

# **Molecular Rearrangements and Reactive Intermediates in Organic Synthesis**

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## **Lecture 44: Organoboron Chemistry**

Welcome back to this NPTEL online certification course of molecular rearrangement and reactive intermediates. In the last three classes, I start talking about organoboron chemistry. I talk about the synthesis of different type of organoboron compound. I talk about in the last class about the hydroboration in depth. I talk about the stereoselective hydroboration, the enantioselective hydroboration. And in the today's class, to talk about another important aspect of the organoboron chemistry as a reducing agent. There are several different organoboron compound which can be used as a reducing agent of carbonyl, acid chloride, esters, acid and many other functionalities. So, lets talk about and learn this because this will be a important topic in any competitive exam. So, in this class to talk about you know the different type of borohydride, I think you must have heard about this. and then they are reduction using borohydrides, we are going to learn about the different type of borohydrides, then the stereoselective reduction using borohydride and then we are going to talk about the enantioselective reduction at the end.

- **Borohydride**
- **Reduction using borohydrides**
- **Stereoselective reduction using borohydride**
- **Enantioselective reduction using borohydride**

So, first thing if you try to learn about the boron and hydrogen, I think one thing you should try to understand once you have this you know boron and hydrogen and you should try to compare the electronegativity. So, this is 2.04 electronegativity, this is 2.20 that means, you can see that if you think about the boron and hydrogen bond the electron density is always towards the hydrogen. So, that is why the you can see the electrons in the boron hydrogen bond are polarized toward hydrogen. So, that is why if you think about the sodium borohydride, if you think about that boron atom bearing negative charge, you can think about the despite the formal charges -1 on the boron it is actually the hydrogen which actually carry the partial negative charges there. Because what is happening if you see in a bond the electron density is lying towards hydrogen that means, the electron density is actually in the hydrogen that is why you can think about the negative charge is actually lying on the hydrogen not in the bond. So, now if you think about these are reagent where

you can see that now this they can transfer the hydride ion to different substrates to form the corresponding product. Now, if you think about this the  $\text{BH}_4^-$  bearing negative charge, there is another important thing which is say  $\text{Na}^+$  in the sodium borohydride. So, that is the sodium borohydride, but we will be going to learn about. So, we can say this is a M and this is a  $\text{BH}_4^-$ , I say I think that is but  $\text{M}^+$  and  $\text{BH}_4^-$ . So, now depending on the size of M, depending on the metallic character of M, the reactivity of this different borohydride depending on the radius and you know all different things I am going to the metallic character everything going to play a important role here.

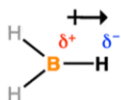
### Electron rich hydride containing boron reagents acts as a hydride donor hence reducing agent:

#### Electrons In The B–H Bond Are Polarized Towards Hydrogen

Electrons in the boron-hydrogen bond are polarized *towards* hydrogen



Also true for sodium borohydride!



- Electronegativity of boron: **2.04**
- Electronegativity of hydrogen: **2.20**



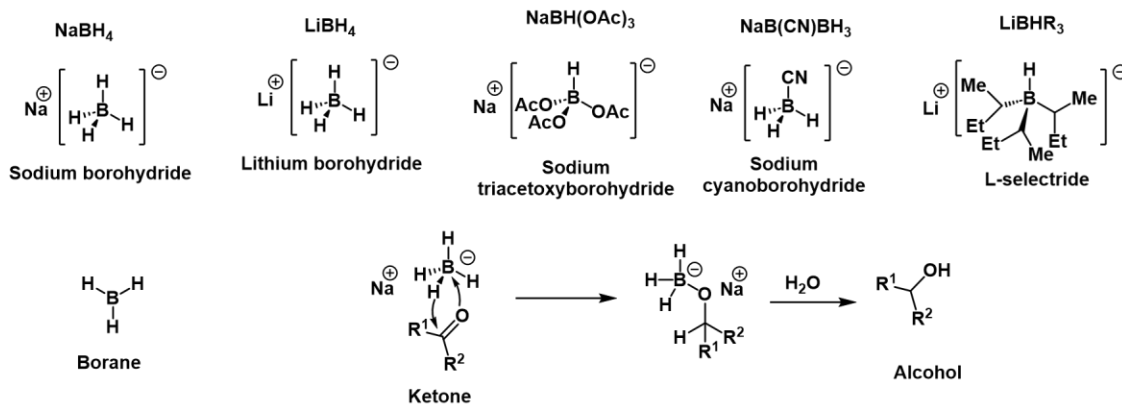
This means that **despite** the **formal** charge of -1 on boron, it is actually the **hydrogen** atoms that bear partial negative charges, and are **nucleophilic**

So  $\text{NaBH}_4$  actually behaves like  $\text{H}^-$  (not  $\text{B}^-$ )

So, first things is that try to learn about what are the different type of this type of reducing agents are present from the boron. So, one of the things is, I think I mentioned is the sodium borohydride you can see sodium with the  $\text{BH}_4^-$  it could be lithium then it will be lithium borohydride, sodium triacetoxyborohydride, sodium cyanoborohydride then the  $\text{LiBHR}_3$  or the L-selectride, where the you know boron with three alkyl group here instead of the three hydrogens. You see three alkyl group here with one hydrogen and then I am going to talk about the another I think you reducing agent is the boron, you have seen there the first reduction already you have seen in the previous class when talk about the hydroboration you see the olefin reduction happen but then we are going to learn that if the boron can not only do the olefin reduction, it can also use for the reduction of the carbonyl group as well. And mostly you can see the reaction what is happening here this you have some sort of a sodium or the the metal plus which actually activate this carbonyl group here which allow now this  $\text{H}^-$  to transfer here to the carbonyl group. After that once you quench with the water you will end up getting the corresponding alcohol, and the other important thing is this type of reaction, I think I am going to explain the solvent play a very important role here. So, not only the solubility is the part, but also you can as you understand these are a

charge species. So, the solubility is one of the important things the solvent also controls the reactivity as well.

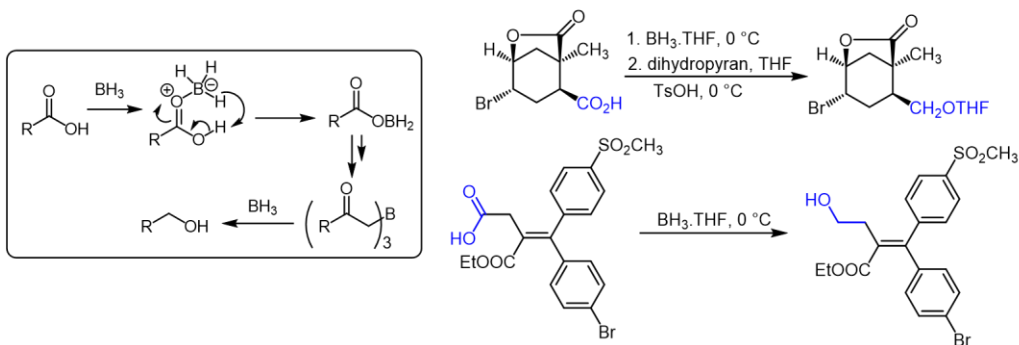
**Electron rich hydride containing boron reagents acts as a hydride donor hence reducing agent:**



So, first I am going to start with the borane because as you see I have already talked about the hydroboration in the last class. So, let's start with the borane. So, we have learnt that the borane can be able to reduce the olefin to form this type of trialkyl boron. So, you have seen that in the previous classes. Now, if you see that if you can treat the boron the important aspect is, it can do a reduction of carboxylic acid in presence of the esters. So, this is a very important thing about the borane, it is not only can be able to reduce in presence of lactones or amides or halides. So, in presence of that also it can be able to selectively reduce the carboxylic acid. It can also in a way be able to reduce the aldehyde, ketones and alkynes which I have already mentioned that it can be able to reduce alkynes, but it can also reduce aldehyde and ketone. But the important aspect is the one which if you try to remember boron, then you should remember boron for another purpose of this chemoselective reduction of acid in presence of lactones or in presence of esters. So let's try to understand I think we already know that the boron not only comes like  $\text{BH}_3$ , there will be always some Lewis base like there will be solvent where the oxygen can give the lone pair or there will be dimethylsulfide, where the Sulphur can give the lone pair. So this can be purchased in the solution. Now if you treat with this substrate where you have this carboxylic acid and a lactone and you have this carbon halide bond also carbon bromine bond. Using borane you can selectively reduce the carboxylic acid and then you can be able to make a tetrahydropyran protection. So, it will be THP here, it will be tetrahydropyran production going to done of this corresponding alcohol. There is another example here you can see there is an ester here and there is an acid in this vinyl carbon, there is an ester and then there is a  $-\text{CH}_2\text{COOH}$  using boron you can selectively reduce that to corresponding alcohol, now the question arises why the boron is so selective to the carboxylic acid, one of the things is once you can think about you have this borane which actually immediately can come to the oxygen because boron is electron deficient, oxygen can give the lone pair to

form this species  $B^-$ . And this  $H^+$  from this acid can form  $H_2$  that will end up making this  $RCOBH_2$  and if it is keep on adding to another two equivalent of carboxylic acid, it will end up forming this, so there will be oxygen here. So, it will end up forming this  $(RCOO)_3B$ . When what is going to happen at the end finally, the borane will be able to reduce the corresponding alcohol, because the chelation of this boron with the carboxylic acid. So, that is the important aspect why this borane can be used for the selective reduction of the corresponding carboxylic acid to the corresponding alcohol which is not happening if you have ester.

- > Borane is commonly used for the reduction of carboxylic acids in the presence of esters, lactones, amides, halides and other functional groups. In addition, borane rapidly reduces aldehydes, ketones, and alkenes.
- > Borane is commercially available as a complex with tetrahydrofuran (THF) or dimethylsulfide in solution. Competing hydroboration of carbon-carbon double bonds can limit the usefulness of borane THF as a reducing agent.



So, this is a list I think you can try to remember some of this, we know that already familiar with the sodium borohydride which is going to give reduce the ketones and aldehyde and acid chloride. But lot of times I think some student ask me question or sometime I have seen in the Phd students are asking me question that sir sometime we have seen the sodium borohydride also can reduce the other functional group. And what happening when you are looking into those reacts and what students are not following that there are some other things also added. Suppose if you think there is a magnesium chloride and sodium, so if you see a reaction is given like that where there is a sodium borohydride is written here and here you have written  $MgCl_2$ . Now you see something happening in the product which is little bit unusual because you always think the sodium borohydride it will be reduce a ketone, aldehyde and acid chloride. But now as soon as you mix with magnesium what is going to happen now it can reduce ester which was not possible using sodium borohydride. and now if you use a  $AlCl_3$  you make aluminum borohydride which can even reduce corresponding acid. So, this is a very strong you can see it can reduce everything in the table and then if you add a calcium again you can see it will be very similar to the magnesium calcium borohydride and then I am going to talk about the zinc borohydride again the zinc borohydride will be much more in little selective it will be very similar to the normal the sodium borohydride, but there are some other things I am going to also bring them again also I am going to talk about this one the cerium using cerium chloride for a

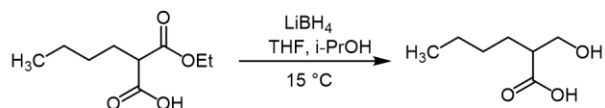
luche reduction I am going to talk about that I am also going to talk about the sodium cyanoborohydride not only they are useful for the reducing of the aldehyde and ketone, but they can also reduce the corresponding imine to form. So, for this there is a reaction called the reductive amination, we are going to talk about that. And then of course, I am going to talk about sodium triacetoxyborohydride. So, that can another important thing it can only reduce the aldehyde, but it can also have some other selectivity if you want to control the stereoselectivity. And then of course, I am going to talk about the lithium borohydride the another one in this table which is coming before sodium and the lithium borohydride can itself able to reduce ester. So, that means if you have a acid and ester here it can selectively take the ester in terms of the acid. and then I think the other one, of course I think already familiar with the lithium aluminum hydride which can reduce every single the functional group here which I have given here even more I think I have not given with the epoxide and some other functional group of course those can be also reduced then the other one is the the called a super hydride is the lithium triethyl borane, it is very powerful one very strong it can even reduce a carbon bromine bond.

Borohydride	Acid	Ester	Ketone	Aldehyde	Acid Chloride
LiBHET <sub>3</sub> (superhydride)	+ve	+ve	+ve	+ve	+ve
LiAlH <sub>4</sub>	+ve	+ve	+ve	+ve	+ve
LiBH <sub>4</sub>		+ve	+ve	+ve	+ve
NaBH <sub>4</sub>			+ve	+ve	+ve
Mg(BH <sub>4</sub> ) <sub>2</sub> (NaBH <sub>4</sub> + MgCl <sub>2</sub> )		+ve	+ve	+ve	+ve
Al(BH <sub>4</sub> ) <sub>3</sub> (NaBH <sub>4</sub> + AlCl <sub>3</sub> )	+ve	+ve	+ve	+ve	+ve
Ca(BH <sub>4</sub> ) <sub>2</sub> (NaBH <sub>4</sub> + CaCl <sub>2</sub> )		+ve	+ve	+ve	+ve
Zn(BH <sub>4</sub> ) <sub>2</sub> (NaBH <sub>4</sub> + ZnCl <sub>2</sub> )			+ve	+ve	+ve
Ce(BH <sub>4</sub> ) <sub>3</sub> (NaBH <sub>4</sub> + CeCl <sub>3</sub> )			+ve		
NaBH <sub>3</sub> CN (NaBH <sub>4</sub> + HCN)			+ve	+ve	
NaBH(OAc) <sub>3</sub>				+ve	

So, first thing I am going to talk about the lithium borohydride because of this important chemoselectivity which I mentioned that if you have a substrate have ester and acid previously, I talk about a reduction where it is selective for the corresponding acid, if you remember I talk about if borane that is taking to give the corresponding carboxylic acid. But if you take a lithium borohydride, it will be going to take ester leaving the acid again what is happening why lithium borohydride is selective to the ester in place of carboxylic because once you have a lithium borohydride going to you are using it is in case of acid, what is happen it is going to form a hydrogen by abstracting this proton from here instead of going for a reduction it is go for a proton extract,

### Lithium Borohydride: $\text{LiBH}_4$

• Lithium borohydride is commonly used for the selective reduction of esters and lactones to the corresponding alcohols in the presence of carboxylic acids, tertiary amides, and nitriles. Aldehydes, ketones, epoxides, and several other functional groups can also be reduced by lithium borohydride.



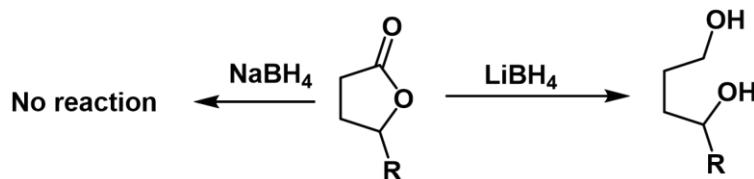
Such as  $\text{LiBH}_4$  is much more reactive over the  $\text{NaBH}_4$  which is attributed to the greater Lewis acid strength and hardness of the lithium cation

The other thing is if you have a lactone here and you want to go for a reduction then the the sodium borohydride will not go for a reduction here because it is a weaker one but once you have a lithium borohydride it is going to for the reduction of the lactone to form this diol. So, what is happening this the lithium borohydride is much more reactive compared to sodium borohydride. So, if you try to think about then you have to understand the Lewis acid strength depending on the hardness of this metal. So, you have to understand the percentage of this the hardness of between the sodium and the lithium. So, if you see the lithium will be stronger compared to the sodium that is why you can see the lithium borohydride will be stronger reducing agent compared to sodium borohydride.

The difference in the reactivity of these compounds is due to properties of both the cations and the anions. However for a particular reagent different solvents also play crucial role for its reactivity.

Such as  $\text{LiBH}_4$  is much more reactive over the  $\text{NaBH}_4$  which is attributed to the greater Lewis acid strength and hardness of the lithium cation

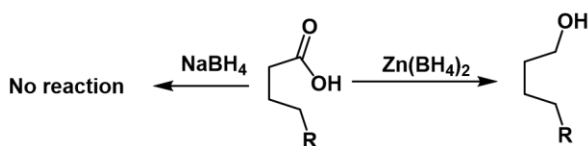
Hence  $\text{LiBH}_4$  can reduce the lactones efficiently but  $\text{NaBH}_4$  can not.



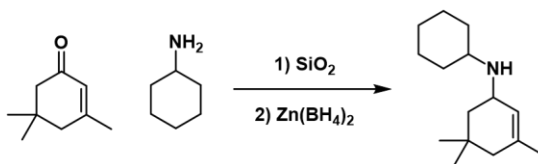
Then I am going to talk about the zinc borohydride here. So, zinc borohydride can also reduce the carboxylic acid to the primary alcohol, but sodium borohydride cannot. In presence of zinc borohydride the carboxylic acid can be reduced to the corresponding alcohol, but of course sodium borohydride cannot able to do it. Again you can think about the Lewis acid character of zinc versus sodium that is also another important factor here and zinc borohydride can be also used for the reductive amination which I am going to explain. If you have a reductive amination reaction you can also use zinc borohydride which can able to reduce the corresponding imine which is going to form here. So, it is going to form a imine first which will be which will be reduced by zinc borohydride to form the corresponding amine. The other important factor using sodium borohydride you must have seen that if you are trying to do a reduction of enone. Then using sodium borohydride you will end up getting a mixture although this will be a major means sometime depending on the substrate you might get 60:40 or of course, so by changing substrate sometime you will see a various selectivity you will get. But the problem is once you get these two it will be very difficult for to isolate,

**Similarly  $Zn(BH_4)_2$  is much more reactive over the  $NaBH_4$  which is also stronger Lewis acid character of  $Zn^{2+}$**

**Hence  $Zn(BH_4)_2$  can reduce carboxylic acids to primary alcohols but  $NaBH_4$  can not.**



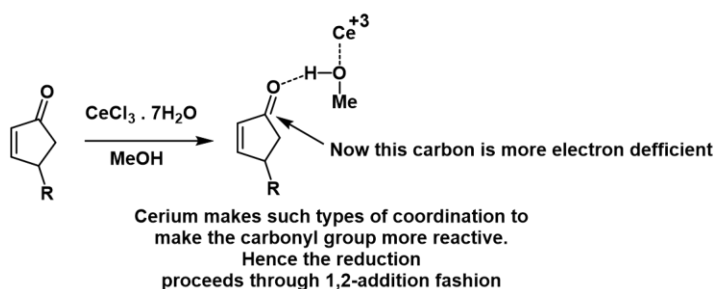
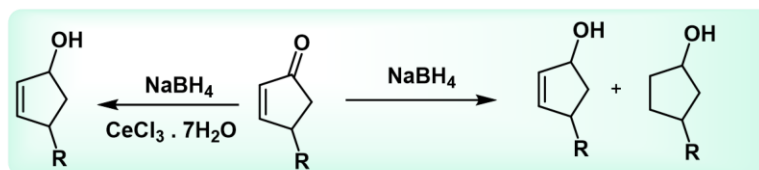
**Zinc borohydride has been found to effect very efficient reductive amination in the presence of silica.**



So that is why you have to find a condition which will give selectively one product that is introduced to the luche reagent or luche reduction, so here you use a cerium chloride in presence of methanol solvent is also very important here because once you use cerium chloride with a methanol then only you see the selectivity that it is selectively going to take to the corresponding allylic alcohol But again if you take a THF here instead of the methanol you will not see the selectivity you will still see a very much mixture. Of course, little more selectivity compared to sodium borohydride but not the exclusive selectivity that comes from adding methanol here. Because what happened the first the cerium actually interacts with the methanol oxygen atom. So it is going to first there is a coordination with the oxygen and the cerium that make this hydrogen acidic because once you have a positive

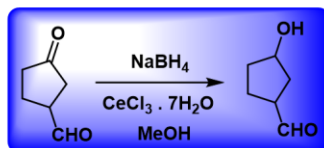
character on the oxygen you see this here. so that can coordinate with the carbonyl oxygen here once you see this H<sup>+</sup> is coordinating with the oxygen, now this carbon center is getting very much electrophilic.

**(Luche's reagent also selectively can reduce the ketone group selectively in a conjugated carbonyl system.)**

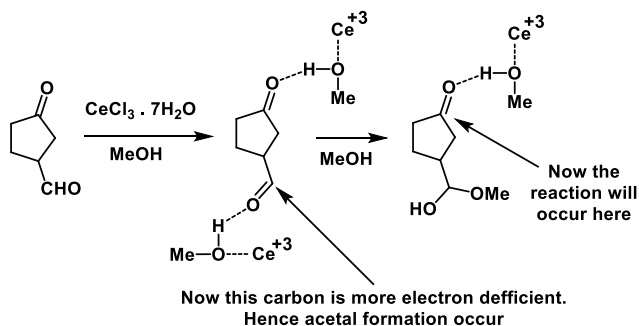


That is why you can see here it can be also happen that because of this protonation happening if you have a aldehyde and you have a this you have this aldehyde and this ketone, in this particular cases the it is end of giving the reduction of the if you see at the end you found that the ketone got reduced, but aldehyde not. You might be thinking we not understand that because sodium borohydride can reduce the aldehyde, but that is not the factor here, there is couple of couple of important thing happening here. One of the important things is that once this is So, this H<sup>+</sup> is binding with the oxygen. So, this can now form say acetal. So, the acetal formation will be faster here. So, once you know this is forming acetal, now the H<sup>-</sup> cannot able to attack here. So, you can see that here it is going to attack to the carbonyl group and at the end this can get quench to come back to corresponding alcohol,

**Sodium borohydride is sometimes used in conjunction with CeCl<sub>3</sub> (Luche's reagent). By the help of this we can easily reduce the keto group in the presence of aldehyde selectively.**

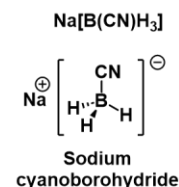






Now the other important reason I talk about the sodium cyanoborohydride. So, if you see by introducing a cyanide, pull some electron density from the boron. So, if you pull electron density then you make the region more selective. So, that is why cyanoborohydride you can see it is very selective reducing agent you can see it can able to reduce the corresponding iminium to the corresponding carbon nitrogen double bond can be reduced to form this corresponding amine here. Also you can have if you do not have a iminium, if you have a amine, if you have imine only, then in that cases if you have only imine sometime you can use a Lewis acid. So, now that can activate. So, now that can activate the imine. So, now the sodium cyanoborohydride can transfer the H- for this reduction.

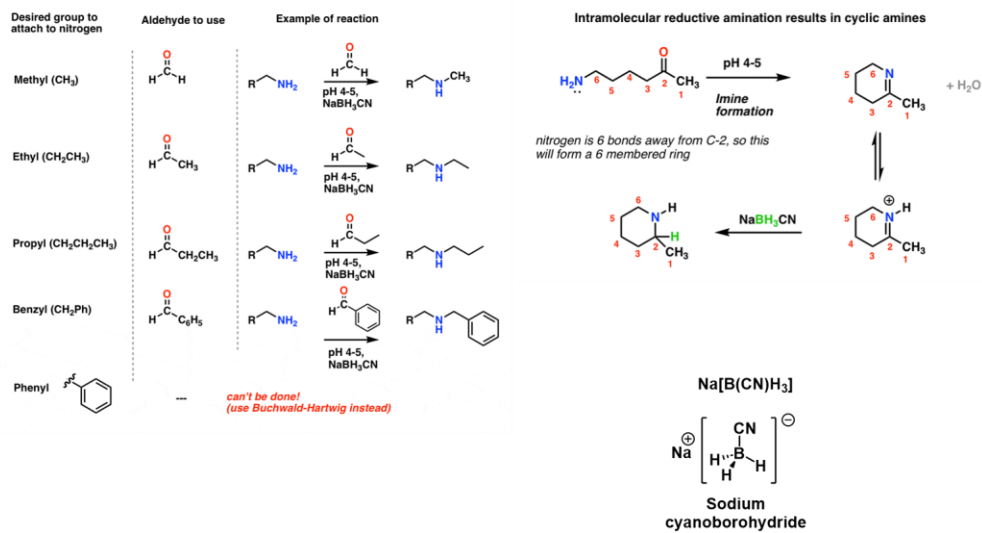
Further incorporating the electron withdrawing group to the boron center again reduce the electron density on the boron. Hence the reducing reactivity gets reduced and the reagent becomes more selective. Such as



Reductive amination by NaBH<sub>3</sub>CN can also be carried out in the presence of TiO/Pr<sub>4</sub> from imine to amine. Here the TiO/Pr<sub>4</sub> coordinate to the imine nitrogen, hence easily can be reduced.

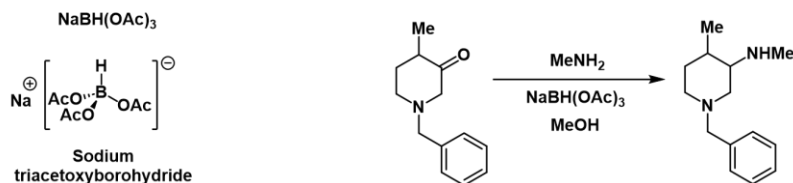
Also, this can be done in a you know if you try to make a imine in the same pot where you can use a cyanoborohydride. So, cyanoborohydride is very much stable on this pH, so now if you takes cyanoborohydride and you take amine and take a aldehyde this is called a reductive amination, you start from the aldehyde and you end up making amine here every cases you can see starting from the aldehyde you are making amine so this reaction called a reductive amination and this reaction done in the pH 4 to 5 using cyanoborohydride in case of aldehyde and amine. so in phase of this pH is what is going to happen this amine and the aldehyde can form a corresponding imine will get activated in phase of the acid that can allow the cyanoborohydride to transfer the H- to form the corresponding amine

this can not only be the intermolecular that can be intramolecular also if you have a carbonyl group here you have NH<sub>2</sub> on that same molecule you take the exactly similar condition which you end up giving you know making to the corresponding pyrrolidine. You can make an able to corresponding six-member nitrogen compound.



There is another important reaction here that sodium triacetoxyborohydride again if you see we have mentioned that the sodium triacetoxyborohydride can also do a reductive amination here. You can first form an imine using that and then if you use a triacetoxyborohydride that can also be able to make an amine. So, now I am going to talk about the other reagent called you know if you have a bulkier group here like this bulkier trialkyl group attached with the boron with this hydrogen with the BH. So, these are actually called L-selectride or K-selectride based on the potassium versus lithium. So, so these are a very bulky hydroboron, so you can see they are bulky you know H<sup>-</sup> transfer agent and these are used if you want to do some sort of a stereoselective reduction of a carbonyl group.

**Sodium triacetoxyborohydride is an alternative to NaBH<sub>3</sub>CN and also has been used for the amine synthesis**

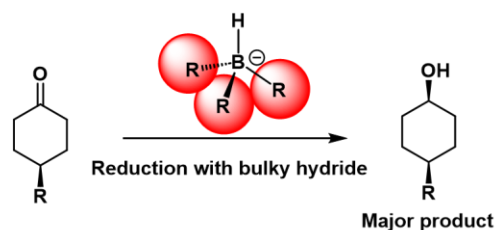


Alkylborohydrides are also used as reducing agents. These compounds have greater steric demands than the borohydride ion and therefore are more stereoselective in situations in which steric factors come into play.

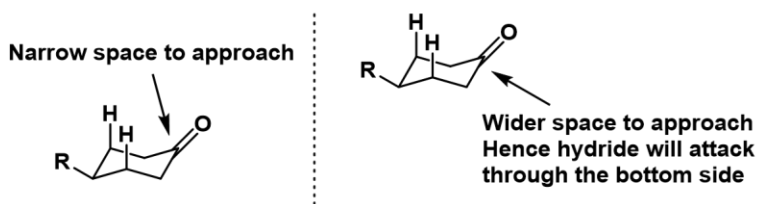


Now going to show one example here so if you have this cyclohexanone you have this position and in the four position you have this corresponding R-group now there is a if you try to draw in the chair conformation now there is a approach can be happen from this side versus the other side Now if you use a smaller H- transfer agent or the corresponding borohydride agent then you cannot get good selectivity it can approach from the either side. But once you use a bulky one now the steric between this group if you try to approach from this side then there will be the steric interaction between this group with the H and the R-group with the incoming the hydride source the corresponding borohydride will be higher compared to if it is going for the bottom phase. that will end up the selectivity in the product that means now what is going to happen if the H- is coming from this you will end up getting to this product as a major product here using this type of hinder the borohydrides.

**The stereochemistry of hydride reduction for the cyclic ketone is greatly dependent on the steric factor of the reducing agent**



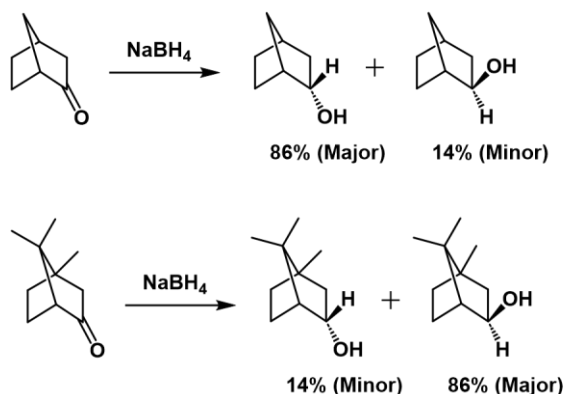
Axial alcohols are most likely to be formed when the reducing agent is a sterically hindered hydride donor because the equatorial direction of approach is more open and is preferred by bulky reagents.



Again if you see in this cases what we are seeing here now this is a depending on the structure if you see here you can get two different scenario here, you can get a 86% major product and 14% minor product here, once you bring some dimethyl group here now you are kind of blocking this the upper phase more in that case you can see what is happening

here, let's try to understand in these cases now if you think about it can the H- be approached from this phase or the top phase. So, what is happening here? Once you increase the steric bulk here, the bottom phase approach will be favourable. Once the bottom phase approach will be favourable, you end up giving this product as a major product.

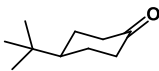

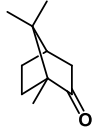
**The increasing importance of steric approach control the hydride approach.**



So, what was happening here? Once you do not have this steric bulk, now if you think about still if you try to compare from approaching from this phase versus this phase, I think previously I talked about this already that here you have a one CH<sub>2</sub>- group to sterically interact, here you have a two CH<sub>2</sub> group. So, that is why you see that approach from the this phase will be feasible like more favorable to give this product as a major product. So, there is another example here of course, you are trying to use this sodium borohydride versus L-selectride. That means again you can see the selectivity as I mentioned there that if you have a sodium borohydride you cannot get a good selectivity there, but once you have L-selectride now you can see the selectivity will be higher. because once you have this bulky group here you can see the hydride will not going to approach from this side, hydride will approach from this side giving you this product with a very good selectivity. Again, it is you know same for the other substrate as well. Again I think you can see here 86% versus 99.6% exo selectivity. So, once you have these dimethyl groups here now this approach will be less favourable. So, the bottom approach will be more favorable giving to the exo product with 99.6 %.

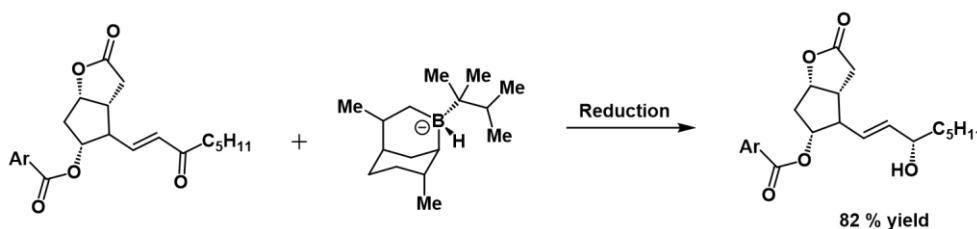
**Comparison among the substrate bulkiness and the steric factor of the reducing agent**



Reducing agent			
	% axial	% axial	% exo
NaBH <sub>4</sub>	20%	58%	86%
L-selectride	93%	99%	99.6%

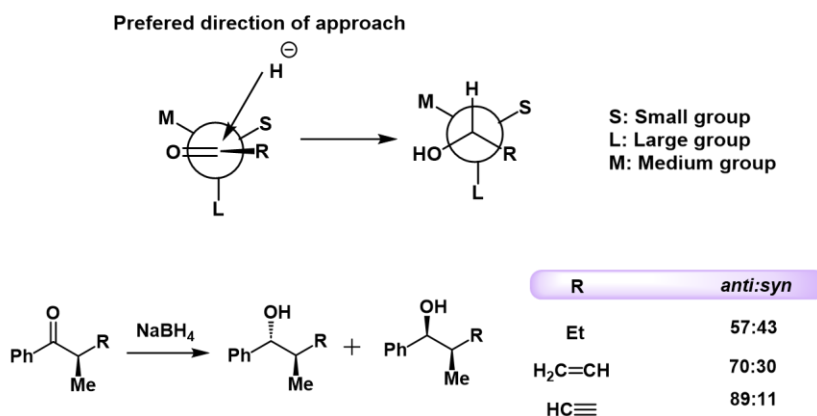
There is an example here in this particular substrate you have this lactone and this  $\alpha,\beta$ -unsaturated ketone. So, you can see this is sterically bulk here now this BH can act to the what is happening the BH adding to the corresponding ketone here because the approach you can see if you are getting to the this particular product as a major product here. So, now if you try to control the diastereoselectivity of the product you have to try different sterically hindered group. So, that you can able to control the approach of the hydride ion.

**Steric factors arising from groups that are more remote from the center undergoing reduction can also influence the stereochemical course of reduction. Such steric factors are magnified by use of bulky reducing agents.**

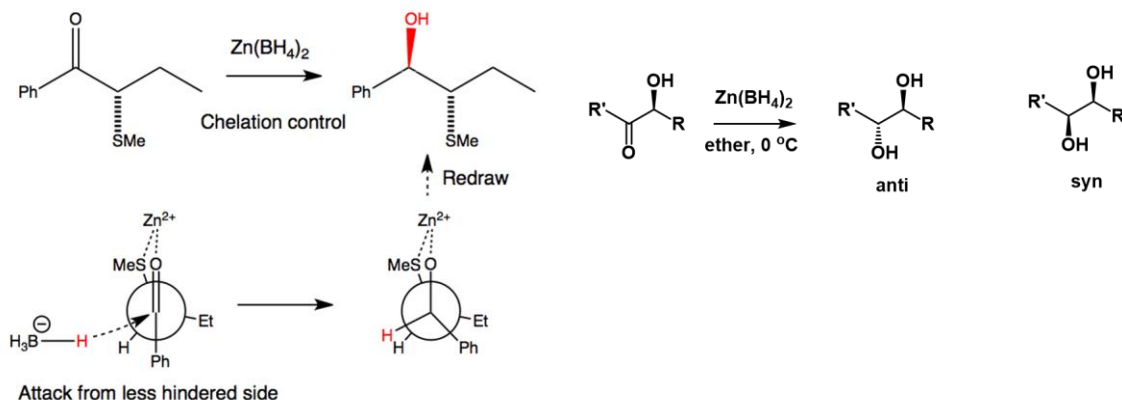


So, here we can also take chiral center here, now we can able to explain them from this the Felkin conformational model that I think you have already learned that in case of Felkin model have a stereochemistry here, we can think there is three different group here. You see H, R and M then you know R is a bigger than you can say this is a large, this is small, this is medium and then now if you try to draw this way the the H- of the nucleophile will approach such a way from this phase to interacting only with the smaller group here. to form this product. So, you can see here in case of ethyl you do not have good selectivity of this anti versus syn means the approach of the nucleophile does not have a much more selectivity still you come to the alkyne which is a smaller group to giving the anti selectivity higher compared to the syn . So, you can see here this will be because clearly you can see it the once you see the size of this alkyne is getting smaller, end up giving to the corresponding product. So, that means what is happening the R-size is giving R- size is controlling the selectivity which is supposed to see from this model also.

**The stereochemistry of the reduction of acyclic aldehydes and ketones is a function of the substitution on the adjacent carbon atom and can be predicted on the basis of the Felkin conformational model of the TS**



Then the zinc borohydride one thing forgot to mention that if you have some sort of a SMe-group or OH next to the carbonyl group here then that can form a chelate with this oxygen. So, it can form some sort of a chelate here. In the corresponding transition state you can see although you might think that both the SMe and oxygen is kind of top each other, but they are forming a chelate with the zinc. Now that is allowing the H<sup>-</sup> to come this phase to facing this H here which is a smaller to giving this product, means this is the corresponding anti product as a major product here. So, that is why in the both the cases using -SMe or -OH end up getting to the anti product as a major product.

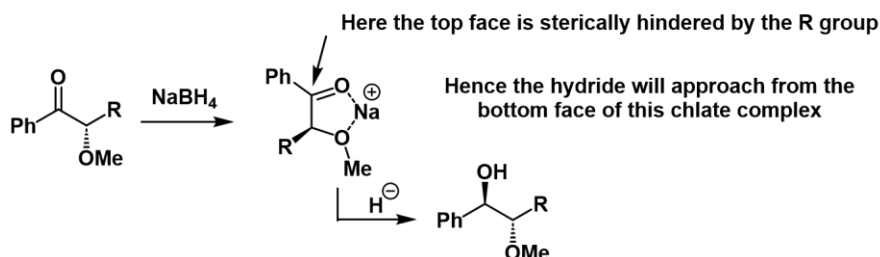


Again, I think if you have a sodium borohydride also you have -OMe group and you are using sodium borohydride also it was found that in the sodium borohydride also there are some sort of compensation happens and it forms the corresponding anti product as a major product.

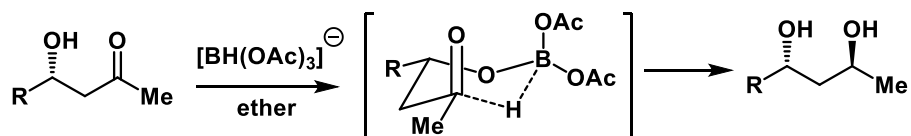
The stereoselectivity of reduction of carbonyl groups can be controlled by chelation when there is a nearby donor substituent

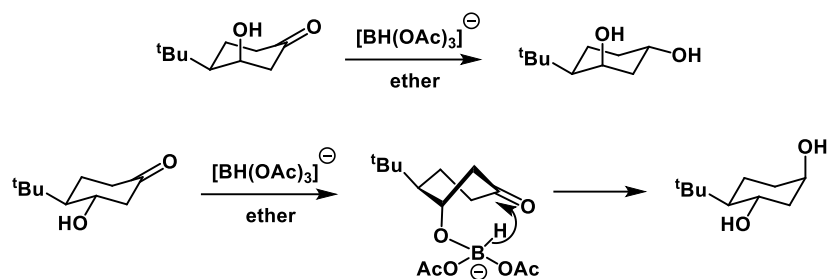
In the presence any electron donating group  
A complexation among the donor group, the carbonyl oxygen, and the metal cation can establish a preferred conformation for the reactant.

The hydride has been delivered from the less sterically hindered face of the chelate



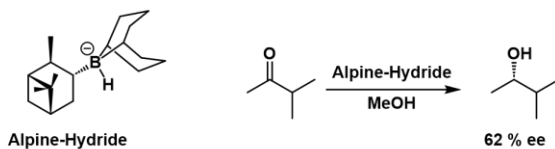
The other important thing is as mentioned the sodium triacetoxyborohydride once you have this. So, you have a  $\beta$ -hydroxy ketone. And now if you do a reduction of this there is two different possibility it can either from this one or it can form. So, it could be syn or it could be anti. So, this could be you can see they are anti or they could be syn. Now that can be control using this triacetoxy group. so what is happening once you have this triacetoxy, the triacetoxy first actually reacting with this alcohol here so this is reacting with the boron and throwing up one acetate from that from there, now if you see this corresponding transition state it is actually thrown one of the acetate and this kind of bound with the boron this bond is formed, so now what is going to happen if you see this alcohol actually in the bottom phase, now the hydride going to transfer from the bottom phase where the OH is there, That's why if the hydride is transforming from the bottom phase, then you end up forming this alcohol from the top phase, that is why you end up getting to the anti product major product here, also if you use the triacetoxy here again you can see there is -OH group here that means you can see that will going to form this BOAc there will be two other OAc and there will be one other So, now this hydride will be coming from the top phase giving this product as a major product which is shown here.





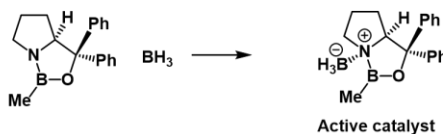
So, I talk about you know the different type of racemic reduction of the carbonyl compound using this different type of borohydride source. Now, I am going to talk about the asymmetric that means the carbonyl have two different phases re and si-phase. Now, if you able to control that means now if the oxygen can form some sort of a chelate with this boron which is electron deficient, it can transfer the BH- the H- through a particular phase of the carbonyl group then you can end up getting an enantioselective alcohol, so that is why this was developed from it is called Alpine- Hydride again you have already used you can see this type of compound. you have already seen before so using this alpine-hydride you can use So, you can see here what is happening this is you have this chiral backbone here in both the side. So, now this can transfer the H-atom to this carbonyl group through the top phase to give this alcohol, with the 62% and then there are several other reagent was developed for this asymmetric reduction of the carbonyl compound using the hydride reagent, the one of the other important one is this the CBS-catalyst the Corey, Bakshi, shibata catalyst where it actually this catalyst was synthesized the corresponding amino acid proline and then once you take this catalyst and then the BH<sub>3</sub> that boron actually bind with the nitrogen from this N<sup>+</sup> and BH<sub>3</sub><sup>-</sup> so this becomes active catalyst once is bound with the BH<sub>3</sub>.

**Enantioselective Reduction of Carbonyl Compounds with Chiral Boranes**



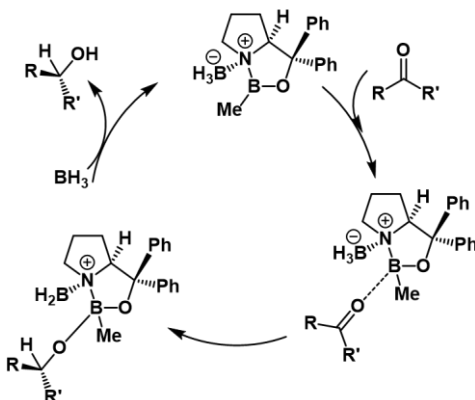
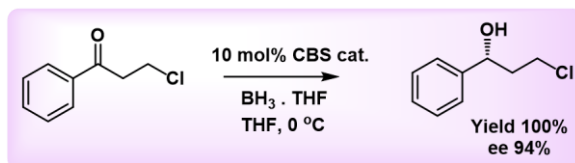
**Enantioselective catalytic Reduction of Carbonyl Compounds with Chiral Boranes reagent**

CBS- Catalyst





So, here is a mechanism here from starting from this compound you can see this is the acetophenone analog using the CBS catalyst in  $\text{BH}_3$ , you can able to get 94 % ee. So, what is happening here as soon as the boron bind here this active catalyst generated in situ in the reaction which now actually once you have a carbonyl group the carbonyl started coordinating with this boron here. So, the carbonyl started coordinating with this boron here for once this happening. Now, one of the phases of this is two different phases here one of the phase is getting blocked because if I think in this transition it will be difficult to see, but once you see a three dimensions of this you can see that this is one of the phase is getting blocked. So, that will allow the hydride to be transferred to the other phase to get the product with very high enantioselectivity.



So in this part i talk about the several different borohydride reagent, talk about the reduction using borane, talk about using the cyanoborohydride the reductive amination and also I end up talking about the asymmetric reduction using the chiral borohydride in a catalytic amount so in there are the references here and again thank you so much for coming to the class. I am going to see you guys in the next class thank you.