Molecular Rearrangements and Reactive Intermediates in Organic Synthesis

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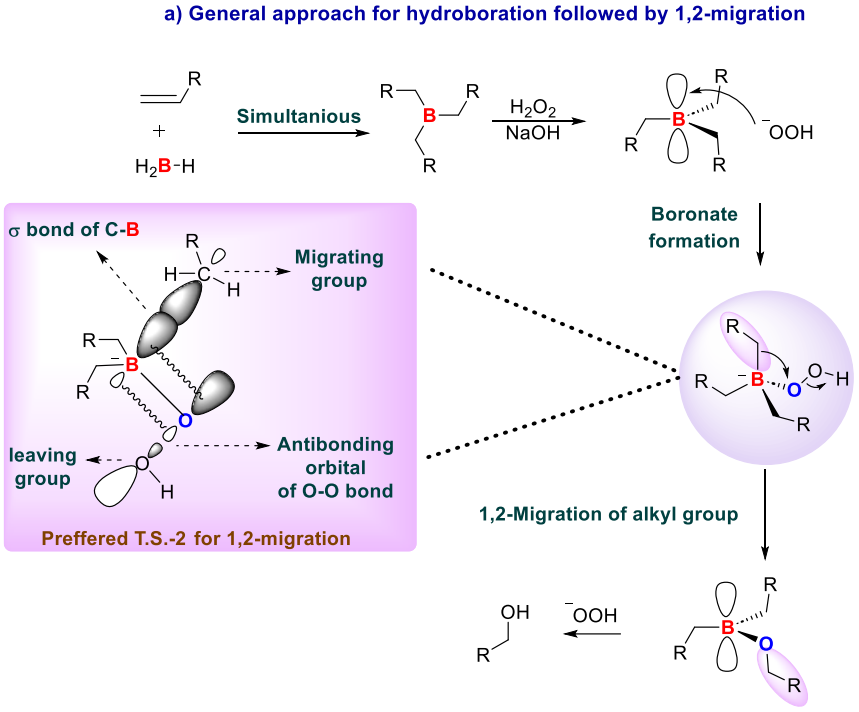
Lecture 46: Organoboron

Welcome back to this NPTEL online certification course of molecular rearrangement and reactive intermediates. In the last couple of classes I was talking about organoboron compounds. So, I talked about very important reaction like hydroboration oxidation, their enantioselectivity and their the stereoselectivity. Also I talked about the suzuki coupling reaction in the last class and the allyl boron compounds the reaction with aldehydes. and then also I think I talk about the the other important reaction is the Hayashi coupling using organoboron compound the one for addition reaction and also about the boron wittig reaction. In the today's class I am going to talk about there are lot of reaction with organoboron compounds which goes via a 1,2 metallic rearrangement. We call it as a 1,2 like 1,2 migration. We generally see a group from the boron going to migrate to the next carbon ok. So, we are going to start about some of this reaction ok and also I am going to talk about other reaction like petasis reaction and some of the other important chemistry using organoboron. So, let us try to understand what is this 1,2 migration I was talking about or what is this 1,2 metallic rearrangement and then I am going to talk about different types of them different types of 1, 2 migration of course, these are the huge topic I am just going to give you a brief idea about it and Then the Matteson homologation one of the I think name reaction for 1, 2 migration reaction and you still find some question coming in the competitive exam from that. And then of course, one of the example from the Agarwal group who have contributed lot in this area and then the zweifel olefination and the the petasis reaction.

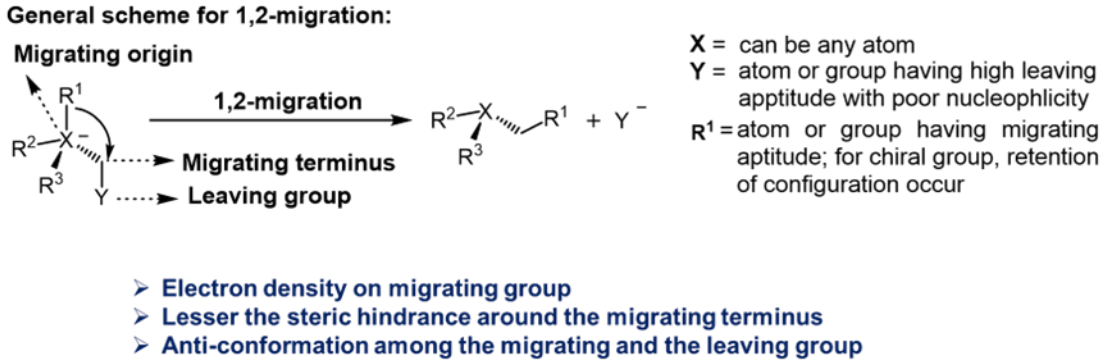
So, let us try to understand first what is 1,2 migration I am talking about. I think if you remember when I was talking about this hydroboration oxidation chemistry first thing we understand there is a syn addition of the boron and hydrogen to the olefin. And then after the consuming 3 equivalent of olefin you end up making to this trialkyl boron compound. But then once you treat with H_2O_2/NaOH you generate this OOH minus in the hydro peroxide anion. So, that is going to attach to the empty orbital of the boron to form this boronate complex. So, once this boronate complex formed you have learned in the previous slide that these R group going to migrate from boron to the oxygen because this Oxygen is acting as a leaving group. So, what is the concept you are learning here that if you have a boron and having a R group ok, having some sort of a boron 8 species then if

you have a X group here and there is a leaving group So that means, if you have a leaving group here then the important thing is now this R can give electron density. to the corresponding sigma star orbital of this xl leaving group bond.



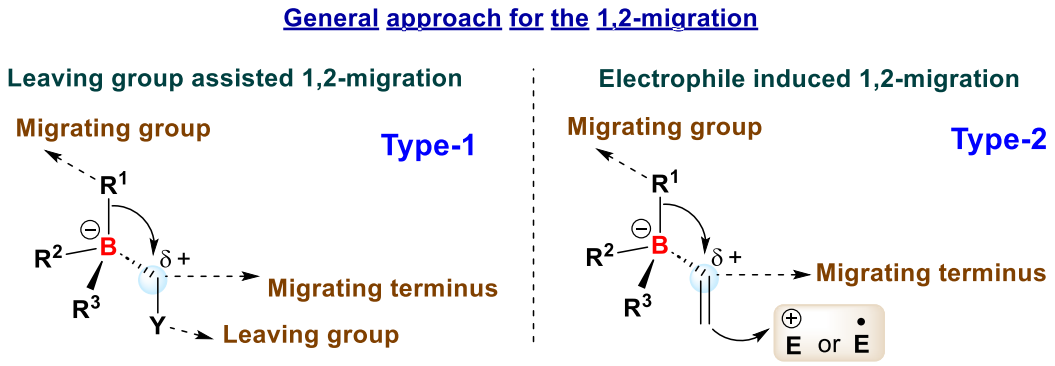
If that is happening then this 1,2 shift is happening to get to the corresponding product. So, that is how you come here in this step first and then after there will be two equivalent of another hydro peroxide going to come and form all the way to this $(B\text{-}OR)_3$ and that is going to hydrolyze to the corresponding alcohol. So, the important thing is here in this particular transition state you have to understand there is a anti-periplanar relationship between these groups. So, then you can see they are literally in a parallel you can think about these two are in a parallel and these are. So, the leaving group and these are actually anti because you can see from here this is the group which is giving electron density to the sigma star and this is the bond which is getting So, this anti-periplanar relationship is very important when there is a 1,2-shift is happening.

I think I talk about that in case of carbocation chemistry when I talk about pinnacol rearrangement if you remember then when this 1,2-migration is happening every cases this anti to the periplanar rearrangement is very important for this 1,2 migration to take place. So, you have learned about oxygen in case of the hydroboration, but further this chemistry was developed and people started using carbon instead of oxygen there.



- Electron density on migrating group
- Lesser the steric hindrance around the migrating terminus
- Anti-conformation among the migrating and the leaving group

Now, if you have a carbon here instead of oxygen and you have a leaving group, then very similarly the boron from the group from the boron will migrate from the boron to the carbon to get to the corresponding product. But now the reaction depends on the electron density of the migrating group that is the the guiding factor. Then the laser the steric hindrance the around the migrating terminus. So, what is the steric hindrance around the migrating terminus? So, that can also hinder some of this migration and most of them importantly the anti-confirmation among the migration group. So, if you not able to achieve their anti-confirmation it will be very difficult for this migration to happen the rate will be much lower.

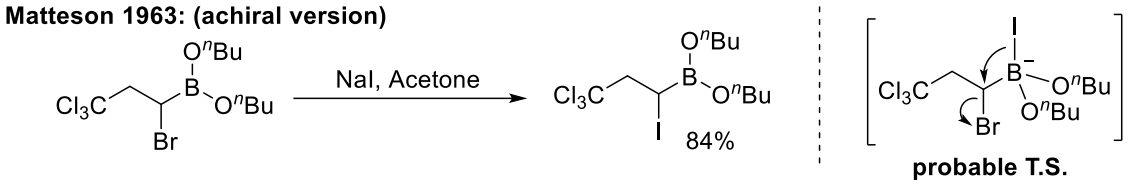


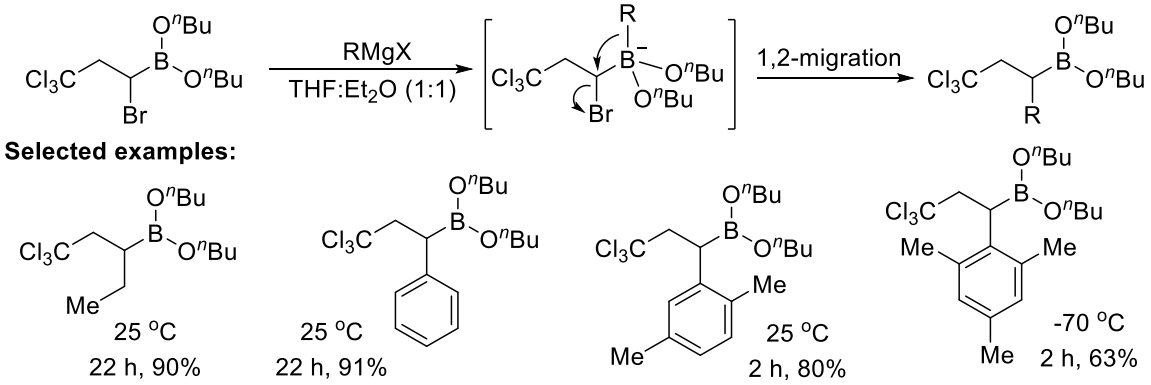
Now, there are several different type again this could be a talk about a entire semester about this 1,2 migration using the boron. and our group are also working in this area. So, there are couple of different type, but I am just going to bring two important type here that first is here that if you have a carbon here which have a leaving group.

So, we are talking about the carbon which we attach to the B minus having a leaving group here, then this can participate in a 1,2 migration this is type 1. Now, there could be a type 2, type 3 and type 4, but I am going to just restrict you to the type 2 now if you have a olefin here. So, now you have a vinyl boron compounds, but the boron is in a

boronate. So, now if you can activate this double bond with a electrophile. now that is going to generate some sort of a delta positive charge that is another thing.

If you generate the carbon attached with the boron in a boronate complex what I am talking here that if you have this groups here and you have a carbon here where if you are you can able to generate some sort of a delta plus character. So, that could be if you have a leaving group then of course, once the leaving group is getting out you are generating a delta plus character. If you have a olefin here and you are giving electron density to the electrophile you can generate some sort of a delta plus character here. So, that delta plus character going to allow you to this migration to happen. Also there are example where you can able to in a radical here you guys have already learned the radical chemistry. Now, if you can have a radical here which can add to this double bond that will be generating a radical next to this boron carbon and now that radical it can become a carbocation. If someone can take the radical from there and become a carbocation that can also allow this bond to migration from the boron to the carbon to take place.

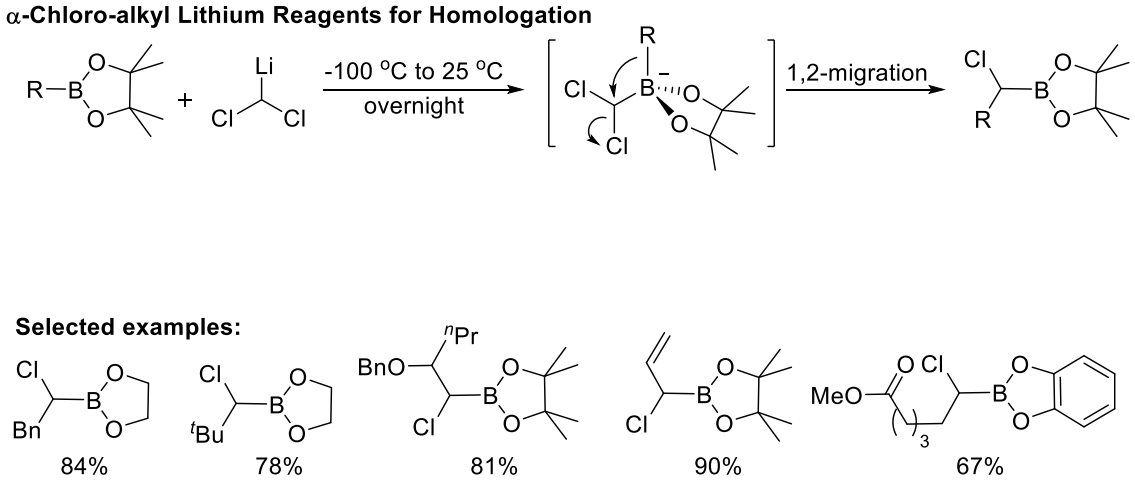




Original the chiral version of from the medicine group if you treat the sodium iodide and the acetone what is happening you are forming this compound very fast and one of the explanation for there that the I minus is attacking the boron. forming the boronate complex and then the I actually moved from the boron to the bromide to get to this compound with a very good rate. So, it is not like a simple SN_2 reaction here it is actually some sort of a reaction with a boron first to make a B minus and then a migration from the boron to the carbon ok. So, now you can see the it could be if you have a something

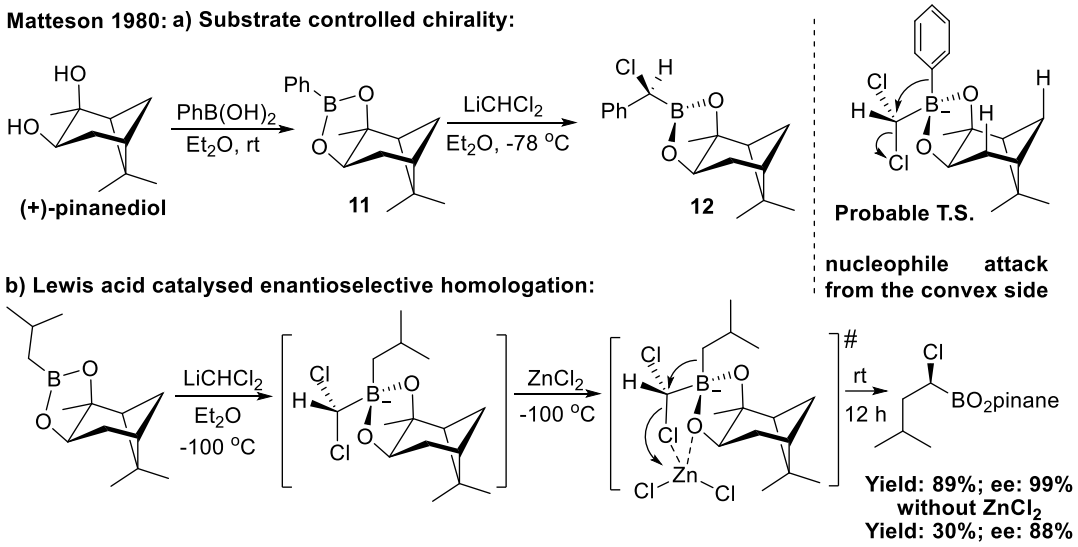
like that. So, we are talking about some sort of a alpha halo organoboron compound. So, we are talking about alpha halo organoboron compound. So, it could be organoboron esters you are seeing it is these are boron esters here. So, if you treat it in a Grignard reagent this R minus that is going to attack to the boron to form this boronate.

Now, that will allow this R to migrate from this boron to eliminate this to get rid of this in the leaving group which is the bromine to get to the corresponding product after the 1, 2 migration and there are several different examples for this. Now, the next example here



that previously we have learned if you have a alpha bromo organoboron compound.

What about if you can bring some organolithium? So, your lithium has a corresponding carbon halogen bond that means, that can also act that means, your organolithium has this living group then that can add to the boron to form this boronate complex first. Now, the R group from boron can migrate here to get rid of the chlorine to form this corresponding alpha halo compound. So, now, we are synthesizing it ok. Now, we are synthesizing the corresponding alpha halo compound again if you take this compound and take another equivalent of Rmgx correct may be in R dot you can replace this chlorine by R dot. That means, you can do simultaneously two reactions. and some of these examples here you can make different type of this alpha halo boron compound from this reaction. Again I think one thing is important in the previous slide I think I should mention you we are going a reaction at minus temperature such a low temperature for this reaction ok. You can understand this as a this is a very reactive species because you have a lithium with a carbon halogen boron So, that is a very important thing and in this reaction. So, that the reaction you want only the it can bind with the boron it cannot do some other reaction. So, that is why you want to make sure the reaction is very low temperature for it for getting a the chemo selectivity right.



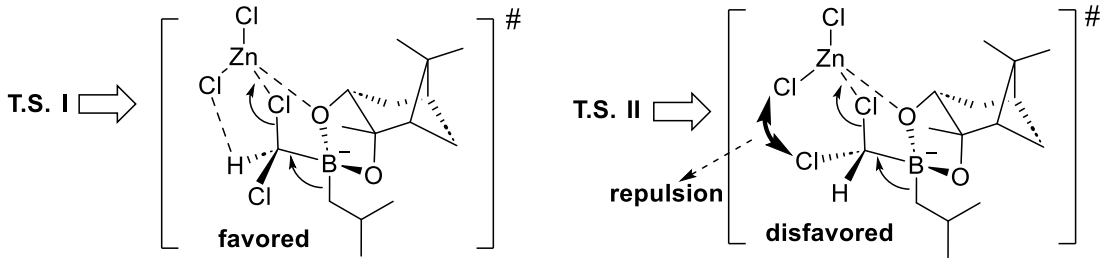
There is another reaction now with the idea is ok we have learned 1,2 migration for this corresponding di chloro compounds. now getting this corresponding alpha halo organo borne compound enantioselective. For that you can able to the matteson actually take this idea that if you take pinanediol and if you take a phenyl boronic acid then you can make this corresponding boronic esters Now, if you can see now you have a chiral group attached here. So, that means, the borne ester has become chiral very similar to you see we have talked about the chiral borne in case of the allylation reaction correct the using allyl borne compound. So, if you treat with the very similar lithium $CaCl_2$ in place of diethyl ether -78°C, now you can able to make this center chiral ok after the 1,2 migration ok. We are going to talk about a very important thing in this reaction to improve the enantioselectivity at the beginning this enantioselectivity was not great. What they find out after several scanning that if you use a zinc chloride in this reaction as additive, then you can improve the enantioselectivity to very high enantioselectivity. So, what is the role of zinc chloride here? So, one of the problem if you try to understand in this reaction. So, you can see with and without. So, you can see the difference in ee and also the yield. So, there is a great difference of yield and ee.

So, we try to understand what is happening here because you can think about in this reaction let us try to understand the two different transition state here that once you have this. So, this is a pro chiral center you can think about there is a two chlorine.

Now, you want to make this pro chiral center. So, that means, there is a two chlorine you can see one is here up one is down right one. So, this is up this is a down. So, if you think about these two different chlorine each of them going to migrate for want to migration

going to eliminate going to make a new chiral center there. So, that means, if you can able to control this diastereomeric transition state that means, if you can make some sort

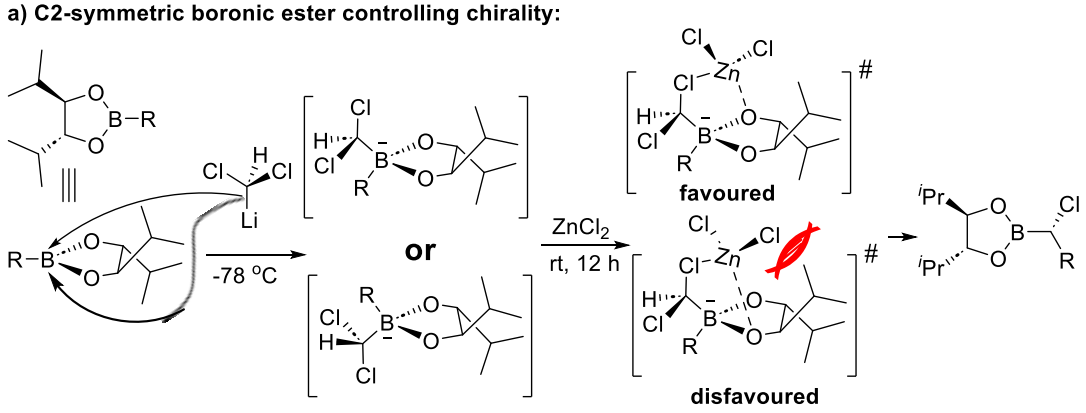
Probable T.S. for hige enantiomeric excess:



of a chelation control then you can able to get to two different type of transition state

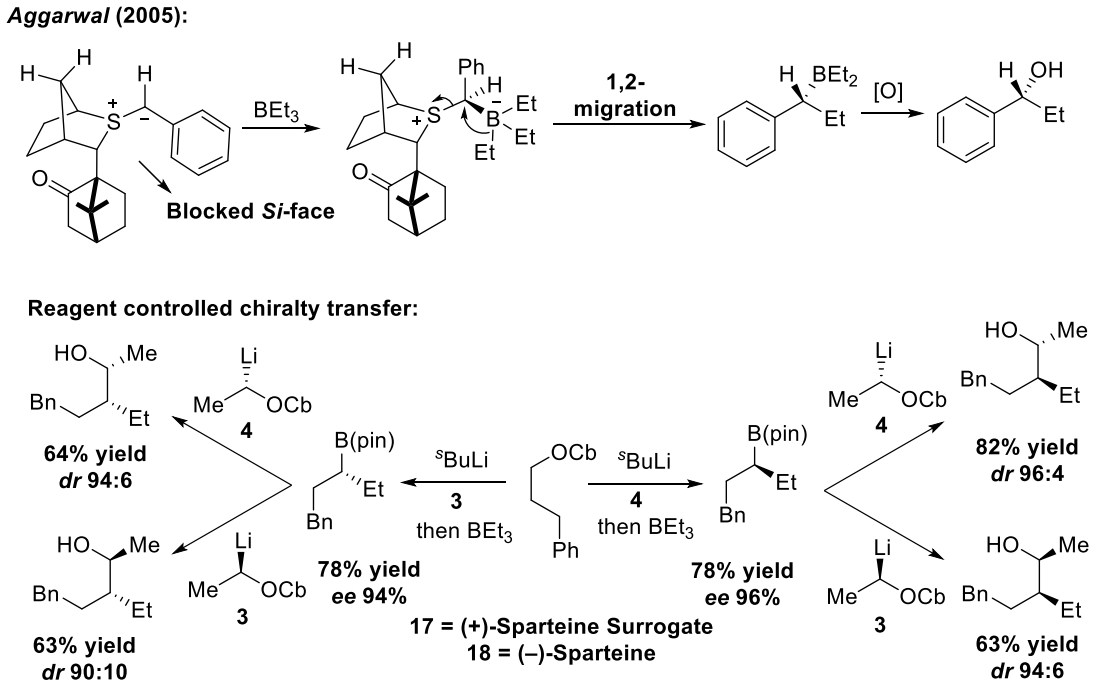
where one could be higher energy than other and in that way that chelation model can allow you get to a one of the enantiomer with a very high enantioselectivity. So, you can see one of the transition state here you can see these chlorines are close enough for a that is why there is a repulsion In other cases that is not happening because they are interacting with this hydrogen. So, now you can differentiate between this pro chiral chlorine. So, the 1, 2 migration can happen only to eliminate this particular carbon chlorine bond to get to the corresponding product with high enantioselectivity.

a) C2-symmetric boronic ester controlling chirality:



Here there is an example if you use a C_2 symmetric boronic esters if you C_2 symmetric chiral boron esters and this corresponding lithium it can generate this corresponding boronate complex here and now if you treat with the zinc chloride here. So, now you are can see now you have used a chiral diols. So, these are the diols which are chiral. So, you synthesize them and then you make a chiral boron esters and then if you treat with this corresponding lithium it form this boronate complex. And now if you treat the zinc

chloride in the room temperature again these are the thing you can see there are two different transition state is going to happen. In a one cases you can see there will be



isopropyl group here they can interact with the chlorine as well. So, these type of interaction now going to differentiate between two different transition state.So, that can allow the reaction to go through this particular transition state to get to this corresponding alpha halo boric ester with a very good yield and and very good ee.

Then later the Agarwal group have done in a lot of contribution in this area they have initially started with this type of acting the sulfur as a leaving group here again you can see this is again you are this is already have a chiral auxiliary here you are generating again a minus plus. So, the minus can act to the boron triethyl boron to make the boronate species. Now, the ethyl group can migrate and the sulfur can act as a sulfur can eliminate to form the corresponding chiral di alkyl boron compounds. the trialkyl boron compounds which can be oxidized to the corresponding alcohol using the 1,2 migration chemistry and their group also find out. So, this is mostly you can see this is a mostly substrate control you are bringing this corresponding in the the minus which is chiral which is adding to the trialkyl boron and there are something called a reagent control. That means, you now start with the chiral boron compounds. So, you either start with the chiral boron compounds or you start with the achiral boron compounds you have two option here. Now now in this cases we are talking about I think generation of a chiral lithium. So, I already talked about that in the organolithium chemistry that this is the OCb now depending on say there is a isopropyl So, now you are using spartan to come here I think

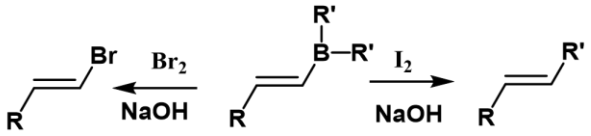
as I mentioned that if you have a lithium which is getting stabilized here through the chelation with the oxygen and you have this chiral spartan which is making a complex with the lithium that is allowing you to the abstracting this proton from here to generate a chiral lithium here. And that chiral lithium once you treat with the organoboron compounds what is going to happen if you take this and if you use the organoboron compound this going to add here correct. So, this is a case you have started with that if you take this type of organoboron compounds with this lithium that can participate in a 1,2 migration ok. Once you have a chiral lithium you can suppose a phenyl bipin also let us take some phenyl boronic esters then what you going to make you going to make the lithium is chiral. So, I am just trying to show you that ok. So, that means, if you lithium is chiral then this is the center already chiral you have this phenyl here and this OCb can act as a leaving group ok and you have a R. So, now, this can this phenyl or the R group can come here to get rid of this OCb to get to this product. So, now, you end up making a chiral boron with a phenyl here ok. Or you can use just a simple lithium not the spartan using BMIDA you can make this simple lithium using sec butyl lithium and now you can use a chiral boron compound. So, if you use a chiral boron compound you do not have to use another things chiral you can you can use that, but of course, you if you use that you can able to make all the different combination what you want of course, in that is the possibility to make a diastole manic cases because you have a two chiral center. Now, if you want to control the two chiral center you can generate a chirality from the corresponding OCb and you can bring the chiral So, that way you can able to control these two chiral center you can able to get all the different the enantiomers. So, you will able to get all the different diastereomeric pair and also the enantiomers. This four

different compound if you have two chiral center you can end up getting these four compounds there will be two of them will be enantiomeric pair and all these four compound can be isolated using this strategy.

Again the other things I am going to talk about that how you activate the the double bond here using a electrophile. So, that can be done using a electrophile like iodine and that is going to introduce you with the zweifel olefination that was discovered in 1967 by Zweifel and co worker. Then if you take a alkyne and if you go for a first if you go for a the hydroboration and if you treat with iodine and in place of a base then you can end up forming this corresponding Z selective olefin. So, we are going to come back to that.

Invention:

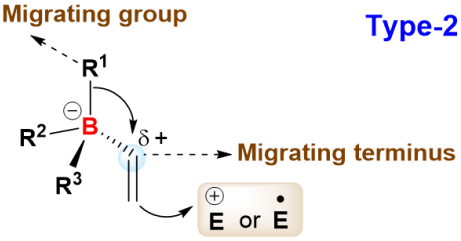
This invention was initiated from the concept of bromination-debromination of vinyl boronic ester, which ended up with vinyl bromides in the presence of sodium hydroxide via a stereospecific *trans*-elimination



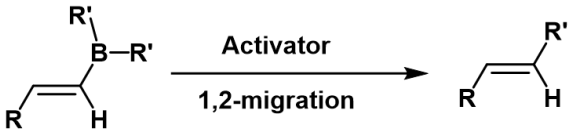
But surprisingly, the iodination of vinylboranes does not produce corresponding vinyl iodides, instead ensued in migration of one alkyl group from boron to the adjacent carbon to give substituted olefins

Electrophile induced 1,2-migration

Type-2



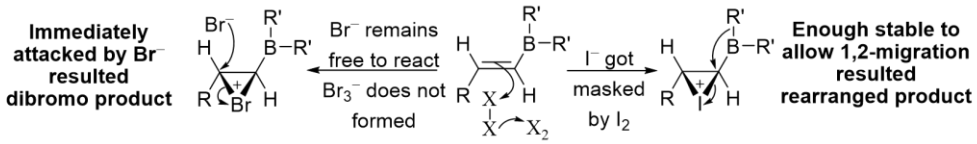
Zweifel olefination: In 1967, it was discovered by Zweifel and co-workers



It can be generalized as the olefin functionalization enabling incorporation of a wide array of groups *via* the coupling of vinyl metals boronic esters.

So, I think in this reaction what is happening I think this will be R dashed will be here I think this is this will be a Z olefin here. So, what is happening at the beginning if you take this corresponding vinyl boron compounds and treat with iodine and NaOH you end up making the corresponding Z olefin. and now if you treat with the bromine and NaOH you do not got to the corresponding vinyl bromide. So, there is two thing happening I think one of the important thing is when you have NaOH when I think we have to understand the corresponding mechanism how this reaction is happening here. So, in the next slide I am going to show you what is the important of using a bromine versus iodine.

The anomaly behavior w.r.t. alternation of halide from bromine to iodine can be anticipated by the stability of the *in situ* formed strained three-membered halonium ion intermediate.

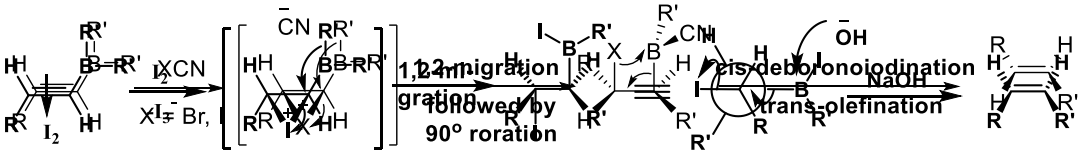


More polarized iodine, having higher energy σ* antibonding it can accommodate another iodide *via* 3c-4e bonding resulting in a stable triiodide. Hence in halogenation, both the bromine and iodine construct halonium ion, but iodide stabilized via I_3^- but bromide does not form Br_3^- and react immediately with the bromonium ion through the less crowded site in *anti*-fashion, ending up as a dibrominated product. .

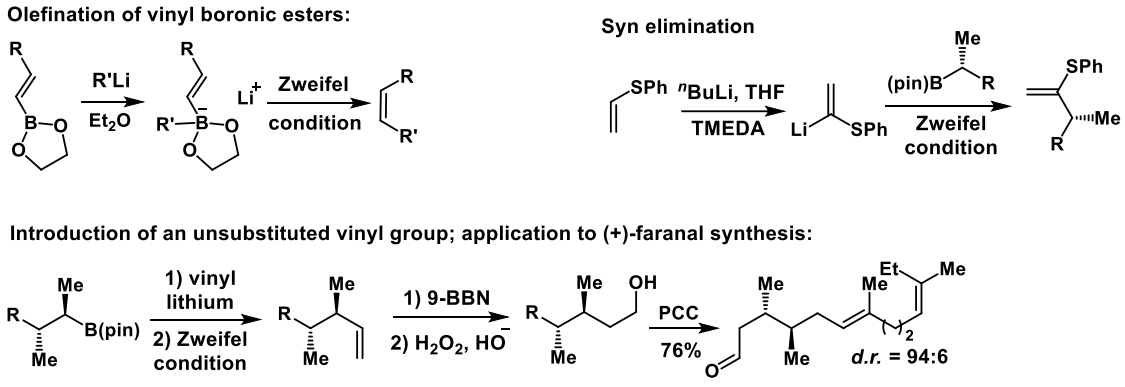
You can see here we can we are clearly going to show you that if you use a bromine here then you will end up getting to this corresponding bromonium and then the the BMI is going to open up the bromonium because this bromonium are not stable. But if you have a iodonium here then you can see ok. So, the it is going to get stabilize by forming this I_3 minus here ok. that is not possible in case of the bromonium ok. So, that is how this corresponding the iodine intermediate will be stabilized that will allow this 1 2 migration from the boron to the carbon to take place. So, this is a olefin activation happening first this is the iodine is coming to the double bond forming a iodium getting stabilized and this 1,2 migration is happening ok. After that there will be elimination going to happen to form the corresponding product here what here what you are seeing starting from this compound once you treat with this I_2 it is going to go for this iodonium you can see this reaction also there will be base that can make this boron as a B minus ok and this can allow this 1,2 migration from this boron to the carbon opening of the iodonium and then you can see now there will be a trans or anti elimination you can see there is iodine here, there is a boron here So, they are opposite to each other they will going to participate in a trans elimination to form this corresponding Z-olefin, but that could be a E-olefin if you

a) General scheme for the iodine mediated *cis*-olifination *via anti*-deboronoiodination

General scheme:

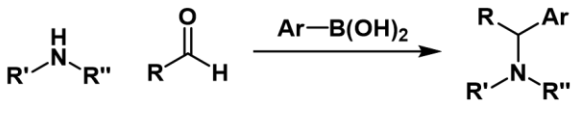


can use this cyanogen bromide. Using that what is going to happen it is going to first form the bromonium, but the CN minus can attack to the boron here you do not have a base. So, it is going to form now this boron going to be become electron deficient. If you remember I talked about the sodium cyanoborohydrate cases also. Now, this X can give electron density to this boron and going to participate in a syn-elimination. They can participate in a syn-elimination to now it going to form the corresponding E olefin. There are several example of it I am just going to show some of the example starting from this corresponding vinyl boronic ester. If you treat it with the R dash then you can form this corresponding boron species. Now under the Zweifel condition using the iodonium and the sodium methoxide you can able to make corresponding z-olefin.



It can be a syn elimination can be happen in this particular compound. Now if you can form the corresponding lithium And now if you use this we can see in case of that you will be able to see the under the Zweifel condition you will be able to get to this corresponding terminal olefin. Again you here you do not have the E and Z selectivity. The other example you can take this type of chiral boron compound vinyl lithium under Zweifel condition you can introduce terminal olefin. So, this is another important thing that you can in this reaction you can also introduce terminal olefin. by bringing a vinyl lithium. So, if you have a chiral boron compound you take a vinyl lithium that will form the boronate complex from here. So, let us write down that if you have a chiral center you

The Petasis reaction (alternatively called the Petasis borono–Mannich (PBM) reaction) is the multi-component reaction of an amine, a carbonyl, and a vinyl- or aryl-boronic acid to form substituted amines



It was discovered in 1993 by Nicos A Petasis

have a boron here Bpin then you are generating one vinyl boronate species ok. Now if you treat with the corresponding the zweifel condition then this vinyl group will be transfer as you have seen. So, now there will be not E and Z, but this vinyl group will be get into the attached with that chiral center. And then now if you can take the vinyl group you can go for another round of the the hydroboration oxidation and you can able to synthesize the corresponding natural product.

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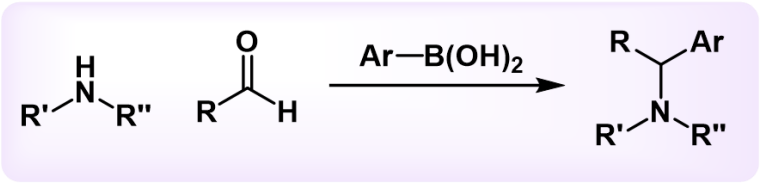
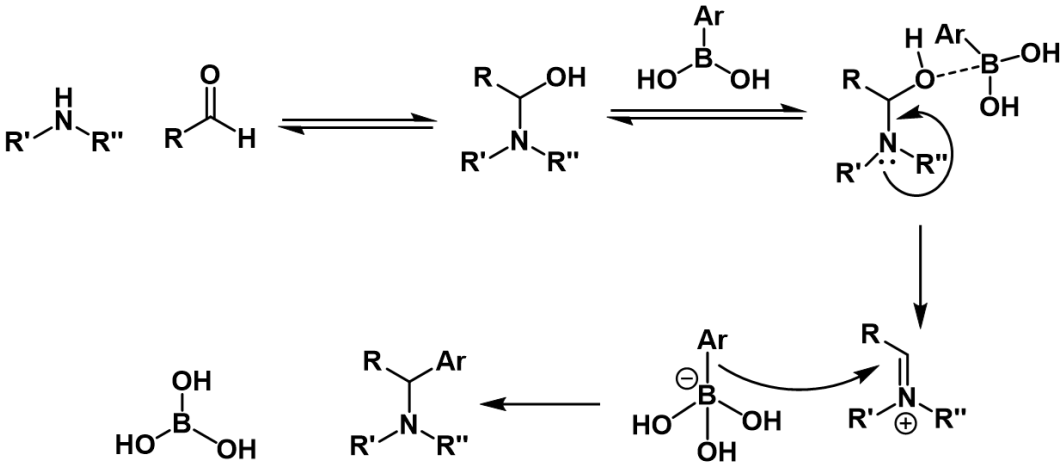
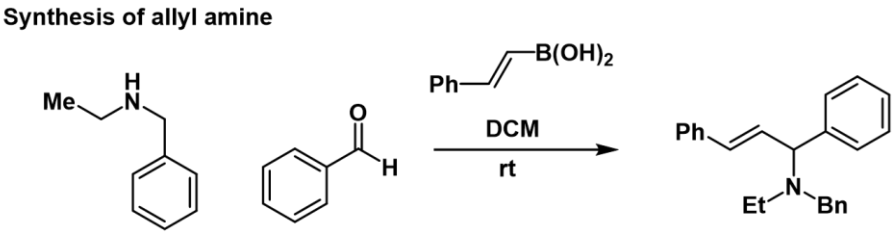
The other important reaction using organoboron compound is the Petasis reaction and we are going to see that that one two migration still going to work here. So, so this is a mostly a multi component reaction and you can see this reaction can be called a Boronomanich reaction. So this reaction was discovered by Nikos A Petasis in 1993. After that this reaction become really famous lot of different example was done even the a lot of this asymmetric and the diastereoselective condition was developed. So, this is a multi component reaction because you can see there are three different component one is

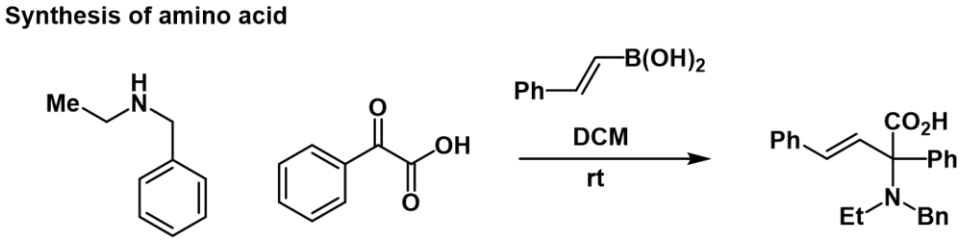




aldehyde one is amine another is boronic acid to get to a secondary amine.

So, mechanistically there are different type of aldehyde was developed it could be sometime you will see that the aldehyde could have some other groups like some other group attached here which can act as a coordinating group you can see it could be a OH could be NH some other things going to be here. which can act as a coordinating group to the boron sometime it can work with simple aldehyde also. But mechanistically first





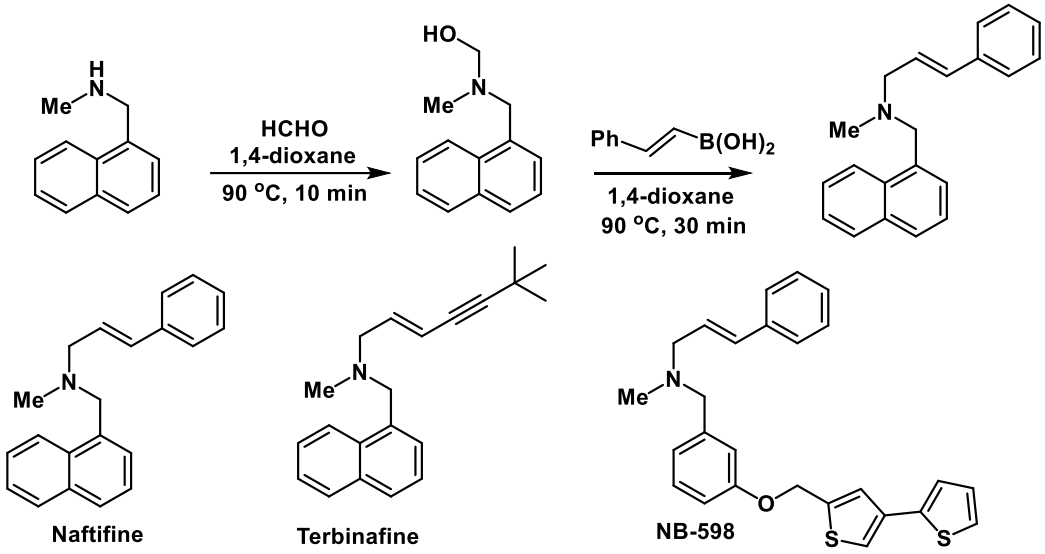
going to happen that if you have a amine and a carbonyl compound aldehyde it will going to form the corresponding imine correct. So, first thing it is going to form this one by attacking this nitrogen to the corresponding carbonyl group and then the boronic acid you go from this OH it can this oxygen can bind with the boronic acid ok. And so, there is two different type of mechanism written in the books you can go to directly to the imine to the iminium you can say it is after the OH from here once it lose the water it will form the iminium and you are forming this corresponding allyl boronate species.

Now, this can be transferred here through. So, this allyl group is acting as a very much some sort of a nucleophile to act to the corresponding amine to get to this type of product. So, this is could be a one type of mechanism there is other type of mechanism which is mentioned that in this particular time when you have a OH here that can bind with this boron. So, you can see this is a OH. So, it is binding with the boron forming a B minus and now this aryl group can participate al group can take part in a migration from this boron to this carbon ok. So, it can it can migrate from here to get and then keep this carbon oxygen bond. So, that is also mentioning in some cases.

Again there is some example you can see synthesis of allylic amine can be done very easily from there you can start with this corresponding amine and benzaldehyde phenyl vinyl boronic acid in the boronic acid and you can get to the corresponding secondary amines. there are some other example to synthesis amino acid now the question I was

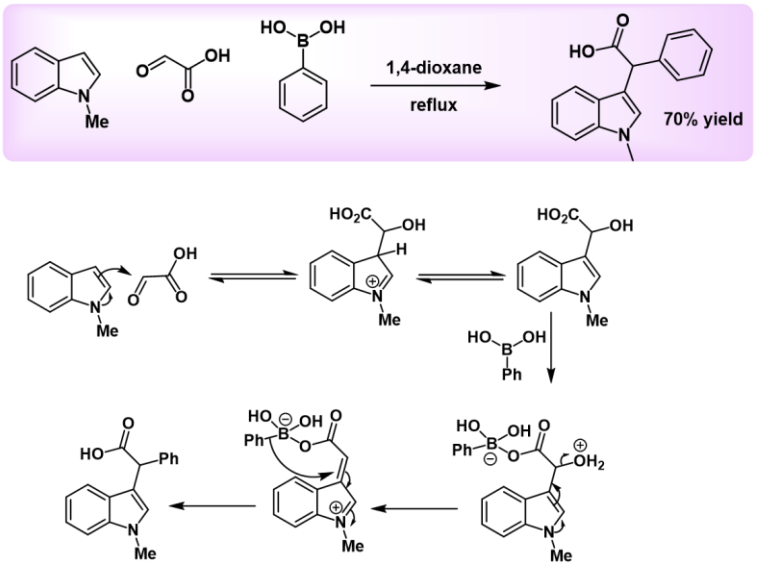
telling you the lot of times you bring a carbonyl with a group like a acid. So, what is going to happen those acid group can or sometimes there will be OH group they can act as a coordinating with the boron. So, that can coordinate with the boron to form the corresponding boron species. So, if you use the vinyl boronic acid it will going to get to the corresponding. So, now you are able to make to the corresponding tertiary amine and as well as this is a amino acid because you have amine and the carboxylic acid.

Yeah first thing again I think you can see this formaldehyde dioxane. So, this is synthesizing of a marketed drugs which is the naphthene using a vinyl boronic acid. So, it can get to the corresponding product with a very similar mechanism and this chemistry was used for synthesis of further marketed drugs and bioactive compounds. Then here



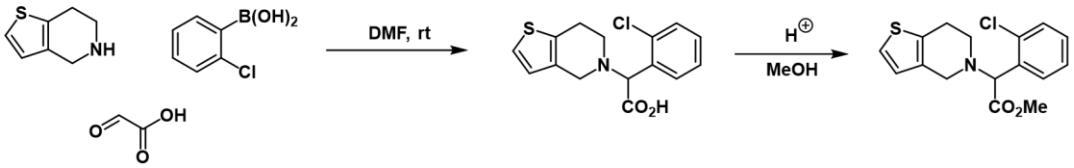
you can see there is an example of the of the synthesis of indole 3 carboxyl by using the petasis reaction here first thing is you can see the once you have this. So, this this carbonyl is very much activated because it is next to a carboxylic acid group which is pulling electron density. So, aldehyde so, the indole you have learned that indole is going to add take a electrophile from the C_3 position add to the corresponding ah the carbonyl group first forming in this species which can after take proton get to this corresponding indole. Now, the borning acid comes into the play ok. So, the boronic acid can able to protonate this to get to this type of intermediate species. Now, it is allowing this 1, 2 migration to take place to neutralize this imine to get to this corresponding product.

Synthesis of indole-3-carboxylic acid derivatives



There are other example for synthase of bioactive compounds here I think again you have this corresponding secondary amine and you have this carbon with the corresponding acid and you have the aryl boronic acid. So, to get to this corresponding product which can be convert to the corresponding ester which is this ah the clopidogrel ok. So, that is

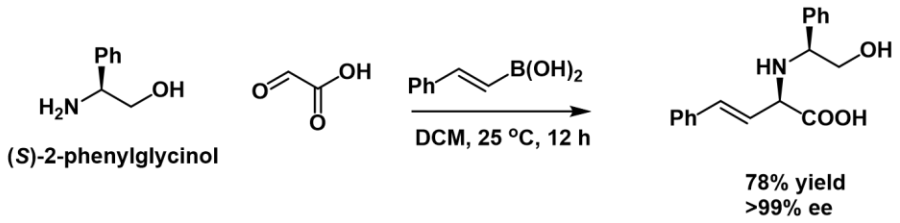
Synthesis of Clopidogrel, an antiplatelet agent,



the compound can be synthesized.

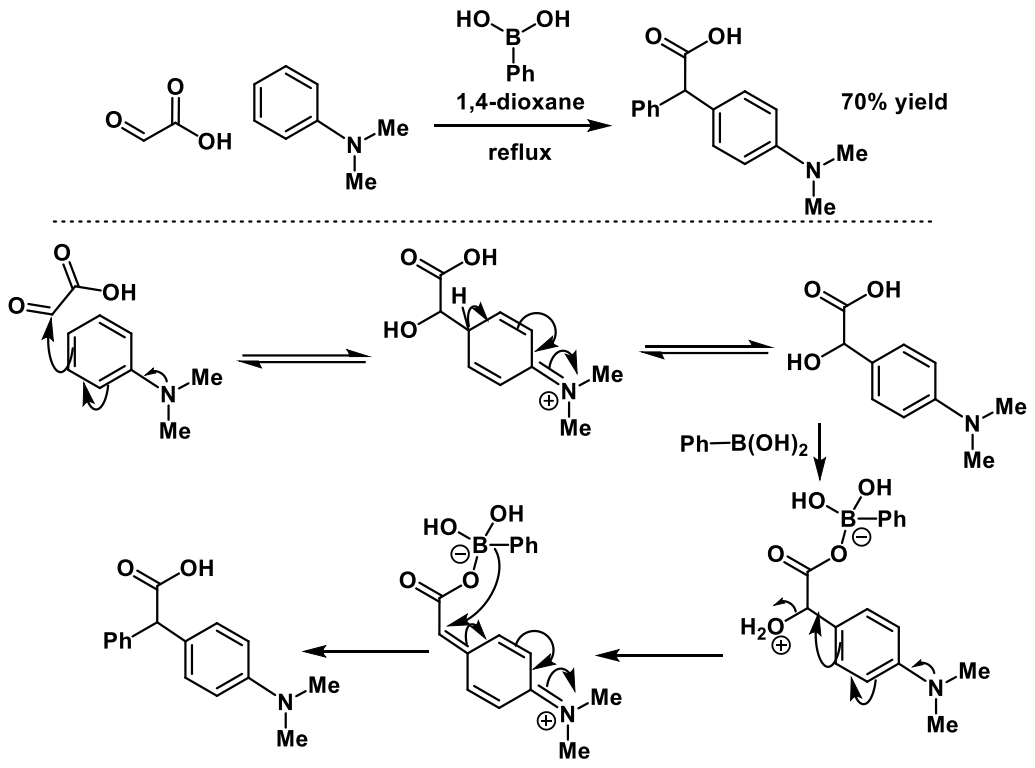
Again if you start with this corresponding chiral amine now you can able to control the the chirality of the in the product this chiral center will be even intact ok. Now what is

The Petasis reaction exhibits high degrees of stereocontrol when a chiral amine or aldehyde is used as a substrate. When certain chiral amines, such as (S)-2-phenylglycinol, are mixed with an α-keto acid and vinyl boronic acid at room temperature, the corresponding allylamine is formed as a single diastereomer.



going to happen here you end up seeing this product what is you end up this this partgoing to be get introduced in the product correct. So, so this is your starting material started with this is the part got introduced. So, now you can able to control you can able to get to the 99% is a mechanism again I am just trying to show you the mechanism here because what is thing happening here now you are trying to do some sort of a de-aromatization of this ring at the beginning to first the reaction to take place very similar to the reaction with indole. So, this is the reaction with the corresponding carbonyl compound taking place and then once you once you are going to re-aromatize it now the phenyl boronic acid going to bind with the corresponding carboxylic acid as I was telling you that if you have a carboxylic acid the boron acid going to bind with it from the boron complex and now you can see that this OH the at the same time it can also protonate this OH to a H_2O this can now this nitrogen can pull the electron density de aromatized and from this sort of intermediate where the phenyl group can transfer from boron to this particular carbon here to get to this product. It is a very interesting transformation you can see starting from this compound you are literally introducing this entire group in the para position.

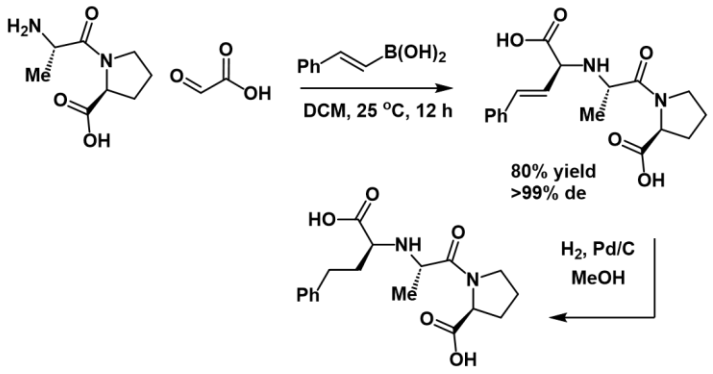
There are more example for synthesis of the biological active compounds again you can see in this particular example you can clearly see here that you have this amine have a



here it is a primary amine here which is reacting with this compound under the petasis condition to get to this corresponding product. You can see this is again there are some more example here you have this boronic acid, you have this the corresponding aldehyde with the carboxylic acid, you have corresponding diamine here and you can see if here what is happening.

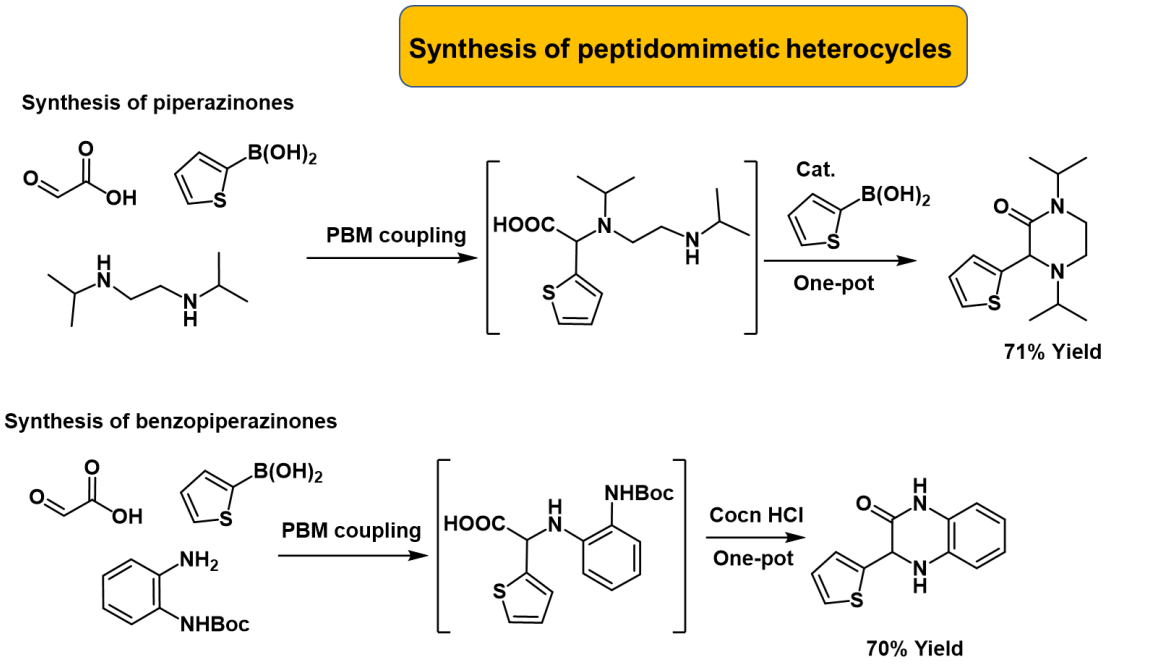
Synthesis of iminodicarboxylic acid derivatives

When used as nitrogen nucleophiles, amino acids can furnish various iminodicarboxylic acid derivatives. High diastereoselectivity is usually observed, and the newly formed stereocenter usually share the same configuration with the starting amino acid.

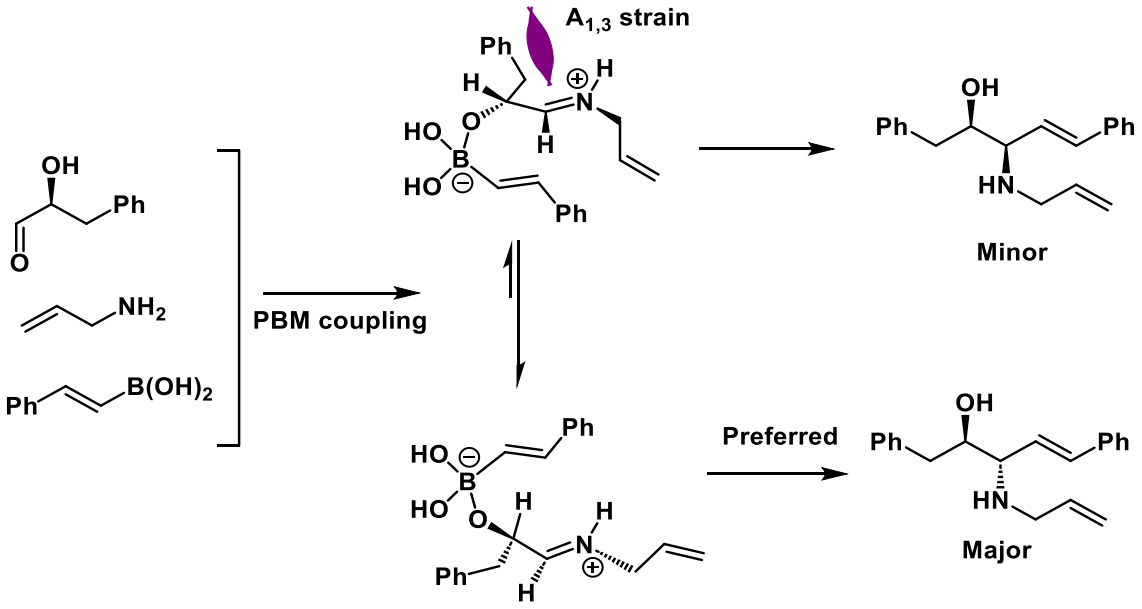


First there is a the petasis reaction first there is a I think the coupling of this with this corresponding ah in the intermediate which is forming here ok. And then there is a petasis

reaction happening first in this part and then what is happening now you have the next a NH can able to react with this corresponding product. So, you can see now I think there is a coupling between this amine and acid which is catalyzing by the borning acid. So, borning acid catalyzed that this amide coupling reaction to get to this similar thing happening here as well. First there is a petasis reaction then there is amide coupling.



Again in some cases there is a particular compound with a a chiral center here. As I was



telling you can do this reaction with a hydroxy group also which can also be kind of directing some of the transformations. So, now if you have that scenario there is two

different case can happen type of transition state can be happening it could be this one or this one and this is more favor versus this. Your first thing if you remember you have this primary amine here it is going to form this iminium here and now based on this iminium geometry you can think about there is a like a double bond then there is this 1,3 allylic strain here can be make a important role here. for the. So, which can be avoided in this particular transition state to get to the corresponding. So, you can see the corresponding anti product is forming as a major product instead of this corresponding syn product to avoid the corresponding 1,3 allylic.

So, in this part I talk about ah I think the 1,2 migration chemistry, you have learned about the Zweifel olefination and then I talk about the petasis reaction, the multicomponent reaction with a boronotic reaction. Again these are the references and again thank you so much for coming to the class, I am going to see you guys in the next class. Thank you.