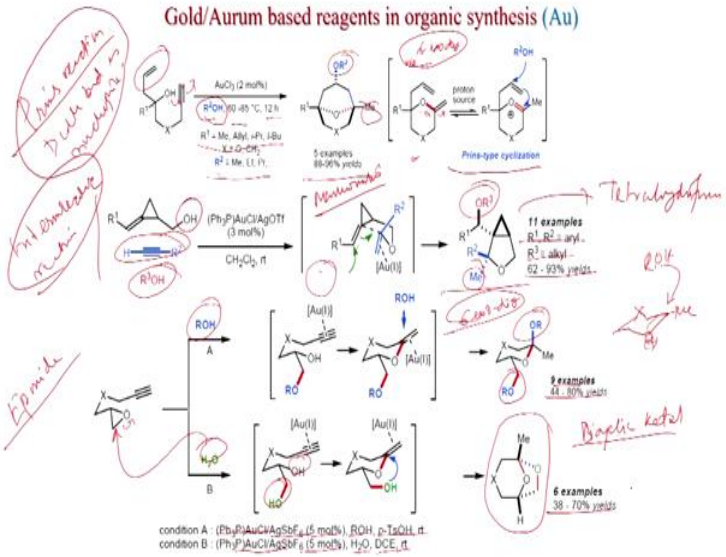

Now we will see that more alcohols reaction here you can see a double bond, already we have seen the double bond did not participate and here double bond has participated and double bond we know it can participate via Prins reaction because double bond double nucleophile then there is a possibility of Prins reaction, that is what is happening here and this is another external nucleophile alcohol gold chloride 2 mole percent, R2H 60 to 85 degrees centigrade 12 hours you get this.

So R2 is here and this oxygen is here and of course this methyl coming from this carbon and R1 can be mthyl, allyl, isopropyl, X can be oxygen CH2 here and R2 can be mthyl, ethyl,

propyl defined alcohols and five examples, it take to 96 percent yield. So what could be the mechanism of this reaction? So first this addition to the alkyne will happen, so 1, 2, 3, 4, 5, 6; so this will be 6 exo-dig. So, first 6 exo-dig will give you this intermediate after elimination of gold.

So now the second reaction is the Prins reaction. So this with photon source this oxonium ion will generate as we have seen earlier also. This enol ether will be protonated to give this oxonium ion and now this alcohol attacks to the double bond like Prins type cyclization you get here and this carbon has to here so that you get a bicyclic compound.

Now you can see three-component reaction. So this is very important, this was intramolecular, this is intermolecular and intramolecular reaction. So an alcohol is refined and alkyne is present and another alcohol, this alcohol is used for the Prins. So here after this if you mix them then you get this, so this is tetrahydrofuran, tetrahydrofuran with cyclopropyl as usual was there earlier, so it did not break.

So here what happens then, in the mechanism so here at first this OH will react here and this OH will act in the Markwonikov fashion. So this is following Markwonikov Rule as to the more substituted carbon of the alkyne that is containing R2 and now this kind of transition state has been drawn to explain the desired stereochemistry, as you can see here this OR3 group and this methyl groups are in the opposite phase.

So this kind of geometry it will orient, the alcohol will come like this and your methyl will be down. So alcohol attack will take place from the top face to generate this one and the methyl will be down and R2 will be up so that you get this. So this is the newly generated carbon-carbon bond here because R3 attacks here then this carbon attacks to here and you will get a methyl group. So this cyclopropyl carbon tetrahydrofuran are obtained in 62 to 93 percent yield and R1, R2 can be aryl, R3 can be alkyl, so generally alcohol like ethanol, methanol, propanol can be added.

Now if you have an epoxide, so this is an epoxide. So with epoxide and alkyne, so if you add alcohol, so what we know that alcohol can open an epoxide, nucleophilic opening of epoxide with alcohol as well as water can be possible and you get after opening of epoxide you get this OH and OR here. Now this OH can do the cyclization with the gold and here of course the 6 exo-dig will happen because you get a 6-member ring here and for the condition A you

have to use Ph3P gold chloride AgSbF6 5 mole percent, ROH, paratoluene sulphonic acid room temperature.

So acid is there and with acid condition you can get this, so oxonium ion will form here after gold eliminates, you get similarly this. So this oxonium ion will generate, now the OR will attack so alcohol will attack and so that you can get this kind of stereochemistry, it is from the top face and this is down face and this product is obtained 44 to 80 percent yields with 9 examples.

So now for water similar condition Ph3P gold chloride, SbF6 5 mole percent water dichloroethane room temperature. Since water is there, water also this OH also will participate, so that we will see now, see here two OH is there. So this is newly OH from the water. So water opens the epoxide and always the attack taking place for the less substituted carbon and you get this secondary alcohol OH again like this coordinates, and now earlier what happened, external ROH was attacking the oxonium ion, here this OH will attack to the oxonium ion and you get this bycyclic ketal, so this is bicyclic ketal. This is formed in 38 to 70 percent yields with 6 examples.

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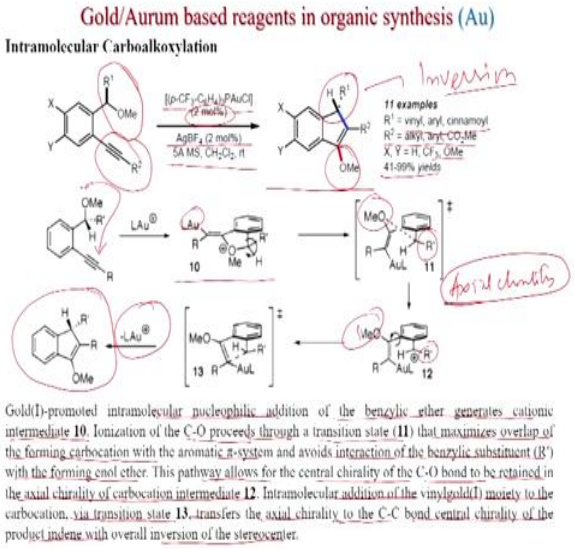

Now we will discuss intramolecular carboalkoxylation. So here if you see this ether is present here of course, this is chiral and here a triple bond is present. There are two things is happening, two important things, one is methoxy group is transferred here and another things the inversion happens. So R1 was earlier up now R1 is down, so here inversion, and here different groups can be incorporated, R1 can be vinyl, aryl, cinnamyl. R2 can be alkyl, aryl, CO2Me. X, Y can be hydrogen CF3 OMe and 41 to 99 percent yield.

And this is the catalyst P CF3 C6H4, P AuCl 2 mole percent, AgBF4 here 2 mole percent, 5 Armstrong molecular shift, dichloromethane room temperature. So what could be the mechanism for this reaction? Because the methoxy group has transferred, so what does it mean? It means the methoxy group has to coordinate to the alkyne and then that bond has to break. So that is how the methoxy can transfer. So what will happen, a gold promoted intramolecular nucleophilic addition of the benzylic ether generates cationic intermediate 10. So this is first form because methoxy attacks to alkyne, of course gold activated alkyne and you get this the trans L Au and O methoxy add in the trans fashion.

Now ionisation there is a positive charge with oxygen now, ionisation of the CO passes through the transition state 11, that maximizes overlap of the following carbo cation with the aromatic pi system and avoids interaction of the benzylic substituent R1 with the forming enol ether. So after this methoxy transfer to the double bond and here carbocation will form and this carbocation will stay in such a way that this R dash and methoxy will be in the further, will stay further so that minimum interaction will happen.

This pathway allows for the center chirality of the CO bond to be retained in the axial chirality of the carbocation intermediate 12. So here this axial chirality will stay of this carbocation because it can stay in a particular orientation. So this is the carbocation and this is 13, so intramolecular addition of the vinyl gold moiety to the carbocation via transitition 13 transfers that axial chiralty to the C-C bond's center chirality of the product indene with overall inversion of the center and now this will attack here, this carbon with having the gold will attack here and after gold elimination you get this indene.

So here this R dash is down so that minimum interaction with this methoxy group and R dash will be there and ultimately you get an inversion. So this is very important process that the methoxy group transferred as well as the inversion of the chiral center and this was published in JACS, 2006.

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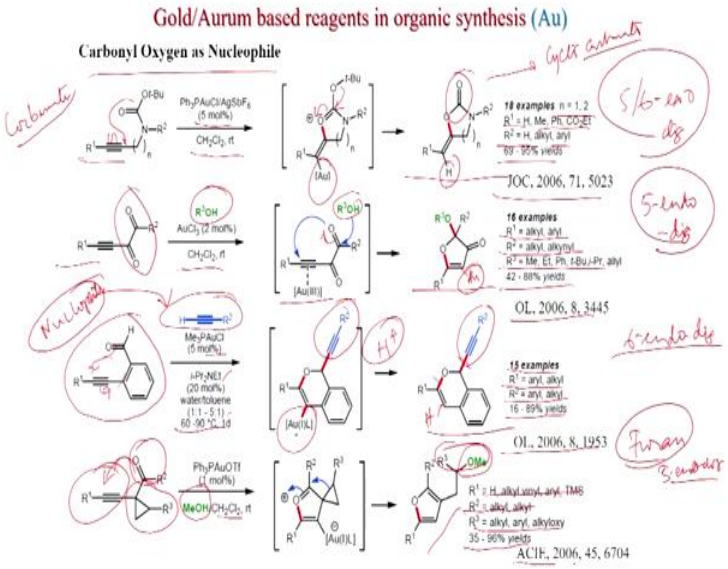

So far we have discussed the oxygen as the nucleophile. Now we will see carbonyl oxygen. So this is also possible. Carbonyl oxygen has nucleophile. Suppose if you see here a carbamate moiety is there. So this is carbamate and a triple bond is present and you get this one. So this is addition is happening here, if you see 1, 2, 3, 4, 5; so this is 5 or 6 depending on a, so this is the exo-dig cyclization. 5 or 6 exo-dig cyclization with Ph3PAuClAgSbF6 5 mole percent, dichlomethane room temperature, you get this cyclic carbamate. So these are cyclic carbamate.

And n can be 1, 2; R1 can be hydrogen that is the terminal alkyne methyl PhCo2Et. R2 can be hydrogen alkyl aryl and you get 69 to 95 percent yield. So what could be the mechanism? The mechanism is like this: So this carbonyl adds to here and generate the exocyclic olefin and this gold will eliminate by a proton. So the proton comes here. And this also will eliminate, so you get a carbonyl here. So this O tertiary butyl will eliminate, so you get a carbonyl. This was published in JOC, 2006.

Another reaction, if you have a triple bond and diketone motif, of course you have to add additional alcohol with gold chloride 2 mole percent, dichlomethane you get this. 5-membered ring is formed. As you can see, red are newly generated bonds, so there are two carbon-oxygen bonds are formed. And R1 can be alkyl aryl, R2 can be alkyl alkenyl, R3 is equal to methyl ethyl phenyl tertiary butyl, isopropyl ally and the products are formed in 42 to 88 percent yield.

So what could be the mechanism? Here also the triple bond is activated by gold 3 here. And now this alcohol will attack to this carbonyl specially so that there is the possibility of the 5-membered ring. So this alcohol reacts, now this oxygen attacks to here in the 5-endo dig. So 5-endo dig cyclization happens and gold of course will be here. And after elimination of gold you get this compound. And the products are formed in 42 to 88 percent yield. This was published in Organic Letters, 2006. There is another reaction, so here this is very important. There is two alkyne, one molecule has an aldehyde group. So this aromatic group attached to the alkyne, and externally another alkyne which has a nucleophile.

So this is actually nucleophile. So gold does not bind with sheets, it is just nucleophile. Gold binds here and with dimethyl phosphine AuCl 5 mole percent, diisopropyl ethyl amine 20 mole percent, water toluene 1 is to 1 to 5 is to 1, 60 to 90 degree centigrade. One day you get this product. So 6-member ring is formed and here also 6 endo cyclization happens, 6 endo-dig happen and this is the external alkyne and this red are two newly generated bonds, one is carbon oxygen, another are the C-C bond and these products are formed in good yields 16 to 89 percent yield, R1 can be aryl alkyl, R2 can be aryl alkyl and this is the intermediate, so this aldehyde will attack here and of course oxonium will generate here and that will react with this alkyne, so the oxonium become single one now and this gold will eliminate with H plus, you get a H here and the desired products are obtained in very good yield. So this was published in Organic Letters, 2006.

Another reaction if you see this one, this is a cyclopropyl group is present, a carbonyl group is there, alkyne group is present and methanol is there externally, so methanol has a nucleophile and with Ph3P AuO trifltate 1 mole percent methanol diclomethane room temperature you get this, so this is furan.

Furan is formed with R1 substituent, R2 substituent and here methoxy group is present and what could be the mechanism? So this carbonyl co-ordinates here, so this is also 5 endo-dig, so 5 endo-dig cyclization gives this oxygen gold around the opposite side, and now this cyclopropyl group because oxonium will generate after the carbonyl attacks to the triple bond.

So what happens? This becomes earlier we have seen here also, you have seen alcohol came here alkyne came and here this cyclopropyl group is present. So the cyclopropyl open because this is with the molecule itself. So because this is hindered so the cyclopropyl group

open and it will react here so that the carbocation will generate here and that one will give will react with methanol to generate this product and R1 can be hydrogen alkyl, vinyl aryl TMS, R2 can be alkyl, R3 can be alkyl aryl alkoxy; the products are obtained 35 to 96 percent yield and this was published in Angewandte Chemie, 2006.

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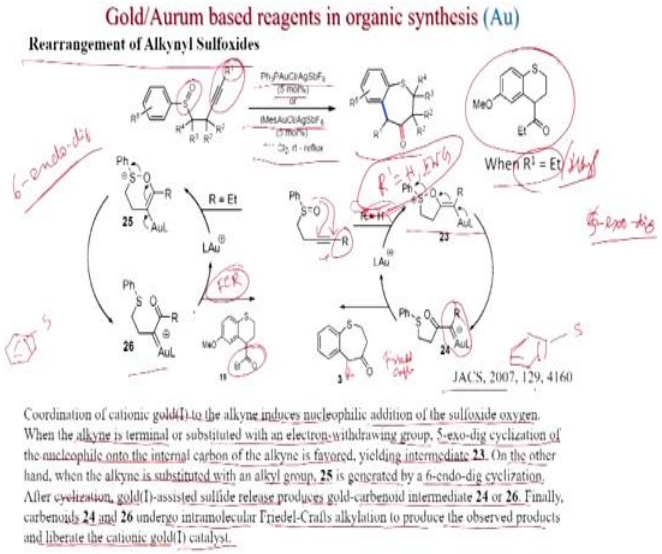

Now we will see rearrangement of alkynyl sulfoxides, so you can see there is a sulfoxide and alkyne motif and now with Ph3P AuClAgSbF6 5 mole percent or imidazole MesAuCl that is the heterocyclic carbon and SbF6 5 mole percent dichloromethane room temperature to deflux you can get the 7-member ring, all these 6-membered. So when R1 is equal to ethyl, so this is the R1, if R1 is equal to ethyl or alkyl then you get the 6-membered and if R1 is equal to hydrogen or electron donating group EWG, then you get this 7-membered ring.

So what could be the mechanism? So there is certain factors that is governing the formation of 6 or 7 member ring, so that we will see now. So if R is equal to hydrogen, here you can see R is equal to hydrogen then this oxygen is attacking here, so 5-5 exo-dig, 5 exo-dig is happening here and you get this 5-membered ring and now this double bond will go here. The double bond will make a carbonyl and this will form, so this is the mechanism that the coordination of cationic gold 1 to the alkyne induces nucleophilic addition of the sulphoxide oxygen. When the alkyne is terminal or substituted with an electron withdrawing group 5-exo-dig cyclization of the neucleophile onto the terminal carbon of the alkyne is favoured, yielding intermediate 23.

So this is formed, this is 5 exo-dig cyclization, so this is Friedel–Crafts reaction because Ph you can draw like this is S Ph and now this carbon will react to here and you get this. So this R is equal to hydrogen that is why R was not shown here, so this is actually R should be here and you get a 7-member ring. On the otherhand if R is equal to ethyl so then what will happen? Then this will happen that the 6-endo-dig, so earlier was 5 exo-dig, so on the other hand when the alkyne is substituted with an alkyl group 25 is generated by 6 endo-dig cyclization. After cyclization gold 1 assisted sulfide release produces gold carbenoid intermediate 24 or 66.

So after that similarly the sulphur oxygen bond will cleave and you get this and now again you have a, if you draw the SPh you can draw like this, so the Friedel–Crafts reaction will happen at this carbon, so this is Friedel–Crafts reaction and here in this case this ketone is outside, so here you get Friedel–Crafts product, so 6-membered ring is formed. Finally carbon has 24 and 26 undergoes intramolecular Friedel–Crafts alkylation to produce the oxa-products and liberate the cationic gold catalyst.

Depending on the substituent on the alkyne either 6-member or 7-member ring can be found, so for 6-membered you have to use alkyl group and 7-member you can use terminal hydrogen or electron withdrawing groups so that the exo-cyclization will happen because then the electron pulling will be there, if R is equal to hydrogen because that will stabilize this one the negative charge which is happening at the carbon connected to the gold because with electron withdrawing group that 5 exo-dig cyclization will be facile. This was published in JACS, 2007.

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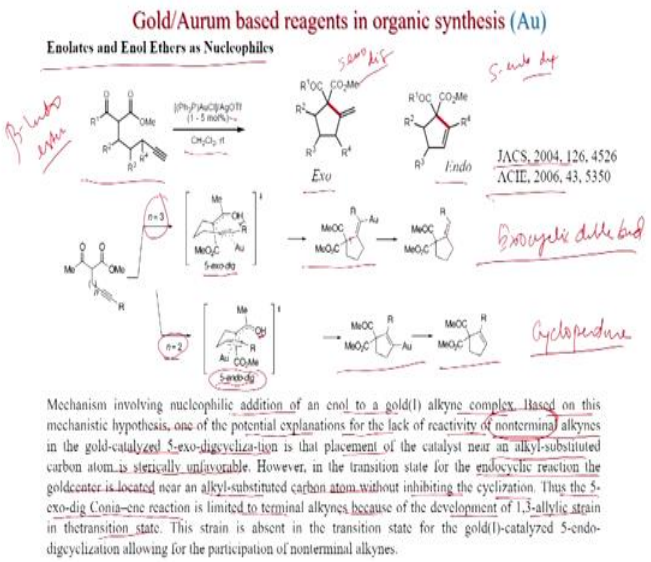

Now we will see enolates and enol ethers as nucleophile, you can see this is beta-keto ester and with the alkyne and this is the catalyst Ph3P AuClAgO trifltate 1 to 5 mole percent dichloromethane room temperature, you can get these exo-endo-products. So this is exo, this is endo, in exo like earlier we have seen the exo-dig cyclization happens. So this is 5 exo-dig 5 exo-dig and this is 5 endo-dig and these are the journals which publish this work.

So we will see the mechanism now, so depending on the n, n is equal to 3 you will see n is equal to 3 then the R is important, so mechanism involving nucleophilic addition of enol to a gold alkyne complex based on this mechanistic hypothesis, one of the potential explanation for the lack of reactivity of non-terminal alkynes in the gold catalysed 5 exo-dig cyclization, so non-terminal alkyne will not react in the 5 exo-dig cyclization.

Is there the placement of the catalyst near an alkyl substituted carbon atom sterically unfavourable? So after 5-dig cyclization this intermediate will form because the this will stay as a enol and this O it will interact with R and that is why this 5 exo-dig cyclization only will happen when R is equal to hydrogen and after this 5 exo-dig cyclization you get this and you can see neucleophile is here added and gold is opposite side so that this olefin will be cis to this CO2Me and group after elimination of gold.

Now on the other hand if n is equal to 2, then you can get 5-endo-dig cyclization and here in the transition state for the endocyclic reaction the gold center is located near an alkyl substituted carbon atom without inhibiting the cyclization.

So in the 5 endo-dig case there is no problem because the gold is coordinated to the other face and OH is here, so there is not any steric interaction. So here the non-terminal alkynes can be incorporated for this 5 endodig cyclization then you get these and after elimination of gold you get this, so cyclopentane is formed here and here the exocyclic bond is there, exocyclic double bond.

If depending on the cyclization is happening that the 5 exodig cyclization if you have a R group then this R group, then it face the steric interaction. So only with terminal alkynes you get the 5 exodig cyclization but 5 endodig cyclization it can work both with terminal as well as non-terminal alkynes.

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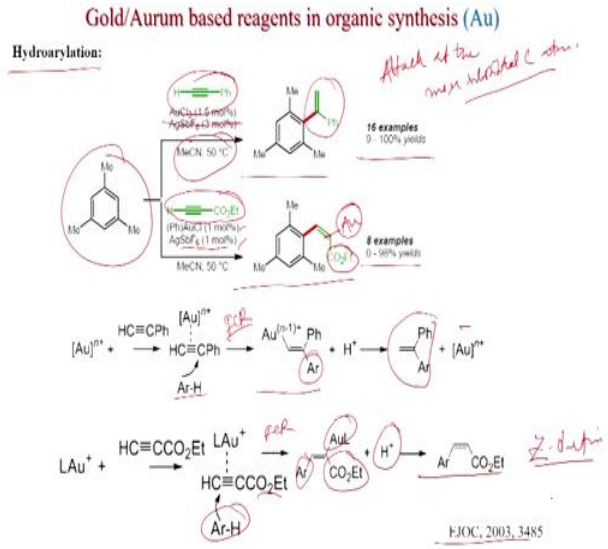

Now we will discuss hydroarylation, so you can see this is mesitylene and with phenyl acetylene you can get this kind of product, of course the attack takes place the more substitutes were attacked at the more substituted carbon atom and you get this with AuCl3 1.5 mole percent, AgSbF6 3 mole percent, you get this product and 9 to 100 percent yield with acetonitrile 50 degree centigrade. On the other hand if you have a electron deficient, electron deficient is there, so this is ethyl propylgyl and with PhAuCl 1 mole percent, AgSbF6 1 mole percent you get this. So what does it mean? Because gold is here so that is the intermediate gold was here, that is why this kind of geometry is formed.

And here this is also following the Markownikov addition because here the most substitute is happening but here the electron that is the electron reach carbon atom will have the ester group, because the ester is electron withdrawing so this carbon will be electron negative and that will be stabilized by CO2 Et group and this also obtained in 0 to 98 percent yields with 8 example.

So this is the mechanism that the phenyl acetylene coordinates with the gold and then the aryl Friedel–Crafts reaction, so this is Friedel–Crafts reaction happens and you get this, the more substituted carbon atom reacts because the gold for the Ph case this will be the less substituted, so here the negative charge will be stabilized and after protonization you can get this gold is eliminated and in this case ethyl propygylate you get this coordination and here the Friedel–Crafts reaction reaction will happen to this carbon because the negative charge of

course will be stablized by CO2 Et group because here a negative charge is present that is stabilized by CO2 Et group and after acidic workup you get this.

So this is the Z-olefin because the Ar and gold are always opposite, so nucleophile and gold are always opposite and that determines the, that determines the stereo selectivity of the olefin, so here Z olefin is formed, this was published in European JOC, 2003.

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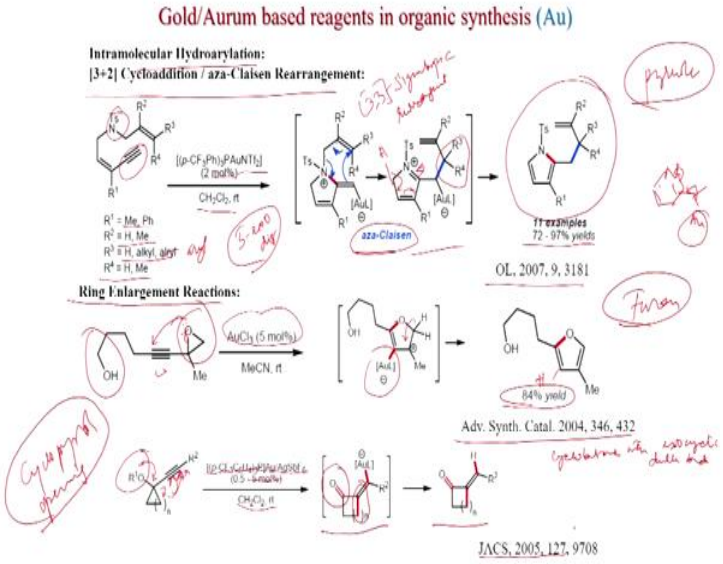

Now we will discuss intramolecular hydroarylation 3 plus 2 cyclo addition aza-Claisen rearrangement, so you can see here a triple bond is present, triple bond, double bond and inter cell group is there and with this one, P CF3Ph3PAuNTf2 2 mole percent, dichloromethane room temperature you get this. So this is of course pyrrole and the substitutions are there and R1 can be methyl Ph, R2 can be hydrogen methyl, R3 can be hydrogen alkyl aryl, R4 can be so this is arryl. R4 can be hydrogen methyl and these products are formed 70 to 97 percent yield, 11 examples.

So what could be the mechanism? So as you know, N-tosyl is a nucleophile here. So N-tosyl will react first here. So this is 5 exo-dig, so for terminal case you can get the 5 exo-dig and 5 exo-dig forms and this N-tosyl carbon nitrogen bond and gold are in the opposite side and after that as a aza-Claisen rearrangement is there because you can see this is nicely fitted 1 2, 3; 1, 2, 3, so 3-3 atoms are present. So that is suitable for the rearrangement, this is the aza-Claisen rearrangement, 3-3 sigmatropic rearrangement.

So this is 3-3 sigmatropic rearrangement and after the rearrangement you get the iminium ion iminium ion and the double bond is found here and R3, R4 is here, quaternary center newly

generated and what will happen? Now hydrogen will be eliminated from here. So you get like this, aromatization and after removal of gold because gold can, now we will see ring enlargement reactions. So here epoxide is there, the epoxide can be opened, so earlier we have seen the epoxide can be opened with external alcohol but here the epoxide is opening itself because the triple one is activated by the gold 3, 5 mole percent, so it is activated and that is why it is neighboring. So what will happen?

This oxygen of course will attack and you get a furan, so this hydroxyl group is not participating, here you get the furan. So what could be the mechanism? So this could be the mechanism after opening. So this opens like this, this oxygen attacks here. So like this you get this carbocation form here and here is the gold. So this is the newly generated bond, oxygen carbon bond is formed, this also newly generated carbon gold and now like earlier the aromatization will take place like this. The H plus will eliminate and H plus will add here, this is the hydrogen is coming from the H plus and a gold elimination you get this product in 84 percent, this was published in Advanced Synthesis Catalysis, 2004.

This is another opening, you have a cyclopropyl group and ether and alkyne is here. So what will happen? Here the cyclopropyl opening is happened, propyl opening because whenever cyclopropyl is connected to ether this is pulling electron pulling electrons. So this will react and that is what is happening. So this is reacting here, here interestingly depending on the N so N can be 1 in cyclopropyl N is 2 is equal to cyclobutyl.

You can get this kind of ring and the carbonyl group is formed here, that is the newly generated from this ether and this is the newly generated bond is formed and gold is here and now after elimination you get this exocyclic olefin and the carbonyl and this is the catalyst P CF3C6H4 3PA Gold AgSbF6 0.5 to 5 mole percent dichloromethane room temperature. You can get this product, so this is cyclobutanone, cyclobutanone with exocyclic double bond. This was published in JACS, 2005.

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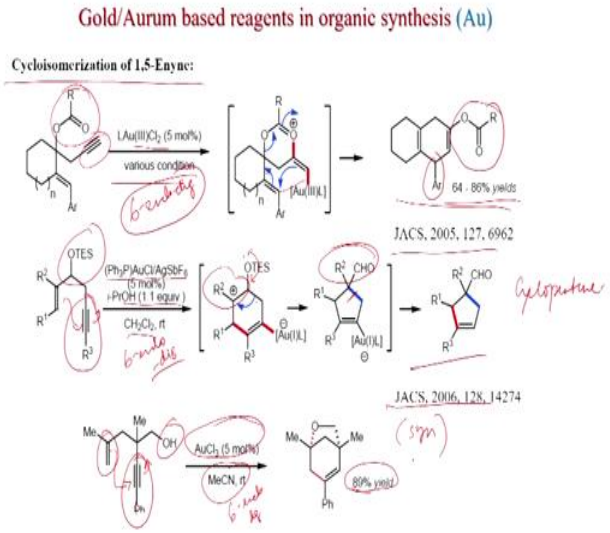

Now we will discuss cycloisomerization of 1, 5-Enyne, you can see here a double bond is present, here a triple bond and here an ester with gold 3 chloride 5 mole percent, various conditions you get this bicyclic compound. So one more cycle has been formed and this product is found in 64 to 86 percent yield. So what could be the mechanism? So here also this will attack first to the terminal double bond and here the 6 endo-dig will happen, 6 endo-dig will give this intermediate, oxonium ion is here and now if you see there will be many reaction because this oxonium ion is pulling the electron, so all electrons will go to that direction. So this is negative charge. This will first attack here, then the double bond will migrate here and this will open and ultimately Ar is here.

So if you see this is the Ar and now this new bond formed and of course gold will eliminate keeping the double bond here and this become COO, so OCOR will form. This was published in JACS, 2005.

If we have a OTS group that also can participate, so we will see now here with a double bond and a triple bond with Ph3PAuClAgSbF6 5 mole percent, isopropanol 1.1 equivalent dichloromethane room temperature you get this cyclopentene. So this could be the mechanism, so double bond reacts here, so 6 endo-dig then you get a carbocation here and now this carbocation because this CS is there so it will push the electrons. So this bond will cleaved, this bond will cleaved and this will ultimately go to aldehyde having a quaternary center. So this is the newly-bond formed and gold will eliminate to give the double bond here, This was published in JACS, 2006.

Now if you have a alcohol, a double bond, a triple bond, this is Ph then also the reaction will happen with gold chloride 5 mole percent acetonitrile room temperature, you get this. So what happens? Here also similarly, this will attack here, here, so 1, 2, 3, 4, 5, 6, 6 endo-dig, 6 endo-dig cyclization will give a carbocation and that carbocation so this carbocation will form, before this the carbocation that then the alcohol reacts and if it is down then it is down face attack. So this is the syn orientation because if it is down then it will attack from the down phase to give this compound in this geometry and you can get up to 89 percent yield.

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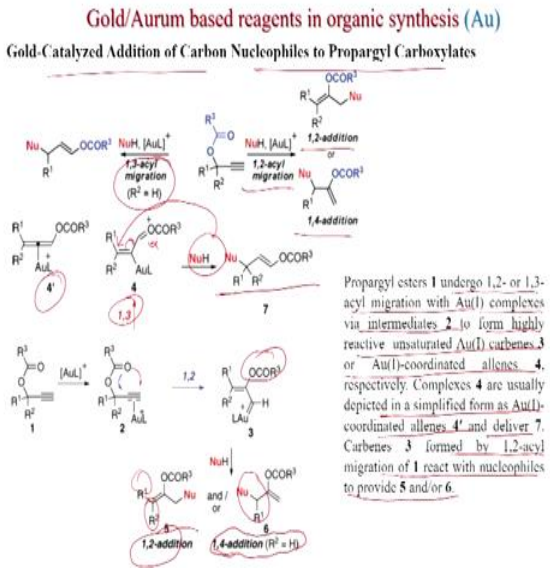

Gold-catalyzed addition of carbon nucleophile to propargyl carboxylate also is possible like this, OCOR3 with nucleophile, you can get 1, 2 addition or 1, 4 addition via 1, 2 acyl migration. On the other hand 1, 3 acyl migration is possible also with nucleophile, gold you can get this. So what could be the mechanism here? So propargylic ester 1 undergo 1, 2 or 1, 3 acyl migration with gold 1 complexes via intermediates 2 to form highly reactive unsaturated gold 1 carbenes 3 or gold 1 coordinated allenes 4 respectively. So either this 1, 2 acyl migration if you see the migration is happening here at this center. So this has opened or 1, 3 for 1, 3 again you can get this 4 which isomerizes to 4 dash actually.

Usually depicted in a simplified form as gold coordinates allens 4 dash and will deliver 7 so, so this will give 7 after nucleophile adds to this. So nucleophile add here, so nucleophile add here and then you get this compound and now this carbene 3 formed by 1, 2 acyl migration of 1 react with nucleophiles to provide 5, 6. So here either 1, 2 addition can be possible, the nucleophile add here. On the otherhand nucleophile can attack here and then the double bond will migrate, so 1, 2, 4 addition also possible and when R2 is equal to hydrogen then that

means this is not sterically hindered because one side of the double bond is open and when both are substituted then this 1, 2 addition is facile.

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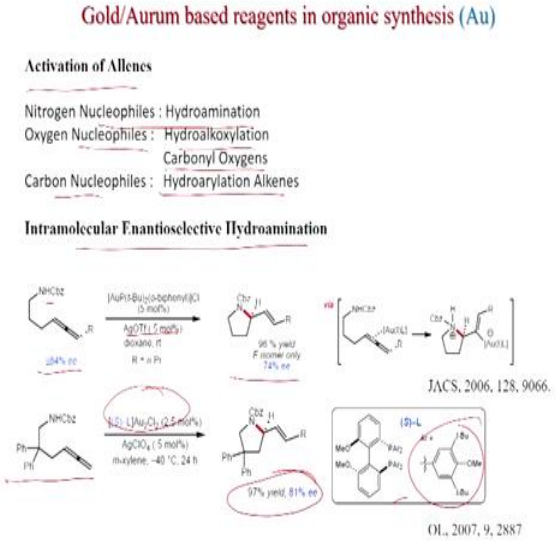

Now we will discuss activation of allenes, nitrogen nucleophile hydroamination, oxygen nucleophiles, hydroalkoxylation, carbonyl oxygens, carbon nucleophiles, hydroarlylation of alkenes, intramolecular enantioselective hydroamination. So this is NHCbz, this is chiral allene with this gold catalyst sliver triflate, you get this product in 74 percent yield. This is the mechanism, similar like alkyne you can also here the activate the allene and you can get this intermediate and after elimination of gold you can get the double bond.

Now with chiral catalyst also you can get, so this is the bisphosphine catalyst with Ar this, you can get the product up to 81 percent ee and 97 percent yield and this was published in Organic Letters, 2007.

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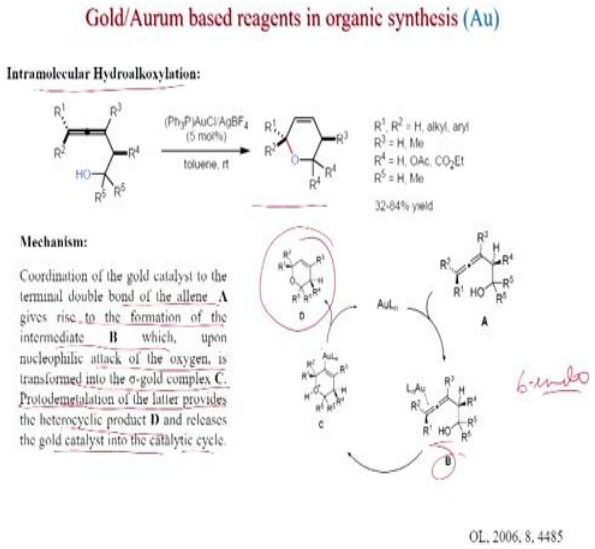

Now intramolecular version is there, intamolecular hydro alkoxylation is possible here, allene OH is there, you can get this 6-membered ring and this could be the mechanism that the allene first co-ordinates with the gold and OH will attack, OH will attack so that 6, 6 endo cyclization happening to get this one and after elimination of gold you get this. So gold catalyst to the terminal double bond of the allene A gives rise to the formation of the intermediate B which upon nucleophilic attack of the oxygen is transferred to the sigma gold complex C. Proto demetalation of the latter provides the heterocyclic product D and releases the gold catalyst into the catalytic cycle. This was published in Organic Letters.

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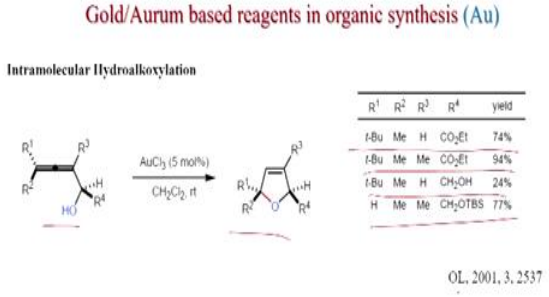

And 5-member ring can be also formed here, you can see these different groups can be tolerated, you can get the products in good to moderate yields, This was published in Organic Letters, 2001.

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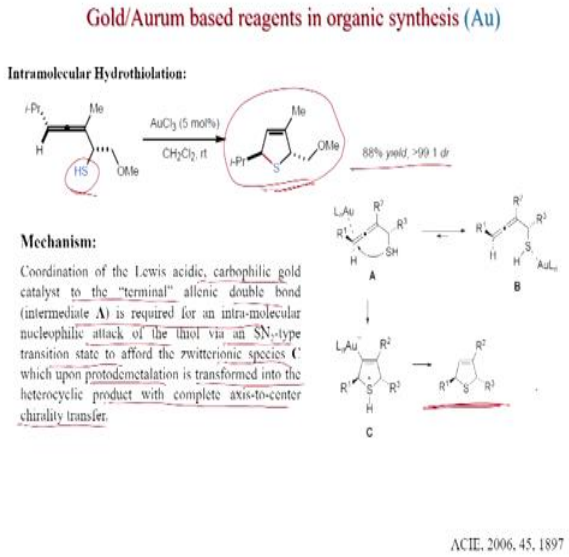

Now we will discuss this one, if you have a thiol then also this cyclization will happen and you can see the chiral product is formed with 88 percent yield greater than 99 is to 1 Dr, so here also the mechanism will be like similar coordinates of the Lewis acidic, carbophilic gold catalyst to the terminal allene double bond intermediate A is required for an intramolecular nucleophilic attack via a SN2 type transition state to afford the zwitter ionic species C.

So this is formed after attack which upon protodemetalation is transformed into the heterocyclic compound product with complete axis-to-centre chirality transfer. So this is formed and this is very important the chirality is transferred to the product as you can see and this was published in Angewandte Chemie International Edition, 2006.

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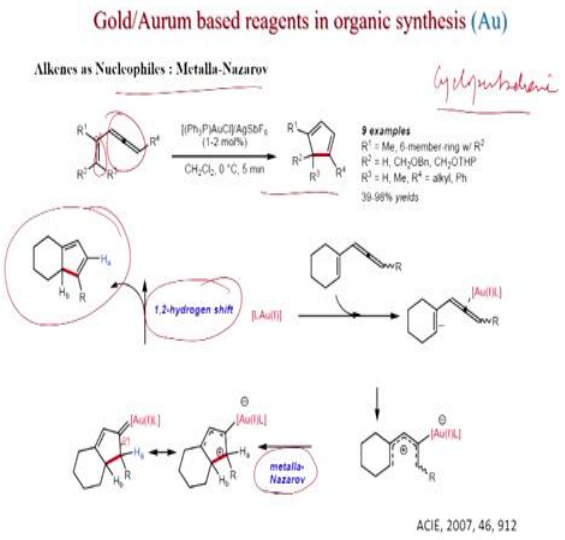

Now will see another reaction, metalla-Nazarov reaction. If a double bond and allene, so this is double bond and allene is present, then you can get this cyclopentadiene. So this could be the mechanism that the gold activates the alkene and then this double bond attacks to the allene, you get this carbocation over 5 carbon atoms and that is the mechanism for Nazarov, metalla-Nazarov reaction happens, this is the newly generated C-C bond and after gold elimination and 1, 2 hydrogen shift, so this hydrogen shifts to here and you can get this compound, this was published in Angewandte Chemie, 2007.

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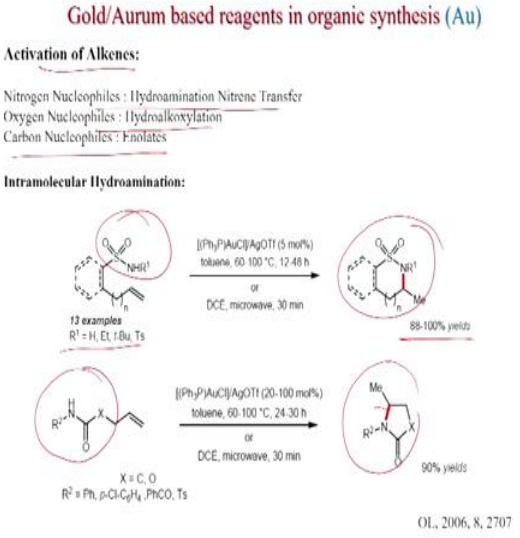

Last we will see activation of alkenes, nitrogen nucleophiles, hydroamination, nitrene transfer, oxygen nucleophiles, hydroalkoxylation, carbon nucleophiles enolate, so this is the hydroamination, sulfonamide is present. You can get this product in 88 to 100 percent yield and you can see this one is present then also is possible, this is the newly generated bond is formed. So this is the hydroamination, This was published Organic Letters, 2006.

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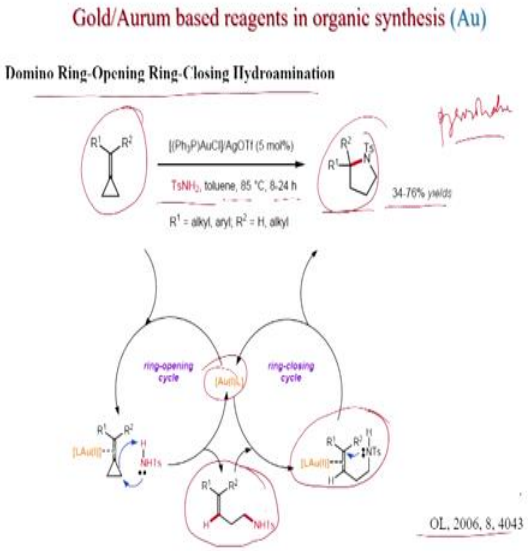

And now we will discuss domino ring-opening ring-closing hydroamination. So here you can see this double bond is present with tosylamine toluene 85 degree centigrade, you can get this pyrrolidine, so this is pyrrolidine are formed in 34 to 76 percent yield and this is the mechanism because of course the cyclopropyl group has been opened. So this is the ring opening cycle and then the so first this activation happens, the N-tosyl group attacks like this and you get this of course. After this opening the hydrogen goes here and N-tosyl here, then it will co-ordinate with the gold again like this way and the cyclization will happen to give this.

So first ring opening followed by ring closing cycle you can get this product, this was published in Organic Letters, 2006.

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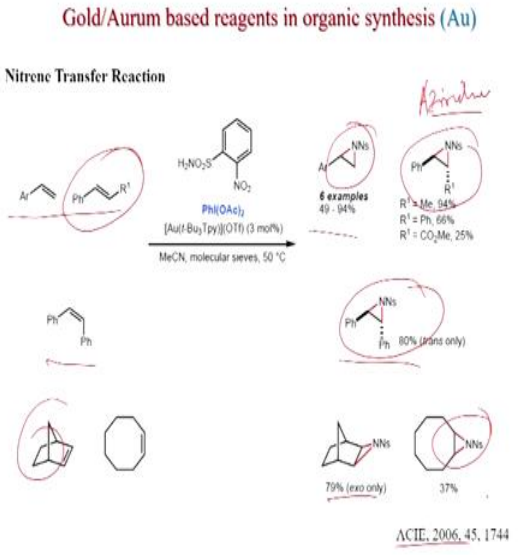

Nitrene transfer reaction, if you have a alkenes then the azide then the aziridine can be formed like this stereochemistry (trans), so the double bond geometry will remain intact like here it is 80 precent trans, here also this formed exo only here this. So this was published in Angewandte Chemie.

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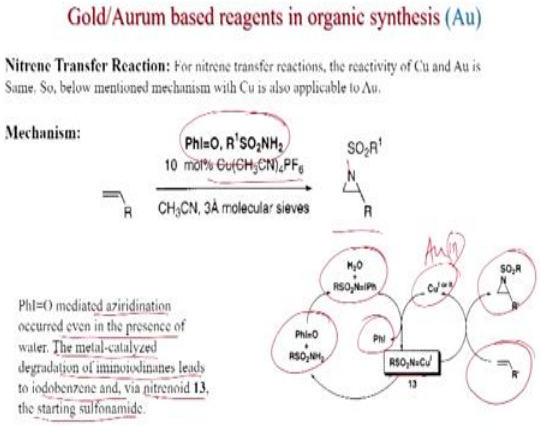

And we will see the mechanism, so this is mechanism with copper, I think similar mechanism with gold also, PhIO sulfanomide you get this one. So what could be the mechanism here? So with PhIO RSO2NH this is from the nitrogen plus and double bond I and that changes with metal PhI elimination with metal. So this is gold also, this will happen, gold 3 and you can get this one in double bond Cu and that reacts with the olefin so that the transfer happens. That is the like cyclopropanation, this is the aziridination. PHIO mediated aziridination occurred even in the presence of water.

The metal-catalysed degradation of iminoiodinane leads to iodobenzene and nitrenoid 13 and the starting sulfonamide. This was published in JOC.

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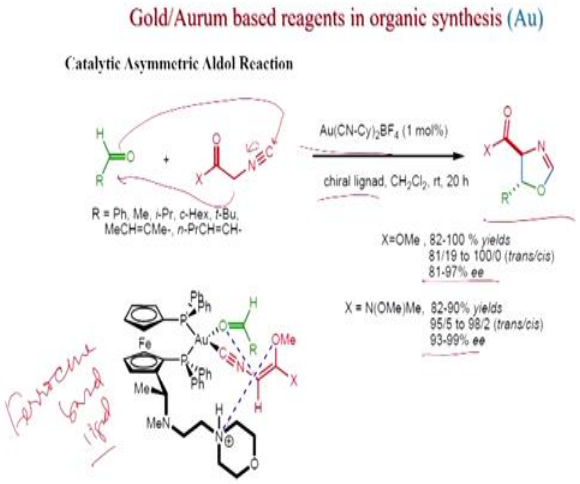

So catalytic asymmetric aldol reaction is also possible with gold, you can see this reacts here and this cyclizes here, you can get this kind of compound with good yield and ee and chiral ligand, if it is there you can get EE also, so this is the chiral ligand, ferrocene based ligand, ferrocene based ligand and you can get this kind of transition state, the aldehyde is coordinated with the gold, also this cyno group is coordinated with gold and this also is making the enolate, tertiary amine. Research published in two journals, JACS and JOC.

So today we have seen different gold catalysed cyclization reaction, first we have seen the alkyne activation and different kind of alkynes can be incorporated in a substrate and with alkene so that you can get defined product, sometimes aromatization and the gold elimination in very facile we have seen and nucleophile and the gold will be in the trans-orientation that will also, that will also fix the geometry of the newly generated double bond and then we have seen the gold can activate allene also and different kind of cyclization we have seen. The allene and the double bond and then we have seen the alkene activation lastly. In the alkyne activation we have seen the cyclopropyl group there.

It can give the first the ring opening and then the ring closing cyclization with sulfonamide and lastly we have seen the aziridine formation with a double bond, so that also you have seen, the iodoxybenzene and sulphonamide, the active nitrenoid intermediate will form, that will attack to the olefin and give the aziridine. Thank you.