Reagents in Organic Synthesis
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Lecture 11
Reduction with Boranes, Diimide and Trialkylsilanes.

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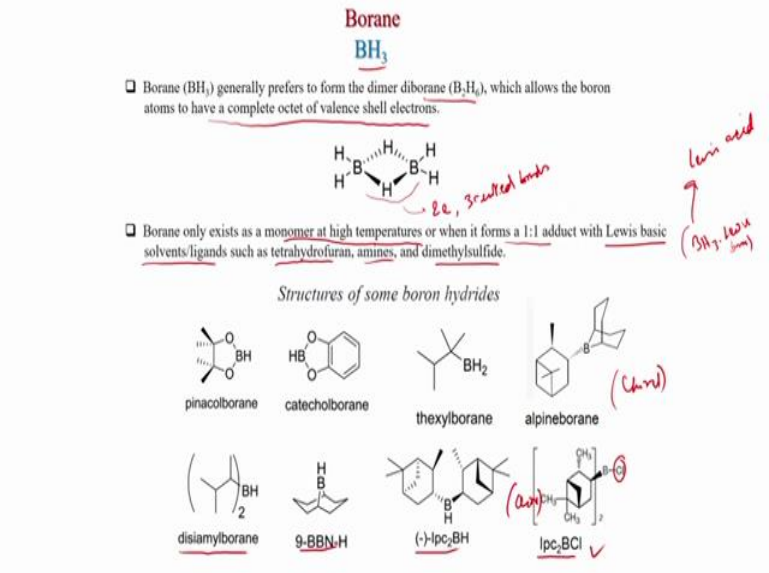

Welcome again. Today we will discuss borane reduction then diimide reduction and silane reduction. So first we will discuss borane. The structure of borane is BH_3 and borane generally prefers to form the dimer diborane, which allows the boron atoms to have a complete octet of valence shell electrons. So this is the diborane structure and if you see this bond this is actually two electron three centered bonds. This hydrogen is attached to two boron. So each boron gets now total eight electrons and completes its octet.

Borane only exists as a monomer at higher temperature or when it forms a one is to one adduct with Lewis basic solvents ligands such as tetrahydrofuran, amines and dimethyl sulfide. In that case, BH_3 makes adduct with Lewis base because BH_3 is a Lewis acid. Structure of some boron hydrides. This is pinacolborane. This is catecholborane because this model is catechol and then borane atom is attached to two oxygen. This is thexylborane and this is a alpineborane.

This is chiral, we will discuss in detail also this borane. And disiamylborane, this is also important borane this is sterically two disiamyl group is there and 9-BBN, this is also sterically hindered borane and isopinocampheylborane**.** This is also chiral, we discussed this is Diisopinocampheylborane this chiral we will discuss in detail and this also discuss Ipc_2BCl

there is one hydrogen is replaced chlorine and we will discuss this advantage also some cases this chlorine and that is the Ipc_2BCl is an effective reducing reagent.

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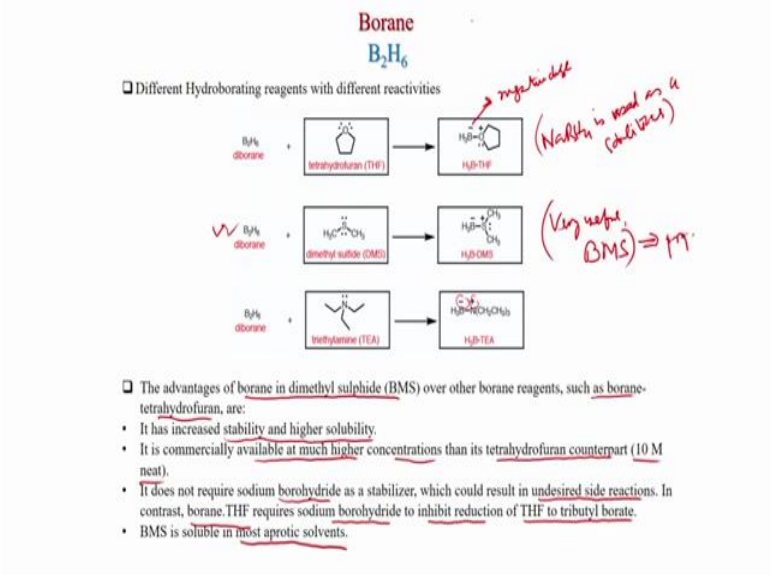

Different hydroborating reagents with different reactivities. So diborane when mixed with tetrahydrofuran then this BH_3-THF complex is formed, so and now, BH3 carries a negative charge here and oxygen has a positive charge. So one lone pair is donating to the borane.

Also diborane when reactive with dimethylsulfide, it forms this BH_3-DMS this is very useful. And it is called BMS. So BH_3-DMS, we will discuss shortly, the advantages of this. And diborane triethylamine even diethylamine also different amine can react with diborane and the complexes are formed. Here also borane carries a negative charge and this nitrogen of the amine carries a positive charge. The advantage of borane in dimethyl sulphide BMS over other borane reagents, such as borane tetrahydrofuran, are, it has increased stability and higher solubility. So this is very useful because it has increased stability and higher solubility. It is commercially available at much higher concentration than its tetrahydrofuran counterpart and you can get up to 10 M neat this reagent BH_3-DMS.

It does not require sodium borohydride as a stabilizer, which could result in undesired side reactions. In contrast, borane THF requires sodium borohydride to inhibit reduction of THF to tributyl borate. So here in a $NABH_4$ is required. Otherwise the THF will also can be reduced. So sodium borohydride is used as a stabilizer. And in this case BMS case, it is not required. BMS is soluble in most aprotic solvents. So this is very useful. Its solubility, its

stability and you do not require sodium borohydride, so that makes the BMS very popular reagent.

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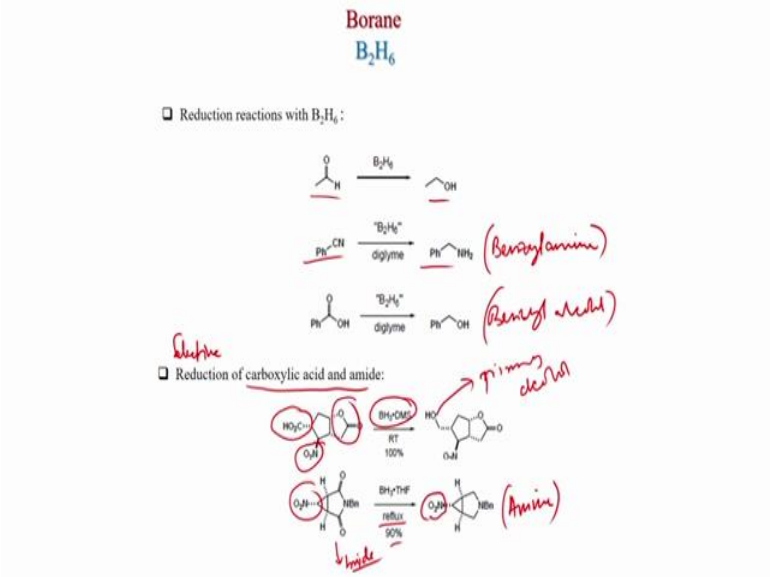

Reduction reaction with diborane. Aldehyde can be reduced to the alcohol. Here Benzonitrile is converted to benzylamine and here, benzoic acid is converted to benzyl alcohol. Reduction of carboxylic acid and amide, so this is very specific that we will see now that the borane is selective for the carboxylic acid and if you see this molecule, here carboxylic acid motif is there nitro group is there, an electron motif is there. And selectively only, the carboxylic acid group is reduced to the primary alcohol with BH_3-DMS reagent in a room temperature. So this becomes primary alcohol**.** And the other lactone group and nitro groups are untouched.

Also, this an imide here and the cyclic imide and nitro group is present with BH3-THF reflux, you get 90 percent yield of this product. So this is an amine product you get. Both this carbonyl groups, amide carbonyl groups getting reduced and nitro group is untouched. So selective reduction, so we can tell this selective reduction. Selective reduction of carboxylic and amide is possible in the presence of other functional groups.

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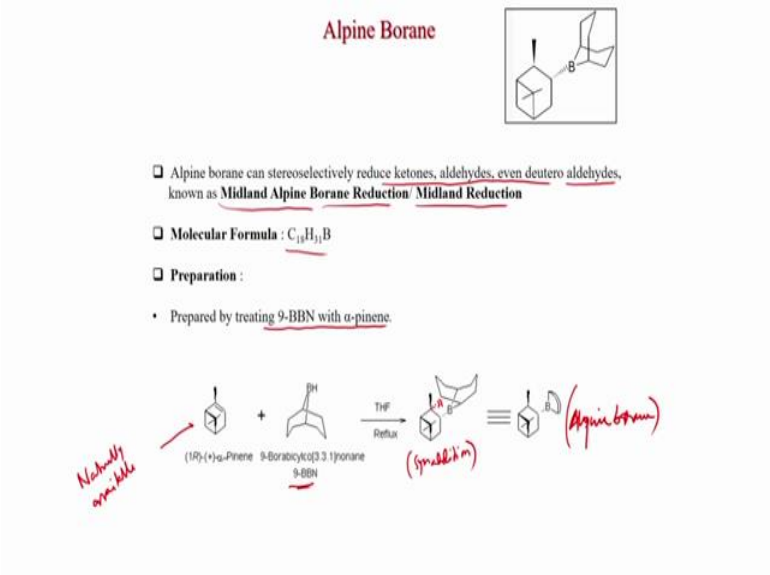

Now we will discuss chiral borane. So this is the first chiral borane that we will discuss. This is alpine borane, alpine borane can stereo selectively reduce ketone, aldehydes, even deutero aldehydes, known as Midland Alpine Borane Reduction Midland Reduction. Its molecular formula is $C_{18}H_{31}B$. So 18 carbon atoms are present and this can be prepared by treating by 9-BBN with alpha-pinene. Alpha-pinene this is naturally available and this alpha-pinene if you react with 9-BBN with THF reflux and you get addition of this borane to the double bond and this is called syn-addition because borane and hydrogen adds from the same phase. And now, this is a chiral borane reagent. So this is alpineborane.

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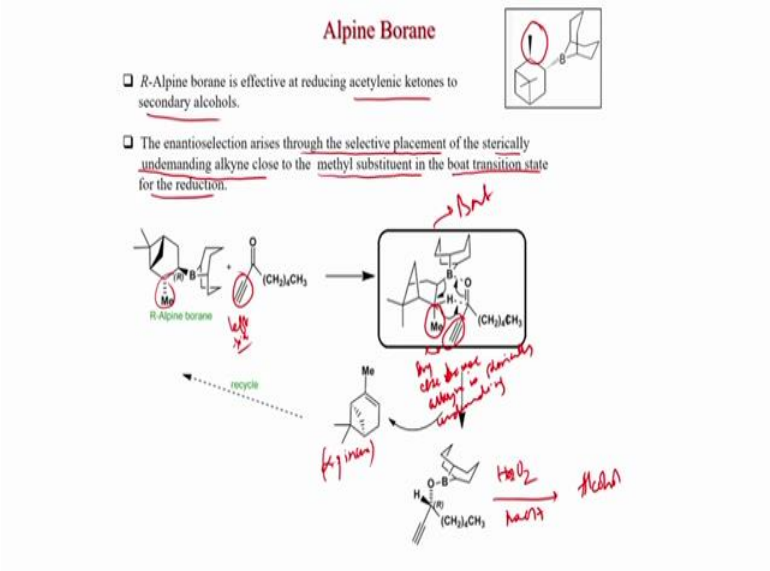

R-Alpine borane is effective at reducing acetylenic ketones to secondary alcohols. The enantioselection arises through the selective placement of the sterically undemanding alkyne closed to the methyl substituent, so there is a methyl here in the boat transition state for the reduction.

And this is the R-Alpine borane, we can write like this and methyl here, if you give the rotation then methyl comes down here and from the downside and now, this is the top side and if you draw the ketone like this with this is the left side. Now, this transition state is like this, so this is sterically undemanding and this methyl group, so they can stay close because alkyne is sterically undemanding.

So this is very small, the steric effect is very small for a triple bond. And now, this boat confirmation, so this is boat confirmation you get here and after that, the dehydroboration happens. So this hydride delivers to the carbonyl and now this borane bond cleaves and to get a double bond so this is alpha-pinene. Alpha-pinene is generated and this complex after H_2O_2 you can get the alcohol. H_2O_2 NaOH get alcohol. Also, this alpha-pinene which is generated in the reaction this can be recycled to make R-Alpine borane.

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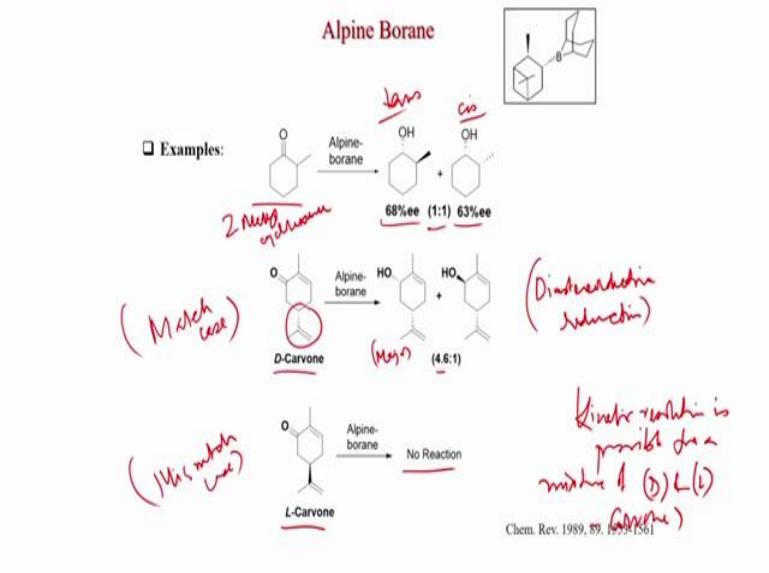

Examples of reduction of alpine borane. Here this two methylcyclohexanone when reduced with alpine borane, you get both diastereomers this is trans and this is cis. So trans you get 68 percent ee and cis you get 63 percent ee and you get 1 is to 1 mixture of diastereomers

Also D-Carvone when treated with alpine borane this is a diastereoselective reduction because you see already a chiral centre is there and now, you get this major diastereomer in 4

point 6 ratio and minor is 1. So this is the minor, this is the major, so this is major. Interestingly, when L-Carvone is used then with alpine borane, no reaction. So what does this mean? That means this is the match case that you get at least product, match case and this is mismatch case. So that means you can do a kinetic resolution also, when you mix D-Carvone and L-Carvone, so kinetic resolution is possible. Kinetic resolution is possible from a mixture of D and L-Carvone because only D will react with alpine borane and L will not react.

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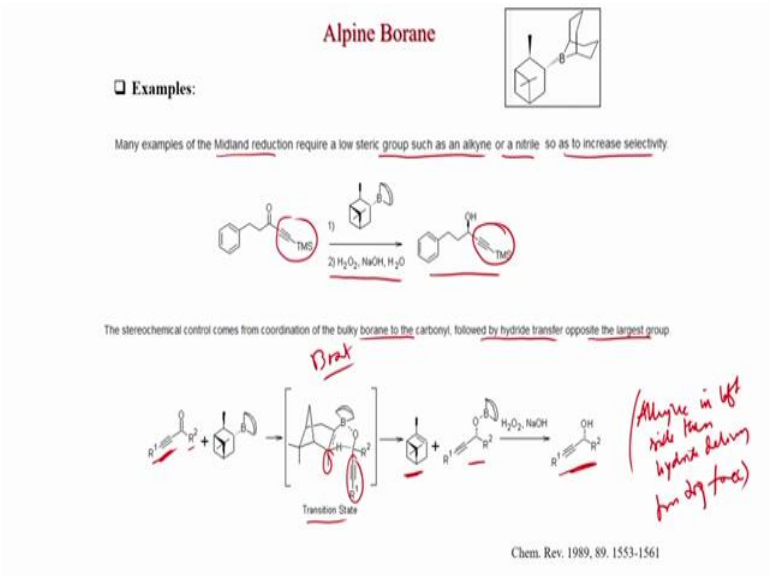

Many examples of the Midland reduction require a low steric group such as an alkyne or a nitrile so as to increase selectivity. Like this, here the alkyne we have drawn the right side so alcohol is like this and this is alpine borane and followed by quenching with H2O2 NaOH water you get this alcohol and this is the alkyne group, TMS alkyne group is present here.

The stereochemical control comes from coordination of the bulky borane to the carbonyl, followed hydride transfer opposite to the largest group. So here again the transition state we have drawn, this is the alkyne and this is R2 group here. So alkyne and methyl they are parallel hence, close to each other, this is the transition state and this is the boat confirmation. And now the hydride will deliver from the top side, top phase so you get the down alcohol here, top side and you get this alkoxy boronate and alpha-pinene after that, H2O2 NaOH treatment you get the alcohol.

So if you write alkyne in left side then hydride delivery from top phase. So in this case, we have drawn right side that is why the alcohol is opposite stereochemistry here. But if you draw like alkyne left side then you get the hydride delivery from the top side.

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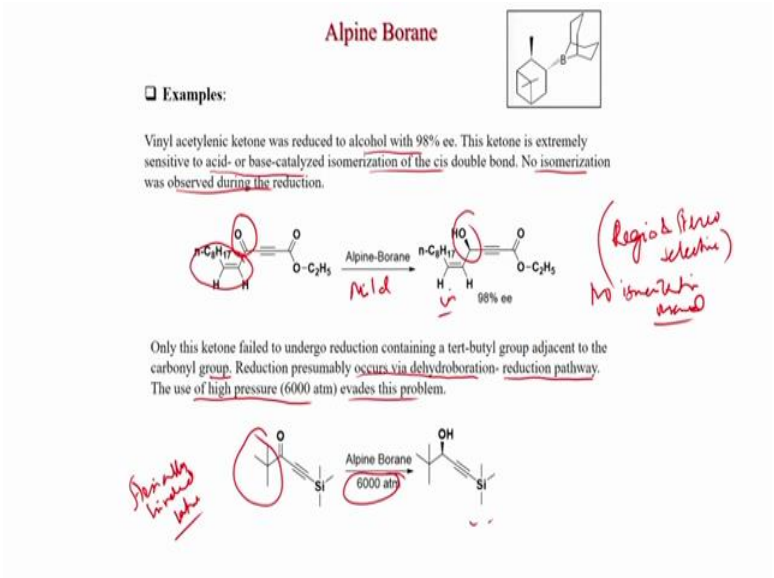

Vinyl acetylenic ketone was reduced to alcohol with 98 percent ee. This ketone is extremely sensitive to acid or base-catalyzed isomerization of the cis double bond. So you can see there is a cis double bond. No isomerization was observed during this reduction. So here you can see, different carbonyl groups are there. Two carbonyl groups is there. So this is regio selective and stereo selective. Because there are two carbonyl groups selectively only this carbonyl group is reduced to the alcohol and the double bond is cis. So here also cis. So no isomerization observed. So that means this is a very mild condition.

Only this ketone failed to undergo reduction containing a tert-butyl group adjacent to the carbonyl group. Reduction presumably occurs via dehydroboration reduction pathway, which we already discussed. And the use of high pressure like 6000 atmospheric evades this problem.

So if a tertiary butyl group is present in the ketone then this is sterically hindered ketone. A tertiary butyl group is attached to the carbonyl group. And now, if you do not use the pressure then you do not get the product. Alternatively, if you use high pressure then you can get the product and high is observed also.

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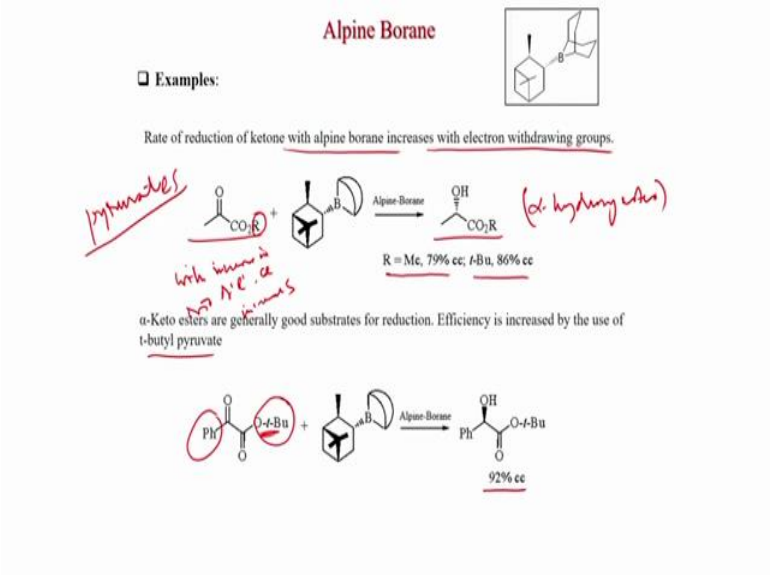

More examples, the rate of reduction of ketones with alpine borane increases with electron withdrawing groups. Like this one, pyruvate system. So if you, methyl 79 percent ee, tertiary butyl is 86 percent ee. So if you increase the steric group then the ee, with increase in size of R ee increases and this is the pyruvates, methyl pyruvate, tertiary butyl pyruvate and with alpine borane you get these products, alpha hydroxy esters.

Alpha-keto esters are generally good substrates for reduction. Efficiency is increased by the use of tertiary butyl pyruvate. So if you use this phenyl group here then also you get the ee. So earlier in our methyl, that is the pyruvate, now if you put phenyl group here and tertiary butyl ester then you get earlier it was 86 so 92 percent ee. So the efficiency increased by the use of tertiary butyl group. So if tertiary butyl group is there then you get the high enhance selectivity.

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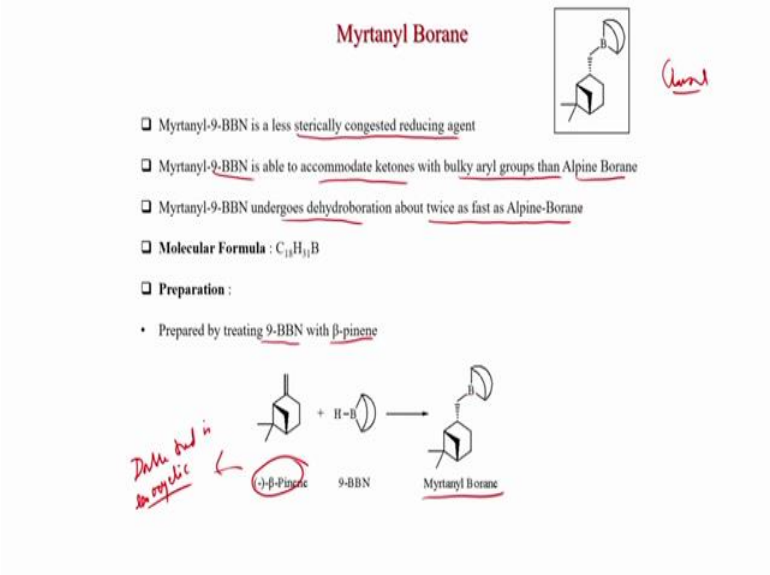

Now, we will discuss another borane, this is also chiral. This name Myrtanyl-9-BBN. It is a less sterically congested reducing agent. Myrtanyl-9-BBN is able to accommodate ketones with bulky aryl groups than Alpine Borane. So this is important, it can accommodate bulky groups, aryl groups also. Myrtanyl-9-BBN undergoes dehydroboration about twice as fast as Alpine Borane. So this is also important, the reactivity is high. And this is prepared by treating 9-BBN with beta-pipene.

So this is earlier we have seen alpha-pinene. So this is beta-pipene. In the beta-pipene the double bond in exocyclic position and with 9-BBN. Then this addition happens because this is terminal olefin and the borane adds to the terminal and hydride to the internal carbon center. And you get this Myrtanyl Borane. Also this addition happens, this is the top facw blocked by this group so the addition is taken from the downside.

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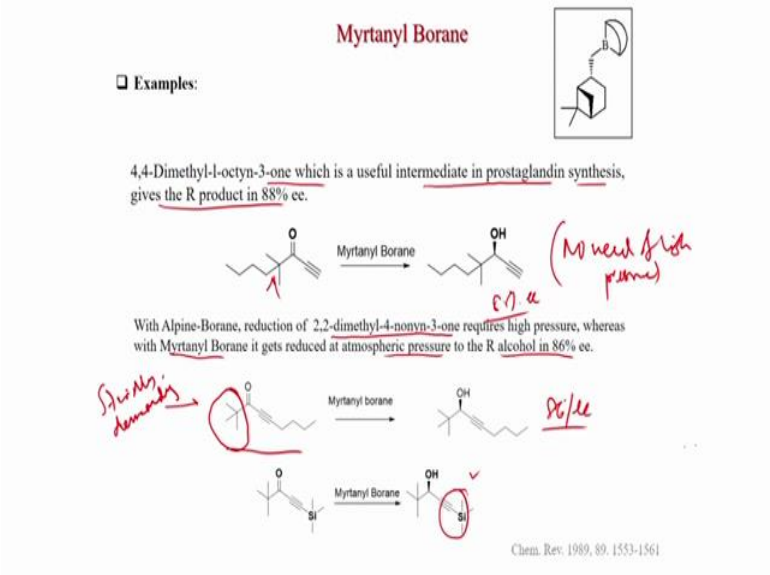

4, 4-Dimethyl-1-octyn-3-one which is a useful intermediate in prostaglandin synthesis give the R product in 88 percent ee. So here you can see this is a quaternary center and with the tertiary butyl group we have seen that the reduction does not happen with alpine borane without pressure. When 6000 atmospheric pressure is applied then only you get the product. But here, no need of high pressure.

So this is very important with Myrtanyl borane you do not need high pressure and you get this 88 percent ee of this product. With alpine borane, reduction of 2, 2-dimethyl-4-nonyn-3-one, so this is the substrate, 2, 2-dimethyl-4-nonyn-3-one requires high pressure. Whereas with Myrtanyl Borane, it gets reduced with atmospheric pressure to the R alcohol.

So here, we have alkyne, we have drawn in the right side, so you get this alcohol in 86 percent ee and you see, this is tertiary butyl group, so this is sterically demanding. So that means sterically depending ketones can be reduced with Myrtanyl Borane. Also, if you have trimethylsilyl group in the triple bond then also the product is formed with affecting this group and you get this alcohol is high ee.

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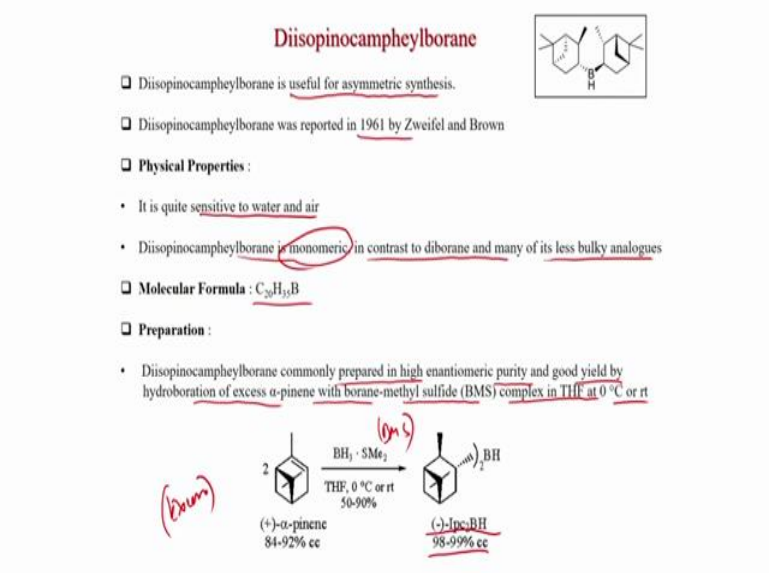

Now, we will discuss diisopinocampheyl borane. Diisopinocampheyl borane also is useful for asymmetric synthesis. It was reported in 1961 by Zweifel and Brown. Physical properties, it is quite sensitive to water and air, so that you have to be careful. Diisopinocampheylborane is monomeric in contrast to diborane and many of its less bulky analogue. So this is monomeric, this is very important and its structural formula is $C_{20}H_{35}B$.

Diisopinocampheylborane commonly prepared in high enantiomeric purity and good yield by hydroboration of excess alpha-pinene with borane-dimethyl sulfide complex in THF at 0 degree centigrade or room temperature. So alpha-pinene you need excess because stoichiometry tells that you need two equivalent of this pinene motif . So two equivalent of alpha-pinene reacts with BH_3 SME_2 BMS in THF 0 degree centigrade or room temperature, you get this borane in 98 percent to 99 percent ee.

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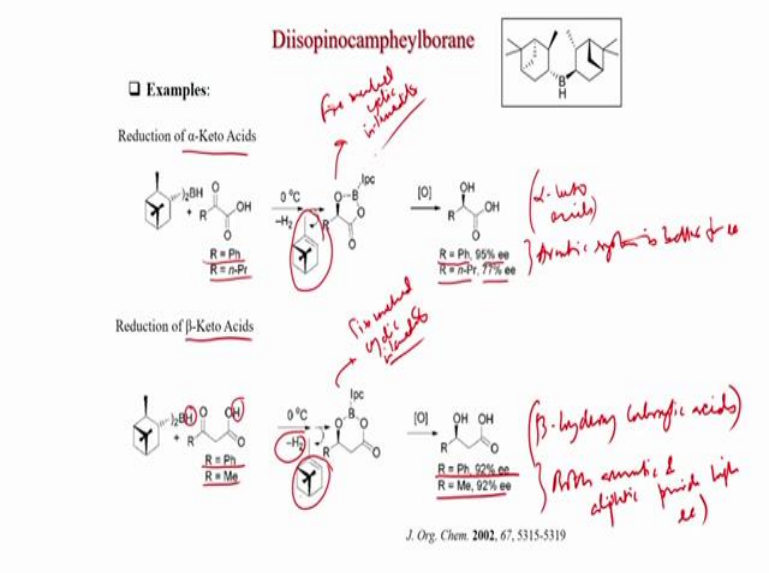

Examples reduction of alpha-keto acids. Like this alpha-keto acids R is Ph, R is equal to n propyl. So aromatic, aliphatic both and when it reduction happens this complex formation, so five membered cyclic intermediate. This fiver membered cyclic intermediate forms and out of two alpha-pinene motif one alpha-pinene eliminates and then this five membered ring is formed and after oxidation you get this alpha-Keto carboxylic acids, so alpha-Keto acids. And when R is equal to Ph, you get 95 percent ee, R is equal to n propyl you get 77 percent ee. So aromatic system is better, aromatic system better for ee.

Reduction of beta-Keto Acids, so this is where in alpha-Keto Acids, beta-Keto, now one carbon is more. And here also the reaction they have studied with R is equal to phenyl and methyl and both cases the reaction happens and unlike earlier case five membered here, six membered. Six membered cyclic intermediate is formed. You see, the reduction already happened and one molecule of alpha-pinene is eliminated also, hydrogen is eliminated because this H is quite acidic.

So this H is acidic and one hydrogen from this borane. So ultimately H2 is eliminated and this six membered cyclic intermediate is formed and after oxidation you get this beta-hydroxy carboxylic acids and when R is equal to Ph you get 92 percent ee. R is equal to methyl 92 percent ee. So here both aromatic and aliphatic white high. So this is important with beta-Keto Acids both aliphatic and aryl groups give high yield.

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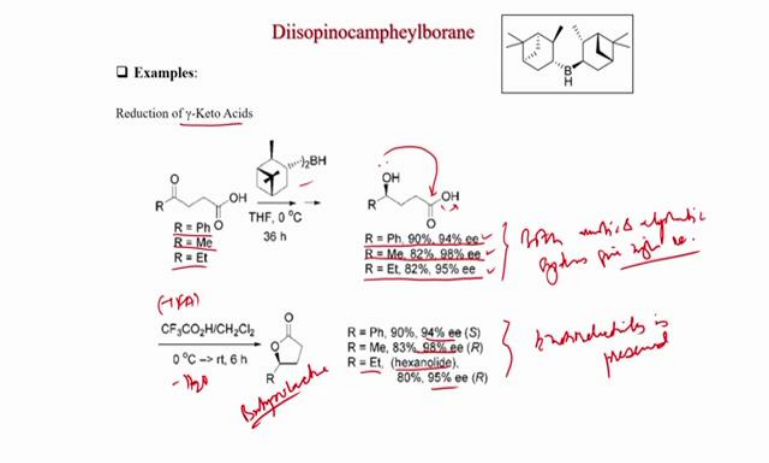

Now, we will discuss one more carbon enhanced that is the gamma-Keto Acids and they have started with R is equals to Ph methyl, ethyl, both aromatic, aliphatic. And here also, with this diisopinocampheyl borane THF 0 degree centigrade you get the reduction and here also the they did not show the intermediate but you get the high ee. R is equal to Ph 94 percent ; R is equal to methyl 98 percent . R is equal to ethyl 95 percent ee. So here also both aromatic and aliphatic systems give high ee. So this is very important gamma Keto Acids here both aliphatic and aromatic gives high ee. And after trifluoroacetic acid treatment,

So this is TFA, you get the cyclization happen, so under acidic condition you get water elimination and you get butyrolactone. And they are enantioselectivity is preserved. So here R is equal to Ph 94, 94, here methyl 98, 98 and R is equal is ethyl who is just called hexanolide, you get 95 percent ee. So enantioselectivity is preserved.

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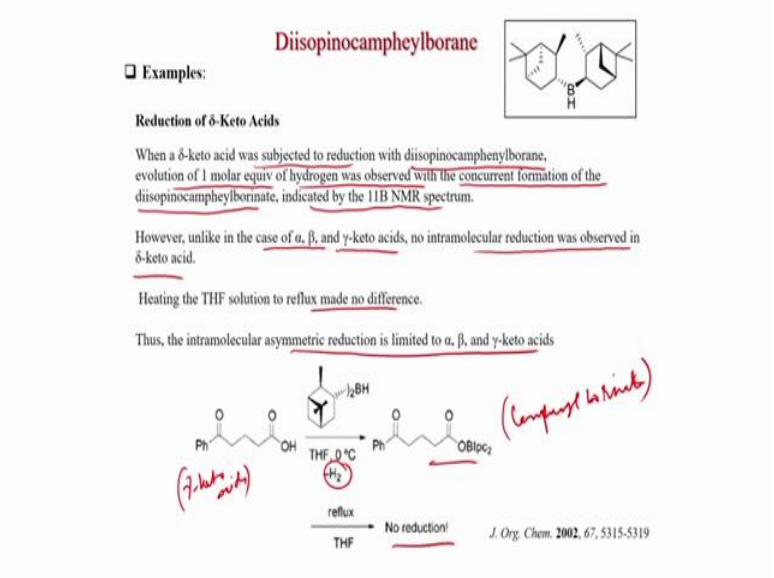

Reduction of delta-Keto Acids. When a delta-Keto Acids was subjected to reduction with diisopinocampheylborane evolution of one molar equivalent of hydrogen was observed with a concurrent formation of the diisopinocampheylborinate indicated by the 11 borane NMR spectrum.

However, unlike in the case of alpha, beta, gama-keto acid, no intramolecular reduction was observed in the gama-keto acid. Heating the THF solution to reflux made no difference. Thus, the intramolecular asymmetric reduction is limited to alpha, beta and gama-keto acids. So this is the delta-Keto Acids and when treated with this diisopinocampheylborane THF 0 degree centigrade only the acid group is reacting with elimination hydrogen to get this camphenyl borinate. Also in reflux no reduction happens.

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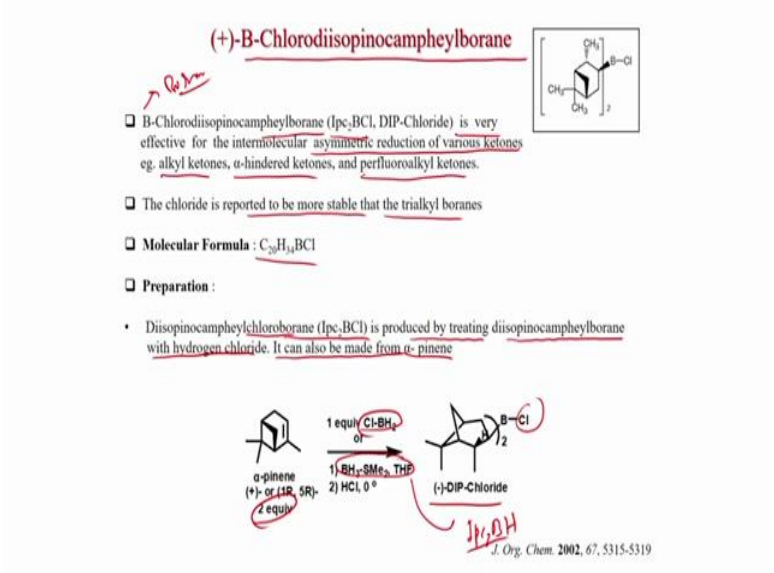

Now we will discuss the hydrogen is replaced with chlorine that is called beta-chlorodiisopinocampheylborane so B means boron. B-chlorodiisopinocampheylborane Ipc_2BCl is very effective for the intermolecular asymmetric reduction of various ketones. As for example alkyl ketones, alpha-hindered ketones, perfluoroalkyl ketones. The chloride is reported to be the more stable than the trialkyl boranes. Molecular formula: $C_{20}H_{34}BCl$ and diisopinocampheylchloroborane is produced by treating diisopinocampheylborane with hydrogen chloride. It can be made from alpha-pinene. So this is the diisopinocampheylchloroborane is prepared by diisopinocampheylborane with hydrogen chloride. Also, alpha-pinene can be used directly for the synthesis of diisopinocampheylchloroborane. So here alpha-pinene two equivalent unit with one equivalent BH_2Cl that Cl comes to here or you can treat BH_3-SMe_2 THF to generate this Ipc2 to borane and then you treat with HCl you get the chloride.

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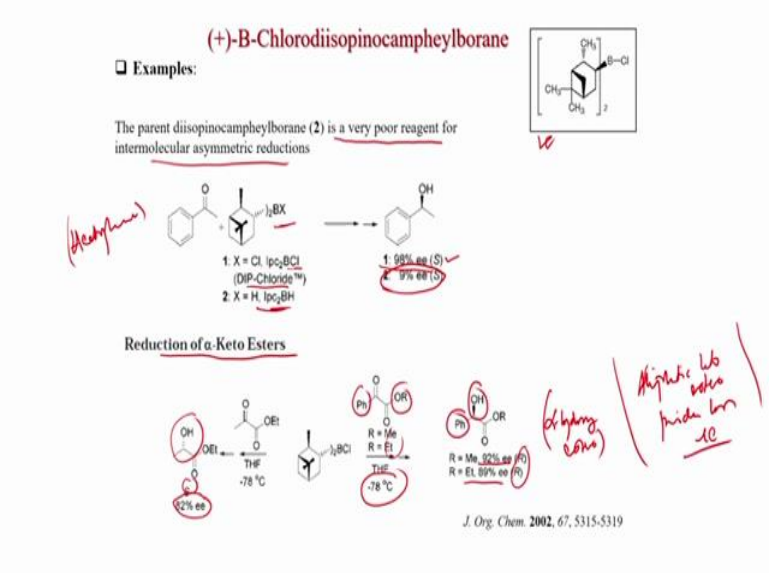

So this parent diisopinocampheylborane is very poor reagent for intermolecular asymmetric reduction. If you consider this ketone like acetophenone when X is equal to chlorine that is the DIP - Chloride and X is equal to hydrogen that is the isopinocampheylborane . So you can see the difference in selectivity here, with this one you get 98 percent ee. On the other hand in isopinocampheylborane borane you get only 9 percent ee.

Not only ketones, Keto Esters can also be reduced with this. So earlier we have seen the keto acid, so this is good for Keto Esters, alpha-Keto Esters like ethyl, methyl, ethyl esters and here phenyl group is there, THF minus 78 degree centigrade, you get this alpha hydroxy ester.

R is equal to methyl, you get 92 percent ee; R is equal to ethyl, you get 89 percent ee. On the other hand, if the phenyl is replaced with methyl then the stereoselectivity getting changed. This is the opposite stereochemistry, earlier it was R and now it is S. And also the enantioselectivity also gets reduced. So aliphatic ester provides less ee. This is also earlier we have seen this alpha-Keto Acids also this observation we have seen.

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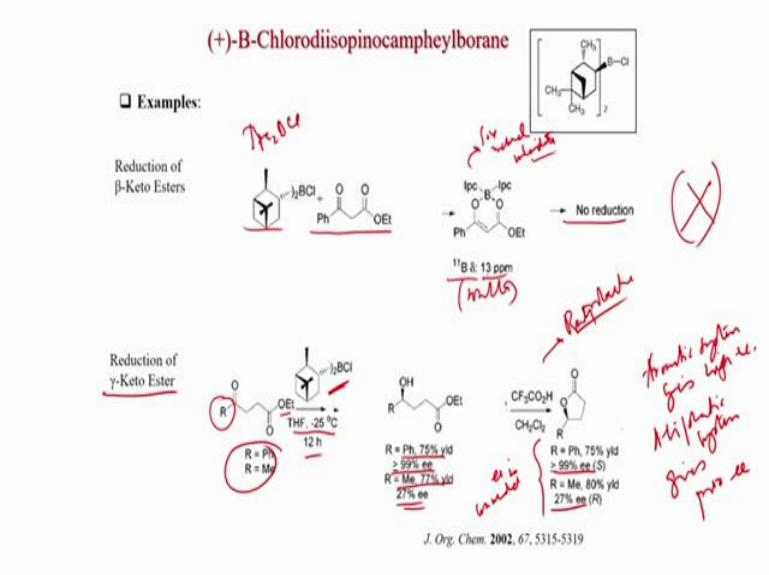

Now, in beta-Keto Esters what happens when this beta-Keto Esters was treated with Ipc_2BCl then you get this enolate is formed and this six membered intermediate is formed. And you can see this ketone is becoming enolate here actually, so enolate is formed. And this 11 boron, it shows 13 ppm this is selective for this and now this ketone is going to enolate that is why there is no reduction.

Now, reduction of gama-keto esters. So what happens with gama-keto esters and there still both R is equal to Ph and methyl with this ethyl group. Now, with this reagent THF minus 25 degree centigrade, 12 hours starring so here reaction work. So here no reaction with beta-Keto Esters. And with gama-keto esters the product is formed, when R is equal to phenyl, you get 75 percent ee and 99 percent ee greater than**.**

R is equal to methyl, 27 percent ee and after trifluoro acetic acid get treatment you get this butyrolactone derivatives. R is equal to Ph 99 percent ee and R is equal to methyl this is 27 percent ee. So ee is conserved. However, the aromatic system works nicely, aromatic system gives high ee. Aliphatic system gives poor ee. So only 27 percent ee is observed when R is equal to methyl.

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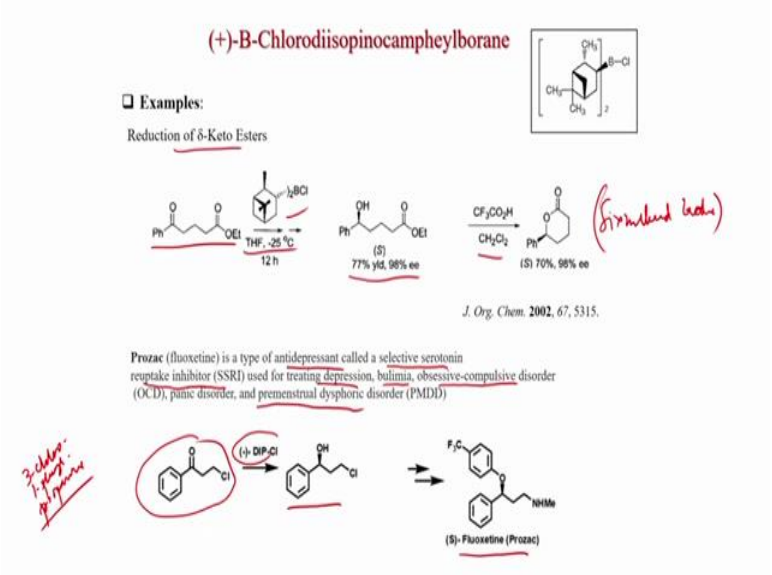

Some more reactions like reduction of delta-Keto Esters. So when delta-Keto Esters like this is treated with Ipc_2BCl under the same condition, THF minus 25 degree centigrade to 12 hours. Here also the reaction occurs and you get the product in 98 percent ee and 77 percent yield and this product when treated with trifluoroacetic acid you get this six membered lactone.

Prozac is a type of antidepressant called a selective serotonin reuptake inhibitor used for treating depression, bulimia, obsessive-compulsive disorder, panic disorder and dysphoric disorder. So this was prepared but by this reaction, so with DIP-Cl you can reduce this ketone. So this is the aromatic ketone, it is called 3-chloro-1-phenyl propanone. So if you treat this 3-chloro-1-phenyl propanone with diisopino chlorocampheylborane then you get this alcohol product which can be converted to Prozac which has many activities.

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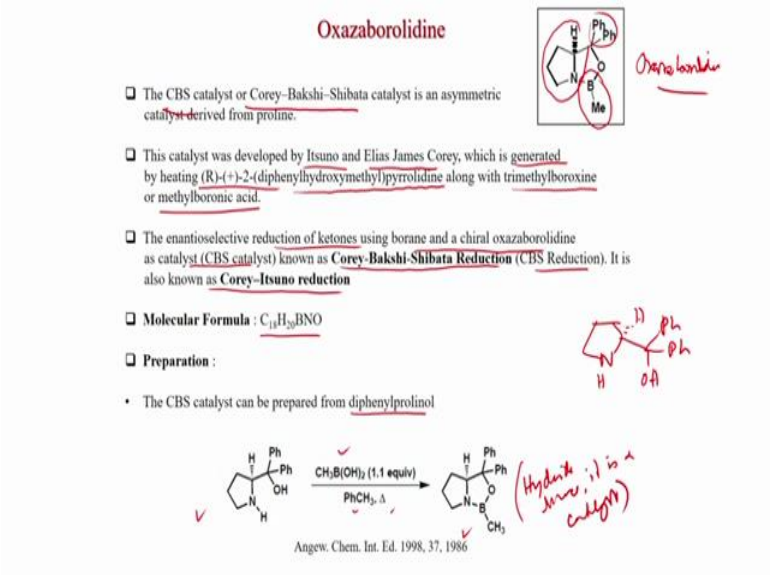

Now, we will discuss Oxazaborolidine. This is called CBS catalyst or Corey-Bakshi-Shibata, the first letters have been taken, is an asymmetric catalyst derived from proline. So this is you can say this structure this is CH2OH which can derived from the COOH carboxylic acid after treating with and now, it have to react with the borane, to get this Oxazaborolidine so this is Oxazaborolidine.

The catalyst also developed by Istuno and Elias James Corey simultaneously which is generated by heating R-2-diphenylhydroxymethyl pyrrolidine along with trimethylboroxine or methylboronic acid. So here methyl group is required. The enantioselective reduction of ketones using borane and a chiral oxazaborolidine as a catalyst CBS catalyst is known Corey-Bakshi-Shibata Reduction CBS reduction. It is also known as Corey-Itsuno Reduction. And molecular formual is C18H20BNO.

The CBS catalyst can be prepared from diphenylprolinol. So this is diphenylprolinol, this is diphenylprolinol with this methylboronic acid and then toluene reflux this Oxazaborolidine is formed. So this is not a because there is no hydride, so this is not a hydride source. It is a catalyst. So Oxazaborolidine is not a hydride, so it is a catalyst. So you need a hydride source for the reduction.

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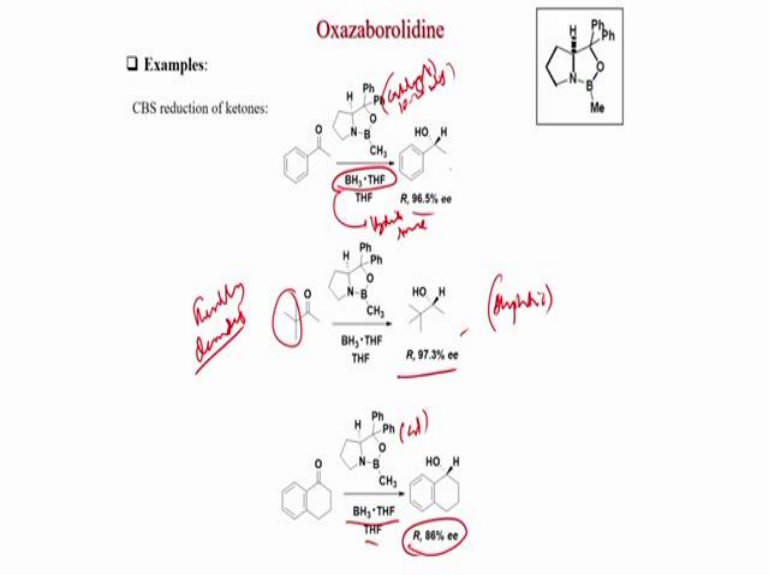

CBS reduction of ketones here this is the catalyst maybe 10 to more percent you need and now BH3 THF this is the hydride source. And acetophenone is converted to this alcohol R, alcohol in 96.5 percent ee. So this is very important, we have seen with Ipc2BCl, also this reduction is possible and tertiary butyl group, so this is sterically demanding. Tertiary butyl group can also be present and you can get 97.3 percent ee of this alcohol. So this is very important aliphatic ketones also give high ee. And this is tetralone, with this catalyst and this is the hydride source BH3 THF, THF solvent you get this alcohol in 86 percent ee.

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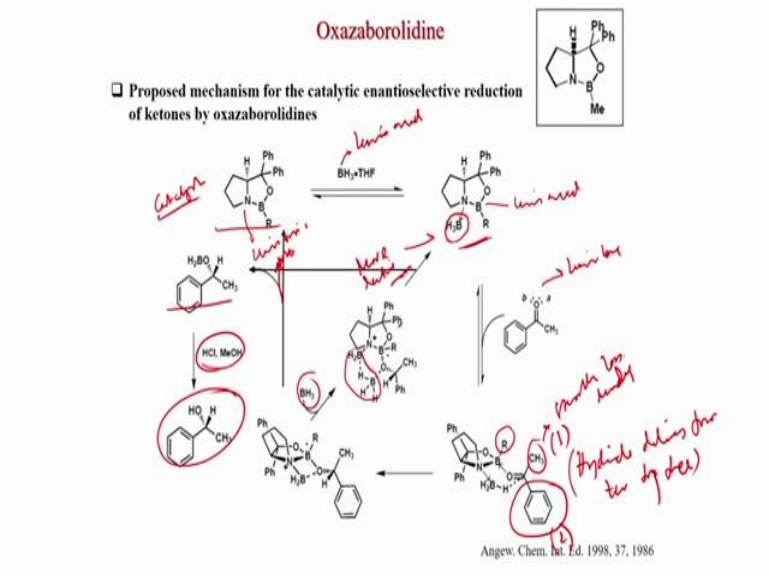

What is the mechanism for this catalytic reduction of ketones. So first is catalyst is reacting with borane because this you can see this is the Lewis basic site. So this is Lewis acid, so that is why this complex is formed, nitrogen reacts with the borane and now this carbonyl, this is also Lewis base and this is Lewis acid center.

So this coordination happens, you can see oxygen borane and this hydride delivery will take place from this borane which is attached to this because this is more reactive, more reactive than BH3 itself or BH3 THF. So this only the borane which is bound to the catalyst only reacts. So this is very important otherwise the ee is not possible and now the hydride delivery will take place from the top phase. Hydride delivery from the top phase and you get the down alcohol, also this large group will be this side because otherwise there will be steric interactions, so this will sterically less demanding.

That is the small, this will be large. So you have to draw a ketone like this and then a hydride delivery will take place from the top phase, so you get this down OH group. And after that, this can be converted to this, after the catalyst liberates you get this complex and after HCl methanol you get the alcohol here actually you get this catalyst back.

Alternatively, one more molecule of BH3 reacts with this complex and then this borane, hydrogen borane this hydride bridge is formed which converted into this active catalyst and this product intermediate is formed here in the borane, alkoxyborane and now with HCl methanol will give this alcohol.

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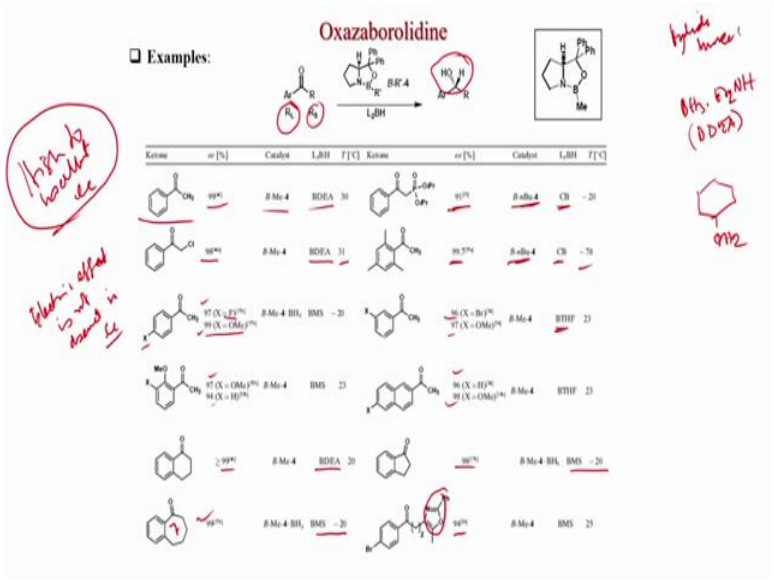

Examples, so R_L and R_S this you have to draw properly, if you draw left side then you get the hydride delivery from the top side, so you get a down alcohol. And different ketones like aryl, aliphatic, so here the acetophenone with BMe4 and BDA this is a BH3 Et_2NH, diethyl I mean, so this is called BDEA, diethylamine that is the hydride source. And with methyl catalyst you get 99 percent ee. Also, when a phosphonate group is there 91 percent B-*n*Bu that is the n butyl group here instead of methyl and CB is cyclohexyl.

So with cyclohexyl borane you get this product in 91 percent ee. Also, chloro group can be tolerated, you get 98 percent ee with BDA is a hydride source and this is the temperature, also three methyl groups can be incorporated and ee can be increased to 99.7 percent with B-*n*Bu catalyst and cyclohexyl borane is the hydride source and minus 78 percent degree centigrade.

Also different electron withdrawing and electron reaches is flow you get 97 percent X is equal to methoxy you get 99. So ee, electronic effect is not observed in ee. So this is very important. And here also, bromo methoxy you get 96 percent 97 percent ee with BTHF that is the hydride source. Here X is equal to OME and dimethoxy compound also high ee and one methoxy acetophenone also give very high ee. This is the naphthyl system here. X is equal to H you get 96, X is equal to methoxy, you get 98 percent ee. This is the tetralone, we have seen earlier, so here the enantioselectivity is very high 99 percent ee with BDA complex that is the hydride source. And five membered means here also you get 98 percent ee and minus 20 degree centigrade BMS is the hydride source.

Here seven membered ring is there, here also high ee and minus 20 degree centigrade, here this motif is exocyclic motif is there. However, only the carbonyl group is reduced 94 percent ee. So what we have observed the high to excellent ee, this is very important for CBS reduction, high to excellent ee for different substituted ketones.

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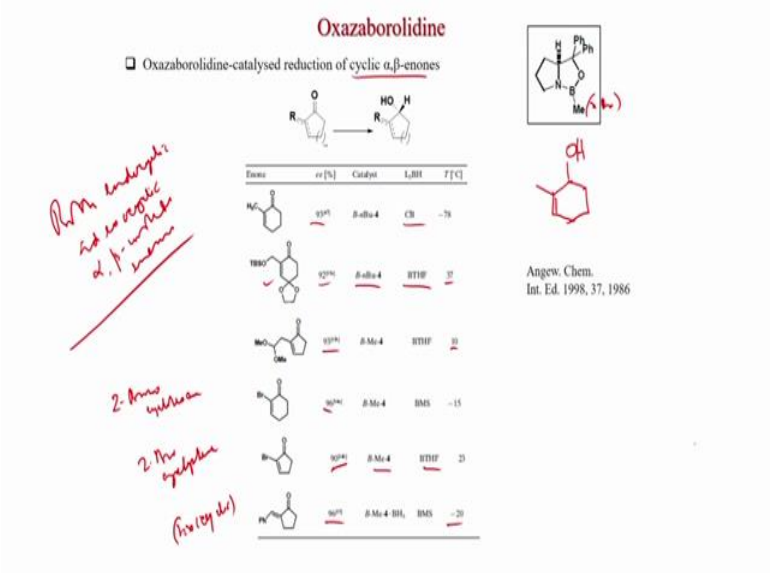

Also cyclic ketones can also be reduced with Oxazaborolidine catalyst like here 2 methylcyclohexanone, you get 93 percent ee, so this is the product, the double bond is now reduced only the carbonyl group is getting reduced. 93 percent ee with cyclohexyl borane and minus 78 degree centigrade. Here this enone, cyclic enone can be the reduced and product can be obtained in 92 percent ee with borane n-butyl this is the n butyl and B-THF the hydride source at 37 degree centigrade.

This cyclopentenone can also be reduced with 93 percent ee, 10 degree temperature. This is the bromo substituted 2-bromocyclohexenone, give 96 percent ee. 2-bromocyclopentenone can also be reduced in 90 percent ee whether ee is a little bit dropped with BMe4 catalyst BTHF borane THF hydride source. And when exocyclic bond is there, that is why we have drawn like this. So exocyclic bond is there that also giving the product in 96 percent ee at minus 20 degree centigrade. So both endocyclic and exocyclic alpha, beta unsaturated enones give products.

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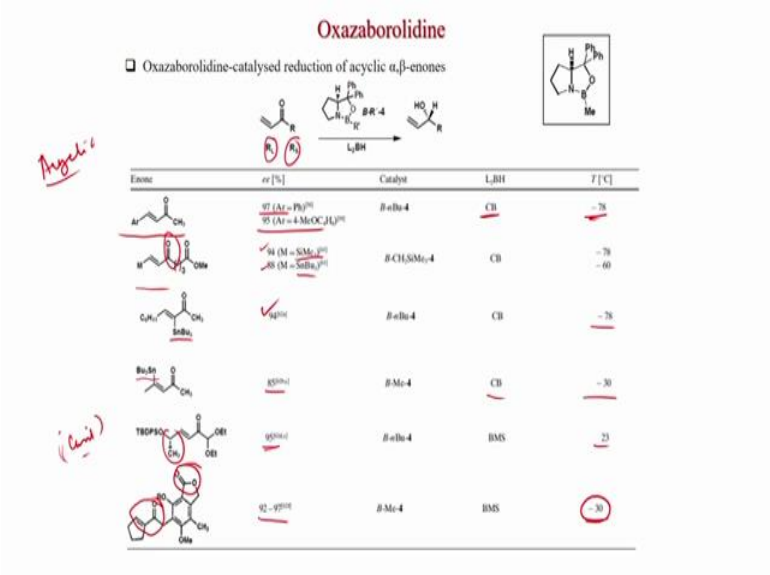

Now we will do acyclic alpha, beta-enones, here the double bond is considered large to explain the stereochemistry and this group is Rs. So this ketone alpha, beta unsaturated as this is the acyclic gives 97 percent ee, Ar is equal to Ph, Ar is equal to 4-methoxy, you get 95 percent ee and cyclohexyl borane minus 70 degree. This one m is equal to SiMe3, SnBu3 case. Also the ketone is getting reduced. So this ketone ester will be untouched and very high ee is obtained so Sn a little bit less ee.

Also, if Sn can be alpha position that case you get the enhanced 94 percent under similar condition. Sn here, Sn butyl then you get the 85 percent ee with minus 30 degree centigrade cyclohexyl borane as the hydride source. And if you have a chiral, so this is chiral enone here is the chiral enter then you a diastereoselective reduction and 95 percent ee you get the product at 23 degree temperature. And this you can see there is a lactone motif is there and this is alpha, beta unsaturated enone. And only the carbonyl group will be reduced with oxazaborolidine in catalyst and depending on the R you get 92 percent to 97 percent ee and minus 30 degree centigrade temperature. So different liner enones can be reduced with CBS catalyst.

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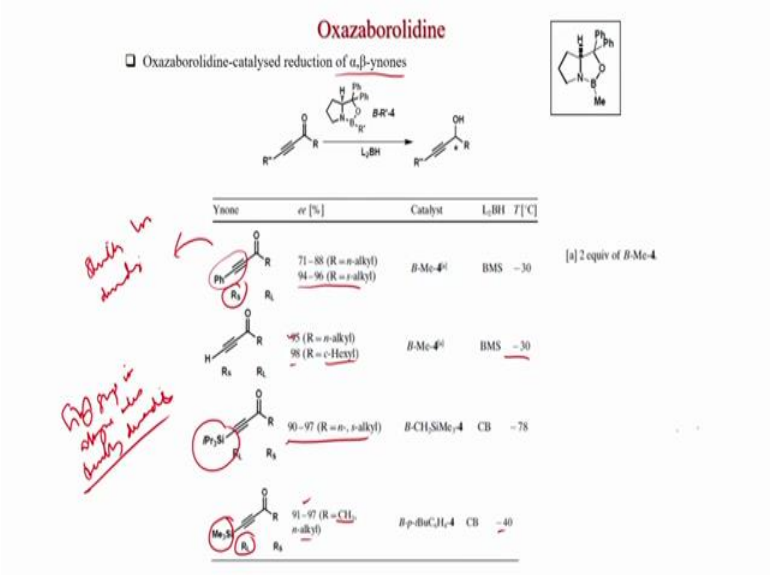

Also not only enones, ynones can be also reduced alpha, beta unsaturated ynones like this. this considered as Rs because this is the triple bond, less sterically demanding or sterically less demanding. That is why it is Rs and this could be R_L and when R is equal n-alkyl then 71 to 88 percent . R is equal to s-alkyl you get 94 to 96 percent ee.

Also if there is no substituent also you get high ee in alkyl and cyclohexyl case you get 98 percent ee and minus 30 degree centigrade temperature. If silyl group is present, then this becomes R_L. So silyl group in alkyl makes sterically demanding. So this is important then this becomes R_L, so you get the opposite stereochemistry but the ee is still very high 92 to 97 percent ee. And here also, this is the dimethylsilyl group is present this is also R_L and within alkyl or CH3, you get 91 percent to 97 percent ee at minus 40 degree centigrade temperature.

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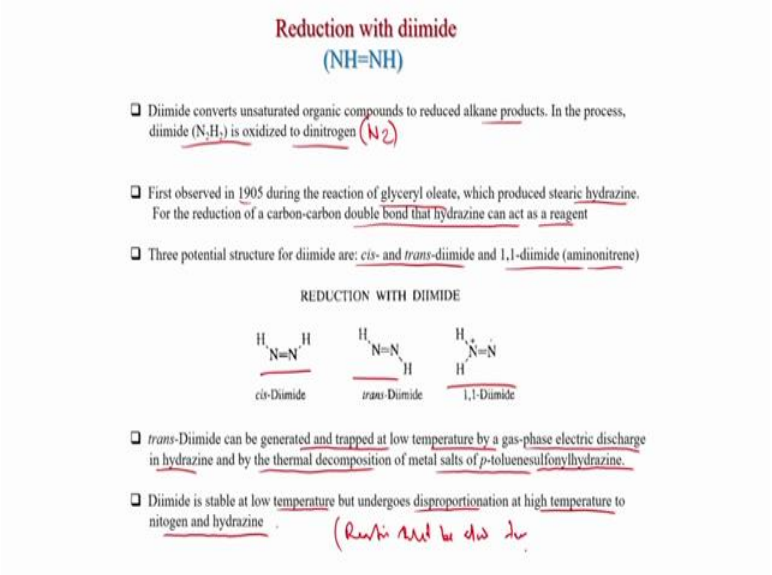

Now, we will discuss reduction with diimide. So diimide converts unsaturated organic compounds to reduce alkane products. In the process diimide is oxidized to dinitrogen. So nitrogen is formed. First observed in 1905 during the reaction of glyceryl oleate, which produced stearic hydrazine for the reduction of carbon-carbon double bond that hydrazine can act as a reagent. Three potential structure for diimide are cis and trans diimide and 1, 1-diimide that is aminonitrene.

This is cis-diimide, this is trans-Diimide and this is 1, 1-diimide. trans-Diimide can be generated and trapped at low temperature by a gas-phase electric discharge in hydrazine and by the thermal decomposition of metal salts of para-toluenesulfonylhydrazine. So hydrazine to diimide can be prepared by electric discharge or metal salt thermal decomposition. Diimide is stable at low temperature but undergoes disproportionation at high temperature to nitrogen and hydrazine. So that means this reaction should be done at low temperature, reaction should be at low temperature. That we will see.

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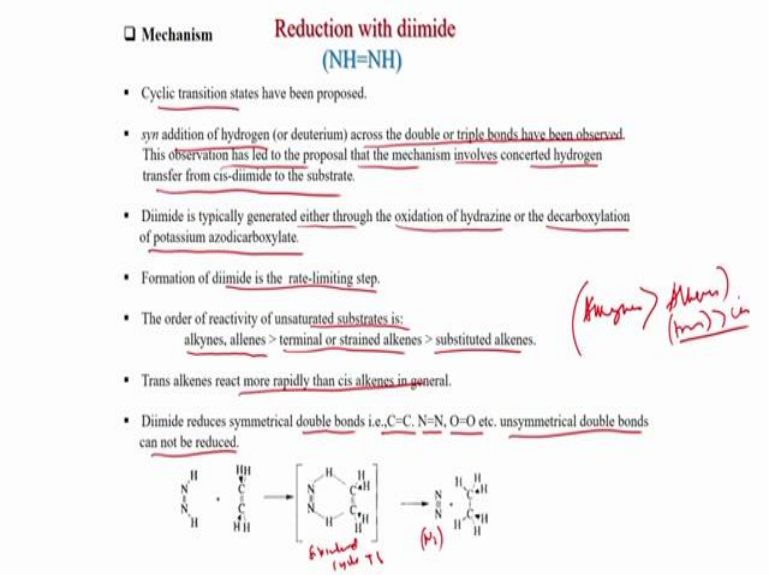

So the mechanism is cyclic transitions state have been proposed for syn addition of hydrogen or deuterium across the double bond or triple bornds have been observed. This observation has led to the proposal that the mechanism involves concerted hydrogen transfer from cis-diimide to the substrate.

Diimide is typically generated either through the oxidation of hydrazine or the decarboxylation of potassium azodicarboxylate. That we will see. Potassium azodicarboxylate can also generate the diimide. Formation of diimide is the rate-limiting step. The order of reactivity of unsaturated substrates is alkynes, allenes, the terminal alkenes and then substituted alkenes. So alkynes more reactive than alkenes and here we will see trans alkenes reacts more. So trans than cis. Trans alkenes react more rapidly than cis alkenes.

Diimide reduces symmetrical double bond C double bond C, N double bond N, O double bond O. However, unsymmetrical double bonds cannot be reduced. So this is very important and this is the transition state the diimide makes a six membered cyclic transition state. And now the hydride delivery will take place and you get the nitrogen here. So this goes at the gas. So reaction goes in the right side very efficiently.

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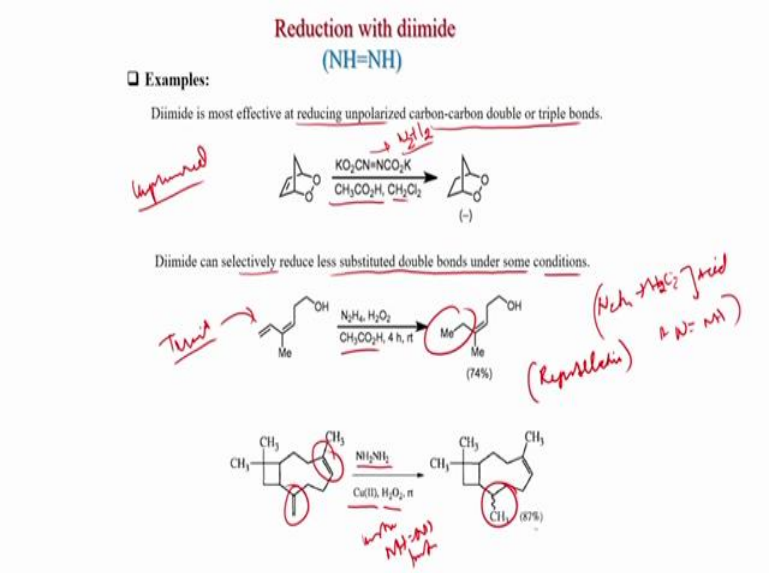

Diimide is most effective at reducing unpolarized carbon-carbon double or triple bonds. Like this is unpolarized and this is the potassium azodicarboxylate, we have shown earlier that, this can generate diimide in situ via decarboxylation and in acetic acid CH2Cl2 you get this product.

Diimide can selectively reduce less substituted double bonds under some conditions. Like here two double bonds are there. So this is the terminal and so this hydrogen, hydrogen also, so N2H4 plus H2O2 oxidation in acid, you get the diimide. So this is the insitu generation of diimide. And now the terminal bonds only getting reduce. So this is regioselective. Here, also you can see two double bonds are here this is internal, this is external means exocyclic and terminal. Here with this hydrogen, copper, H2O2, ins itu formation of NC2NH formation and you get only this double bond is getting reduced to get 87 percent yield.

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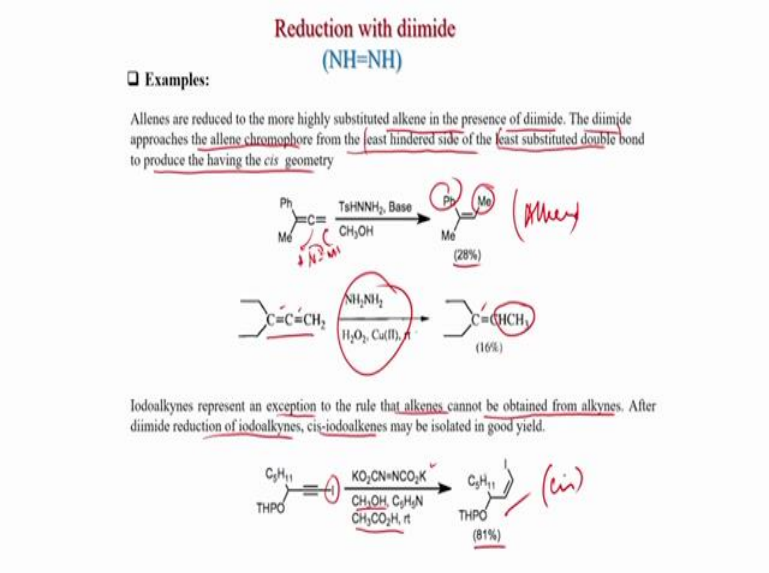

Allenes are reduced to the more highly substituted alkene in the presence of diimide. The diimide approaches the allene chromophore from the least hindered side of the least substituted double bond to produce the product having the cis geometry. So this you can see this is the allene and now hydride delivery takes place from this so NH, comes like this.

And from this side hydrogen air so methyl and phenyl we have cis. So less hindered side and least substituted less hindered side and least substituted double bond. So this is the least substituted double bond of allene. So this double bond is getting retained and you get the alkene in 28 percent. Also in this allene similarly this double bond is getting retained and this only getting reducing this terminal and you get this methyl group here with insitu generation of the diimide.

Iodoalkynes represent an exception to the rule that alkenes cannot be obtained from alkynes after diimide reduction of iodoalkynes, cis-iodoalkenes may be isolated in good yield. So alkenes generally not reduce but if you have a iodo group is there then you can get this azodicarboxylate potassium which generates insitu the diimide with methanol solvent and acetic acid as the acid you get this product in 81 percent. So this is the cis product, this two group are cis.

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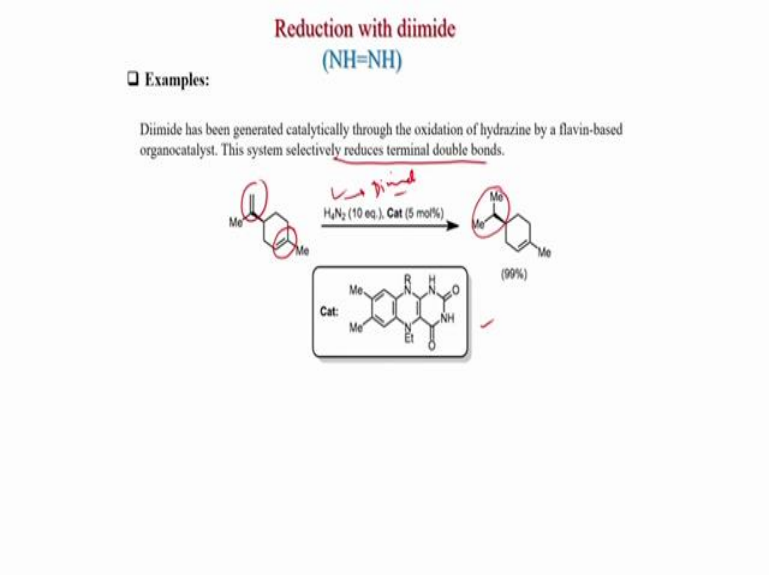

Diimide has been generated catalytically through the oxidation of hydrazine by a flavin based organocatalyst. This system selectively reduces the terminal double bond. Here, you can see this is internal, this is terminal and this group only getting reduced and with this catalyst and 10 equivalent of hydrogen. So catalyst regenerates the hydrodiimide. So that helps oxidation of hydrazine to the diimide and then the reduction happens.

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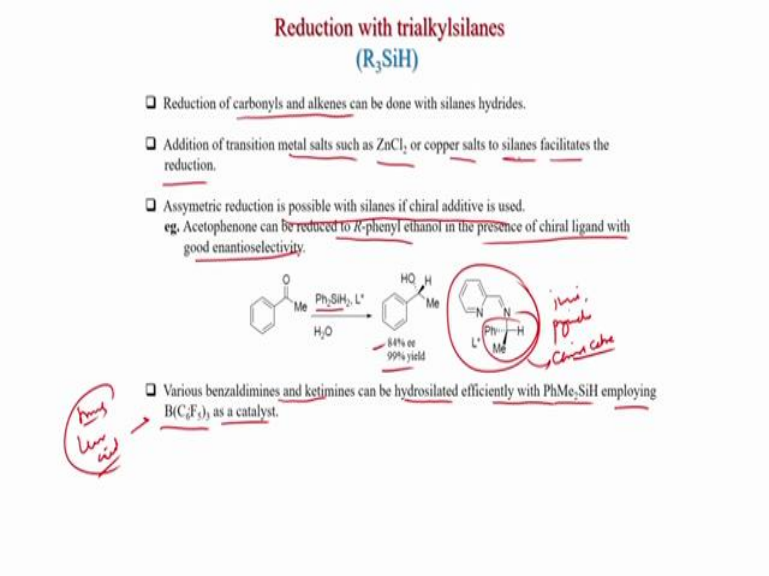

Now, we will discuss silane reduction. So reduction of carbonyls and alkenes can be done with silanes hydride. Addition of transition metals such as zinc, chloride or copper salt to silane facilitates the reduction. Asymmetric reduction is possible with silanes if chiral

additive is used like acetophenone can be reduced to R-phenyl ethanol in the presence of chiral ligand with good enantioselectivity. So this is the chiral ligand, you can see there is imine and pyridine molecule is there and this is the chiral center. This is a cylinder, ethylcylin with this ligand you get 84 percent ee and 99percent yield. Various benzaldimines and ketimines can be hydrosilated efficiently with PhMe2SiH employing B(C6F5)3 whole three as a catalyst. So this is Lewis acid, strong Lewis acid because now this fluorine group is there.

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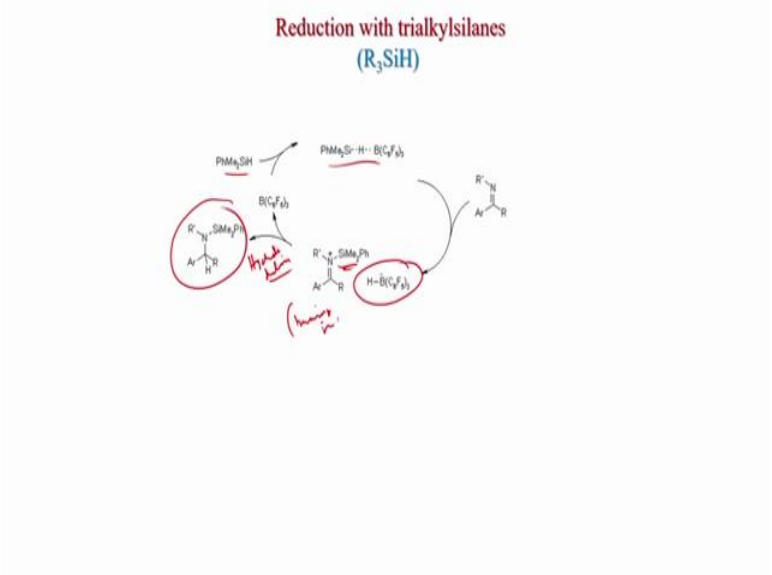

So now this hydride will be attached to the borane and now this complex will be formed because this is a Lewis acid and now this borane was a Lewis acid, now hydride attached to this borane. Now it is Lewis base because borane as a negative charge. Now this imine becomes iminium ion, iminium ion because there is a silyl group now. And now this hydride delivery, so this hydride delivery will take place to get this amine and this catalyst will be regenerated after that react to the active catalyst.

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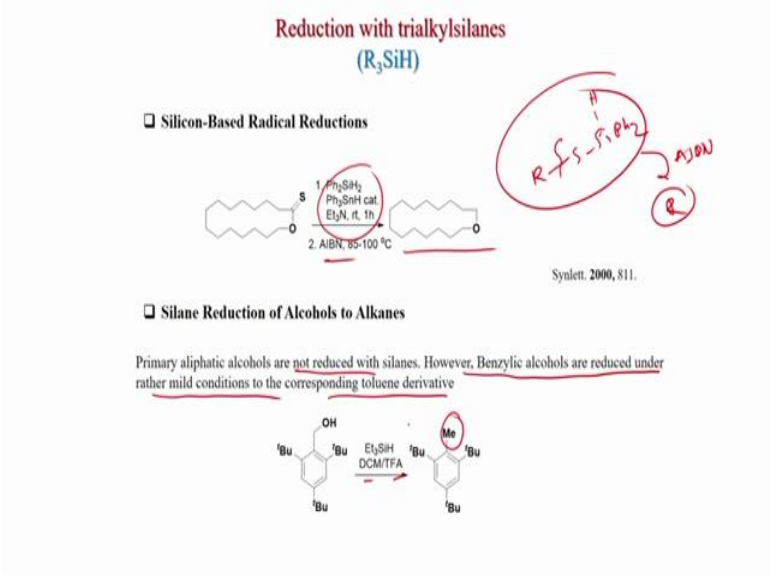

Silicon Based Radical Reductions like this if you have thioesters like this C=S double bond, so with this system the diphenyl silane Ph3SnH, so you get a SiH Ph2. So this you get the intermediate after that AIBN you get R only. So which AIBN you get this cleavage of this C=S bond. 85 to 100 degree centigrade, you get this either.

Silane Reduction of Alcohols to Alkanes primary aliphatic alcohols are not reduced with silanes. However, Benzylic alcohols are reduced under rather mild conditions to the corresponding toluene derivatives. Like this Benzylic alcohols with diethyl silane, DCM, trifluoro acetic acid you get the methyl.

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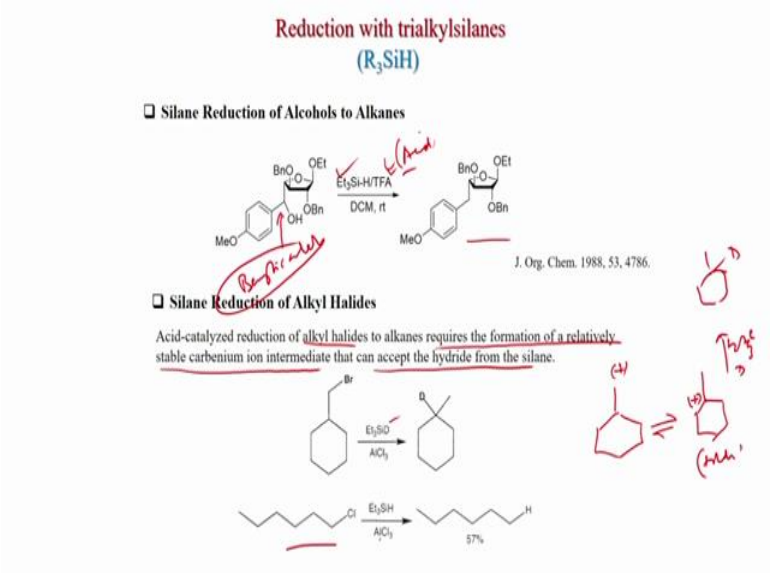

So more Benzylic, so this is also Benzylic alcohol and generally it follows the carbocation intermediate, so you need the acid to generate the carbocation and then the triethylsilane to make the reduction feasible to get this product. Silane reduction of alkyl halides. Acid-catalyzed reduction of alkyl halides to alkanes requires the formation of a relatively stable carbonium ion intermediate that can accept the hydride from the silane. Like this if you treat with triethylsilane, deuterium here aluminum chloride you get this deuterium.

So what happens, so first this carbocation form and then this rearranges to this. This stable, so this is stable carbocation and now this reduction happens, so now Et3SiD comes and you get the product. Also this long chain alkyl halide can be converted to the alkene with trithyl silane in aluminum chloride catalyst.

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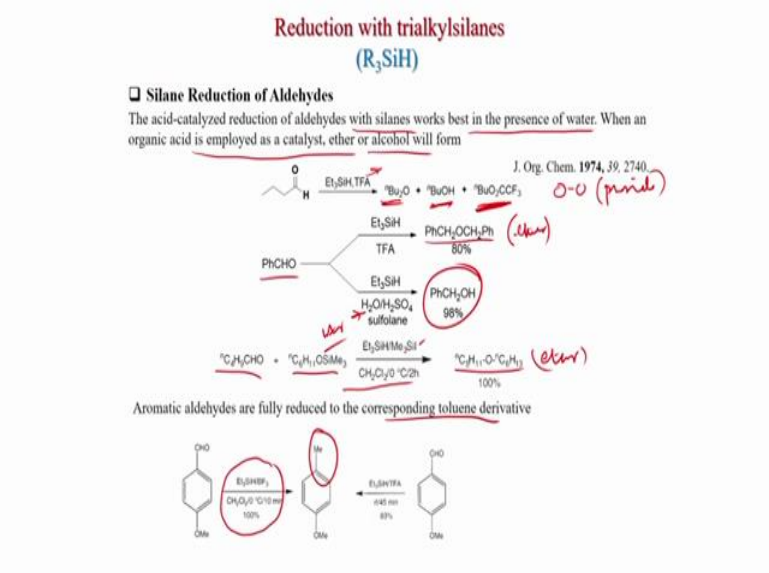

Silane reduction of aldehydes. The acid-catalyzed reduction of aldehydes with silanes work best in the presence of water. When an organic acid is employed as a catalyst, either or alcohol will from like his Et3SiH with trifluoroacetic acid you get the ether, alcohol and a product is formed actually. And now benzaldehyde when treated with triethyl silane TFA you get this either. So this is the peroxide actually. Peroxide is formed.

And here ether is formed when triethyl silane water, so water is added here then you get the alcohol with H2SO4 as the catalyst. Also this aldehyde and this alkoxysilane when treated with triethyl silane and with Me3SiI as a catalyst in dichlomethane solvent you get the either in 100 percent yield. Aromatic aldehydes are fully reduced to the corresponding toluene derivatives. That is also possible like Et3SiH TFA room temperature 45 minutes in the para

methoxybenzaldehyde can be converted to methyl group here. So where we have seen this might be lower temperature that you get the ether and here it goes with the toluene derivative. Also, EtSiHBF3 CH2Cl2 0 degree centigrade means you get the methyl.

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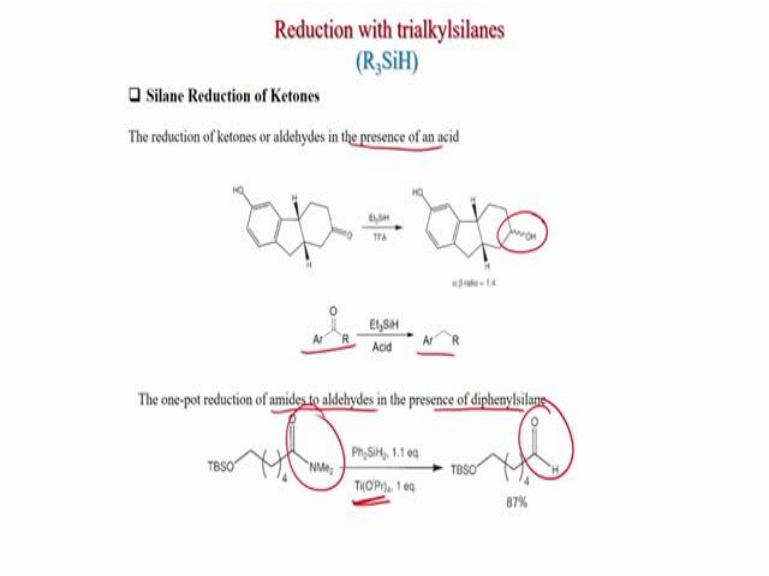

Silane reduction of ketones. The reduction of ketones or aldehydes in the presence of an acid like this ketones is going to secondary alcohols. Also this is aromatic ketones going to alkene. The one pot reduction of amides to aldehydes in the presence of diphenyl silane is possible. This is amide, we are going to aldehyde with titanium isopropoxide non equivalent.

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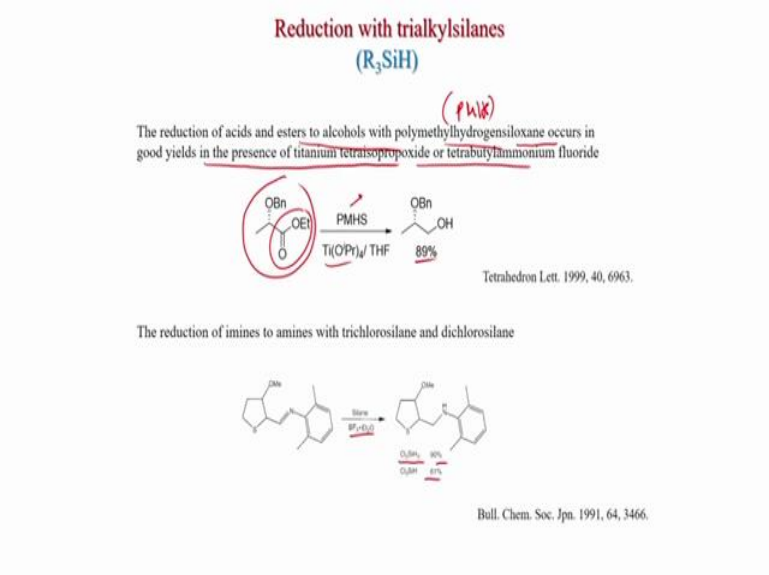

The reduction of acids and ester to alcohols with polymethylhydrogensiloxane occurs in good yields in the presence of titanium tetraisopropoxide or tetrabutylammonium fluoride. Here the so benzyl ester which PMHS this is the PMHS with titanium isopropoxide you get this benzyl diol in 89 percent yield. So this ester group is getting reduced with alcohol. Imines to amines with trichlorosilane and dichlorosilane, so this imines BF3Et8 to activate imine and get the reduction with good yield when dichlorosilane is used the 90 percent at least possible.

So today, we have discussed first the borane and borane we have seen that borane BH3 is not stable, so it has to be complex for commercial availability like BH3 DMS dimethyl sulphide that is very popular and that has similar advantage about BH3 THF and then we have discussed the chiral borane like alpine borane we have seen that it is very good for the reduction of propysalic ketone. So if a triple bond is there then the ketone can be reduced selectively to high ee.

And one drawback of this case is that when a tertiary butyl or sterically demanding group is there then high pressure is required like 6,000 atmosphere pressure is required and this problem was solved with Myrtanyl Borane is use the enantioselectivity was high for this triple bond propysalic ketones. And however, with Myrtanyl Borane the pressure is not required.

Then we have discussed isopinocampheyl borane and this is very useful for the reduction of defined ketone acids. So alpha-Keto Acids, beta-Keto Acids. alpha-Keto Acids we have seen the aliphatic gives less ee but beta-Keto Acids, gama-Keto Acids and delta-Keto Acids we have seen they give the products. And one drawback of this isopinocampheyl borane was the aromatic ketone like acetophenone reduction. In that case we have seen that Ipc2BCl when chloro diisopinocampheyl borane is used the enantioselectivity was high.

Also different esters expect beta-Keto Esters, alpha-Keto Esters can be reduced to the product also gama-Keto Esters and delta-Keto Esters can be converted to the product. And this product can be converted to the lactone derivatives also. Butyrolactone five membered or six membered by acid catalyzed cyclization method.

And then we have seen the diimide reduction. So diimide is very useful reduction because the hydride delivery takes place at syn orientation and it is very useful for the reduction of nonpolarized double bond. So C double bond C, O double bond O, N double bond N. Also

allenes can reduce much faster rate than trans-alkenes and trans-alkenes can reduce much faster than cis- alkene.

Also we have seen the regio selective reduction is possible. So allene case, it is the less hindered side and least substituted carbon that getting hydrogenetic. And also, the terminal double bonds are getting reduced when a regio selective when an internal double bond is there that double bond is added only the terminal double bond is getting reduced with diimide.

And lastly, we have seen silanes. So silane are very useful reducing agent with chiral ligand you can get the enantioselectivity also sometimes defined acid additive or metal additive are used. So this BC6F5 whole three that is quite strong Lewis acid and it can reduce defined amines in high yields. Also you have seen the silane can reduce aldehydes to alcohols. Also, it can generate the ether and in case of para methoxybenzaldehyde we have seen the aldehyde is getting reduced to the toluene derivatives. Thank you.