Essentials of Biomolecules:
Nucleic Acids, Peptides and Carbohydrates
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Lecture 08
Synthesis of nucleosides

Hello everyone and welcome back to the lecture again so in the last class we have talked about the synthesis of the nucleobases. In the last lecture we have talked about the synthesis of the purine nucleobases which has 2 rings and that is one 6 membered ring fused with a 5 membered ring and we have seen how the synthetic methodologies can be used to produce these compotes industrially as well as in the level for the laboratory use.

At the same time we have also talked about few experiments to understand prebiotic chemistry. How these molecules such kind of molecules would have been synthesized millions and millions of years ago in on earth where there was when there was no biological molecules when there was no life. So, the prebiotic chemistry when you have talked about the experiments are basically the hypothesis or the postulates actually which tried to understand the mechanism of synthesis of that larger molecules out of the smaller molecules that were likely to be present in that prebiotic earth.

Prebiotic earth means I am talking about the primordial soup which had the basic compounds or the elements the basic compounds and the gaseous compounds for example methane carbon monoxide carbon dioxide water ammonia and all sorts of the smaller molecules. And of course there was very less amount of oxygen so it is currently an aerobic condition one thing is of course we have to keep all the thymine mind is that that has been happenings millions and millions of years they were there in that in that soup.

And the environment was quite drastic that time it was pretty high temperature and then a lot of electric spark were used to be there so the very drastic conditions now when we when you look at the experiments and that tried to mimic those prebiotic earth are actually cannot be mimicked in exact type because of mainly of course 2 reasons first reason is that time that the reaction was happening on the earth where prebiotic earth the reaction was happening since millions sometimes billions of years time frame.

And that much time you cannot provide when you are doing the same thing in the laboratory so that is one issue. Second one a temperature and pressure very much you can create in the laboratory you can recreate the similar kind of conditions in the laboratory but time is one thing that you cannot recreate. And second is of course the degrees of freedom the earth was very much open so the molecules were floating all around high very high degrees of freedom for the molecules and the liquid that was there we call it primordial earth or primordial soup.

And when you do the same thing in the laboratory in a small container your degrees of freedom are really restricted so the molecules cannot float around or cannot roam around as much as they used to be in the in the beginning of the earth. So, these are 2 these 2 are the issues that are associated in mimicking the primordial reactions or the prebiotic reactions in the laboratory. But so whatever I have shown here are basically the hypothesis that which suggests that the synthesis of the nucleobasis particularly may have happened in the same fashion.

The mechanism could have gone through the way that we have seen okay. So, today so I have covered the synthesis of the nucleobases both pyrimidines and the purine nucleus. So, the next thing is the nucleosides.

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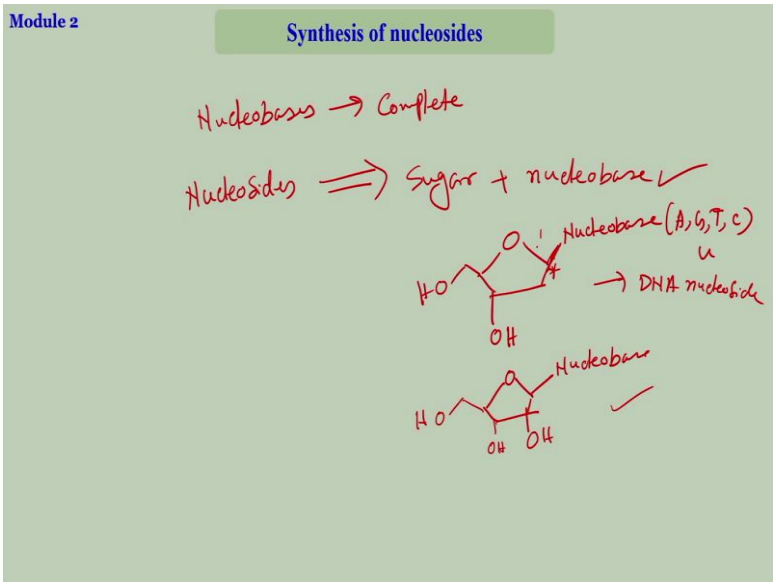

So, nucleobases are complete now so we are trying to go up to the synthesis of the nucleic acid so which means DNA the full synthesis of DNA or the full synthesis of RNA. So, we have seen how the nucleobases can be synthesized in the laboratory now comes the nucleosides. So, nucleosides basically means the sugar plus the nucleobase so this has been done. Now we have to see how you can attach the nucleobase with the sugar.

So, your target molecule is something like this here is the nucleobase it can be adenine can we guanine can be thymine can be cytosine for DNA or can be uracil for RNA. And when we are talking about DNA then this is the sugar chemistry or sugar conformation. This is the for the DNA, DNA nucleoside. When we if we talk about RNA then your target would be here nucleobase there will be hydroxyl here this would be your target.

So first we will start with the RNA one because this is more general this as the hydroxyl group present here also then we will go specifically to the DNA. So, here what is the target is you already have synthesized nucleobase. So, a target is how to connect the nucleus with the sugar moiety at this position. If you do look at the numbering this is called the C1 prime over or 1 or simply if we can write one prime position.

So, nucleobase; connection of nucleobase at the one prime position of the sugar that is your prime target now;

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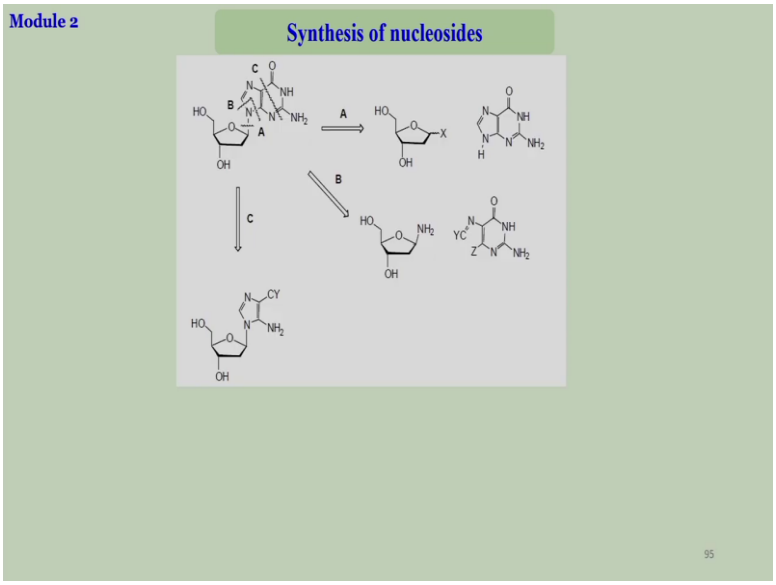

So, there can be lot of alternative methods I will show you that in this slide you can see so there can be other ways also to synthesize the nucleus with the sugar attaching at the C1 prime position. First one is of course as I have talked about this is your nucleobase that you can attach the whole thing you can attach to the C1 prime of the sugar and of course it will be kind of a nucleophilic substitution reaction.

So, therefore in the sugar moiety you need to have a good leaving group so that the nitrogen on the nucleus can attack as a nucleophile and eliminate that so you can have this compound your target molecule that is pathway b and this is what we will mostly follow in this. There can be other ways also one is so B and C pathway B and C both involve that you are synthesizing the nucleobase on top of the sugar.

So in this case nucleus was synthesized separately sugar was synthesized separately and then they were coupled together. But here you can see that using this you are synthesizing the whole of the nucleus on top of the sugar. So, with amine free again 2 ways one is keeping the 6 membered ring that and forming the 5-member ring here or alternatively you start with the 5 membered ring on the sugar and synthesize the 6 membered ring. So, both of these ways are as we have seen before but only thing difference is that you are synthesizing the whole molecules on the sugar.

We do not use these methods much nowadays mostly people use this method where you synthesize the nucleobase separately sugar separately then couple them together.

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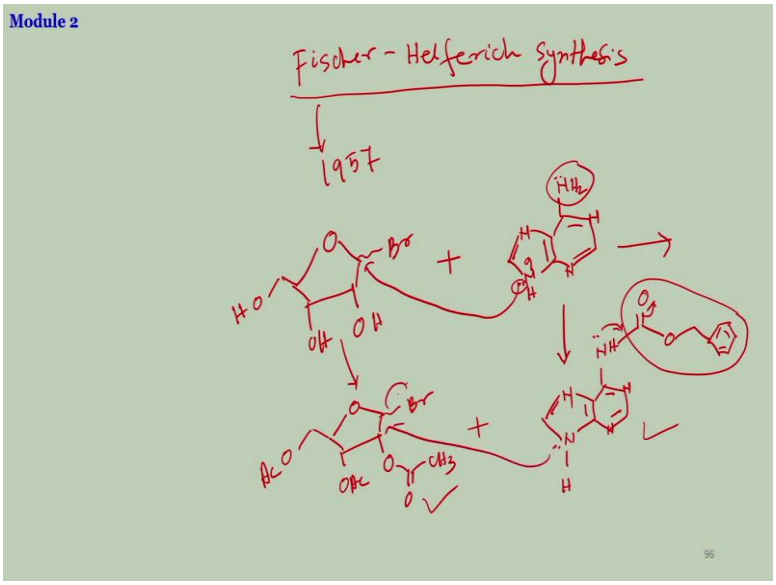

So, first kind of the synthesis was done by is name reaction Fischer Helfrich synthesis this is one of the first kind of successful synthesis of the nucleobases nucleosides and for which Fisher is very famous actually for his synthesis of the purine especially the purine nucleotides and nucleotides. And Fischer received Nobel Prize in 19 long back 1957 for his famous purine synthesis protocols. So, in this case what they have done is you have the sugar with a living group as I have said and then you start with this with a living group here.

And for example you start with adenine is amine here and you have this is what is your adenine and you try to couple them together. Now look at the problems here so what is your target your target is basically here this is the N9 position of the adenine which should react so this nitrogen basically should react this carbon eliminating the bromide. So, this is your target. Now what are the problems associated with this reaction.

First one is of course that you have the other hydroxyl groups in free form which can also react which can participate in the reactions giving you all the unwanted products unwanted side materials. So, the first need is to protect these hydroxyl groups so that they do not react or they do not hamper into your desired reactions. So, first thing that they had to do is protection of the sugar this sugar has been converted to protection means if you make the alcohol so these are basically this is secondary alcohol or secondary alcohol this is primary alcohol.

If you convert the alcohols into the acetates which is an ester basically an ester are very less reactive because esters have internal resonance within themselves. So, if their reactivity is pretty much less compared to the free alcohols. So, if you convert the alcohol to the ester that will protect the alcohol from doing the reaction. Similarly I will not writing the whole so this is AC CH 3 CO is acyl group which is usually termed as AC.

So this would be OAC and you can convert this also with OAC. So, then you can protect the other functional groups which could participate in the reactions. Now your target is only here so that the bromine can be eliminated fine. Now on the other hand you have the nucleobase here what problem could happen see your target is that N9 should react with the bromine. So, this is the nucleophilic center which means in this case if you use this form exactly then the lone pair of the nitrogen should act as the nucleophilic center and attack the C1 prime.

Now here if you see you have an amine group also which also has a lone pair of electrons and this would be more reactive because this is second amine and here the lone pair is very much it is inside the ring. So, lone pair is very much involved in the aromaticity on the other hand this is a free amine form which is more reactive. So, if you cleave this amine free then you will get the most unwanted reaction that this amine will react to the C1 Prime.

Hence you need to protect the amine also first and this can be done using NH, amine can be also protected by isolation. In this case a very good protecting group is this you can use the simple acyl also as we have seen for the other one. Here this is one protecting group that is being used for the protection of the amine kind of functional groups. Here also the same thing once you do the protection the lone pair of electrons on the amine is very much involved into its internal resonating structures.

So in their internal resonance so that the lone pair of electrons is not available to do the reactions with other molecules. So, that is how the amine can be protected. So, you have to start with this sugar with the protected ones and with the protected version of the nucleobase. Now if you mix them together you will try to do the reactions. You can pretty much expect to have nucleophilic substitution between this and this.

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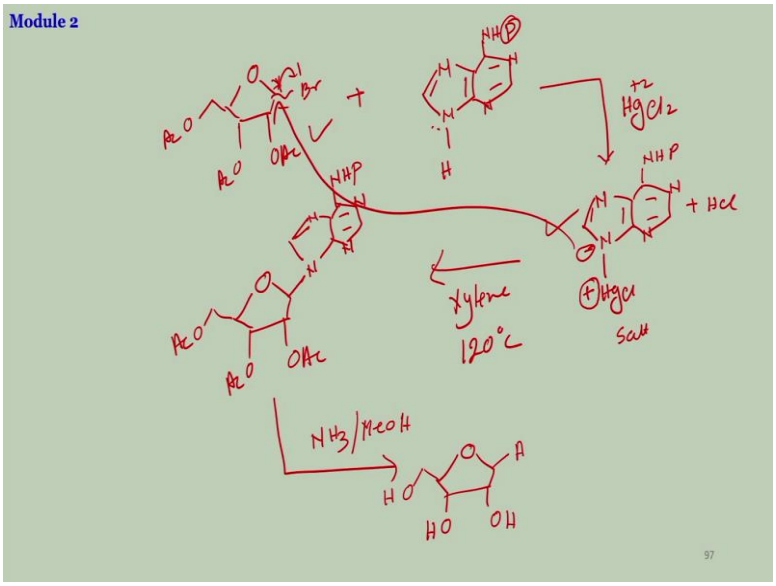

But still it does not work fine the reason is here you have OAC here you have OAC here you have OAC plus NH I am not drawing the whole production group I am writing P. So, in this case this I am terming as P for protection so, NHP. Now if you see the sugar chemistry sugar chemistry is actually pretty hard to do because the carbons are not very much reactive they are not much electron deficient carbons. So, doing nucleophilic substitution is not very facile here.

You have these are in this carbons these are prime or secondary alcohols here you have a primary alcohol in this carbon which is our target hetero atom is attached there but that does not make the carbon much electron deficient. If you have other electron withdrawing groups such

as carbonyl and all these things that would have made the carbon more electron deficient number one, so, sugar in general are not very reactive.

On the other hand nucleobases are not reactive either much nucleobases are not very strong bases so there nucleophilicity is less and the lone pair of electrons as I have told you earlier they are involved in the internal resonating structure so it is a part of the aromatic system so they are not available much. Reactivity of the nucleobases is also less therefore if you do if you mix this and this together then you are not going to get much of your product. So, the need is that you need to activate the reactivity on the nitrogen.

So, that you do by one of the old method is that if you treat this with mercury chloride then that takes away a proton here leaves you with HCl and HCL will be eliminated NHP nitrogen-nitrogen. So, you have in HCl bond this is the new bond that has been formed. Now why mercury chloride we have used I will tell you. So, mercury has high electron electro positive it is an electro positive element. So, it will try to remove the electron from there it wants to be in the positive charge form.

So, therefore this bond is not really a covalent bond it exists very much as a nitrogen minus and HgCL plus because my mercury is stable as a cation Hg+ form you have started with Hg 2 plus mercury chloride so this very much exists kind of an ionic bond less a covalent bond more of an ionic bond or you can call it a kind of a salt. So, therefore positive charge mostly restores on the mercury and that leaves you with the negative charge distinctly on the nitrogen. So, now you have on a good nucleophile with almost a free negative charge and this is the reason that it wants to release away the electrons.

So, now if you treat this molecule with the sugar and typically they do it in an organic solvent xylene 120 degree Celsius temperature that gives you the nucleophilic substitution here and you have your target molecule OAC OAC OAC here it mostly goes Nn here you have the NHP double bond that is it this compound but you have to get back your the free forms we protect it this protection you can done you can do by treating with ammonia in methanol it will detect both of these both acetylate and here.

This will leave you with free hydroxyl free OH here and here you will have the free adenine form so you have your adenine synthesized.

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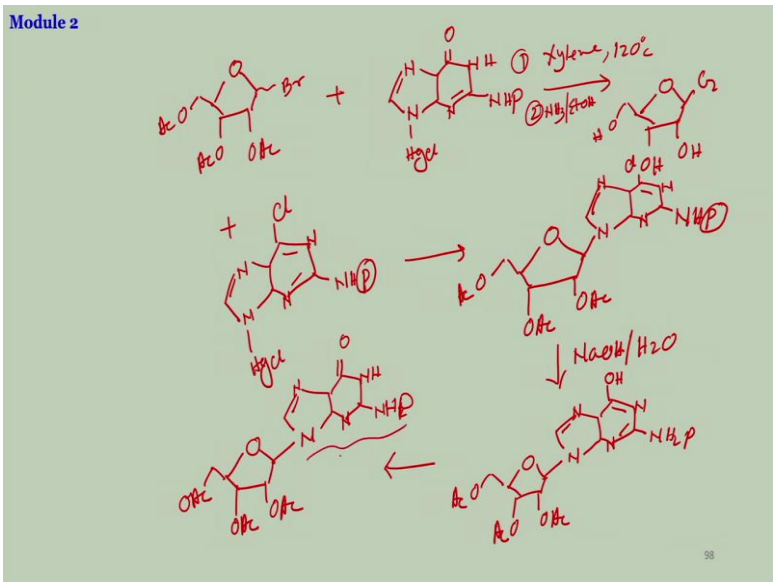

Now similarly if you want to synthesize the guanine for example you start with this OAC protected OAC this is also protected plus you can start with the guanine which is this amine H and here instead of H of course you have to use the HgCL same treatment xylene 120 degree Celsius and you can have your guanine. Of course this is after so it is not only guanine this is the 4 step second step is you have to de-protect everything else that can be done by using the same way ammonia in ethanol or methanol will give you the OH all the way it should be coming here.

There is another way actually to synthesize the guanine instead of instead of using this if you use that gives a better result actually that is why I am showing. Here instead of using the free guanine if you use this form this derivative of one in I am sorry here the NH2 requires a protection the same protection of course NHP so NHP and you instead of using the keto form you start with the chloride there and HgCL then what you get is this molecule.

Here you have the CL N N NHP here you have OAC OAC in here in double bond here now you have to get rid of the chloride if you do the hydrolysis in sodium hydroxide a little bit water then that will replace; you will have the nucleophilic substitution kind of thing here you will have OH there and once you have H of course this is the ienolate form so it will immediately go back to the keto form. So, this will go to the keto form in here you have NH NHP in here that will double bond here this so you have your guanine and then you can go for the de protection. So this is your guanine.

Now I will just briefly explain that say you have started here if you look at the stereochemistry of the sugar C1 carbon we have started with the arbitrary stereochemistry it could have been the after plane it could be the down the plane. So, both cases doesn't matter what is the stereochemistry here whether this is up the plane whether the bromine is down the plane. For ribose sugars you always get the nucleobase which comes up the plane.

So independent of the stereochemistry of this you always get the nucleobase of the plane which is your desired stereochemistry of the nucleoside. In the nucleoside always your nucleobase comes after plane of the sugar this is the up the plane this is down the plane and that is the reason I will just explain in a brief while why this happens. This has to do with the rule that is known as the Baker's rule. So, this is for the pyrimidine adenine or guanine that you can go this way.

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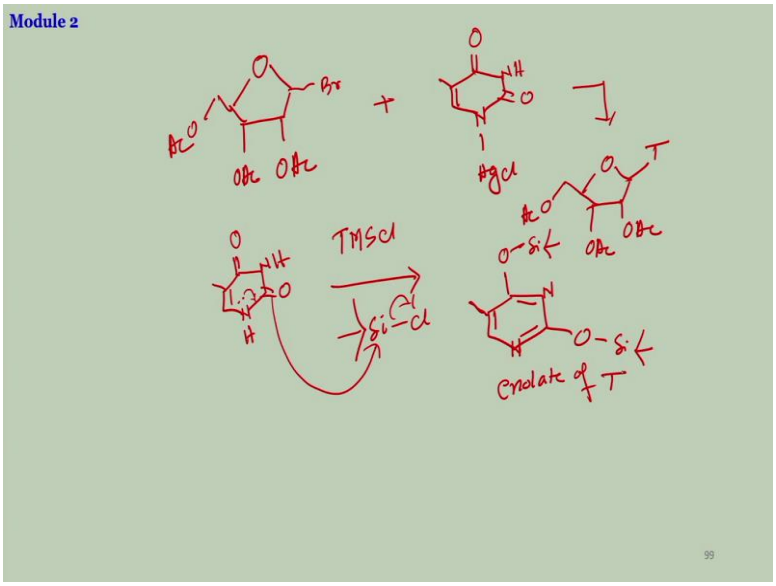

Now if you think of the pyrimidines thymine or cytosine I will give an example of the thymine here OAC bromine now the similar way you can use the thymine with the HCL this is your metal double bond O NH double bond O so this will react will give you the correct compound up the plane it gives you the thymine. I am keeping these protection groups you can use the same methods ammonia methanol treatment to get rid of the protection.

When you say you with cytosine, cytosine has one amine group here so in winter project amino group first and then do this chemistry. Now it is what we do we use an alternative method which is more facile or which is which will give you better result bit and the yield of the

reactions are much higher where instead of the HCL if you treat if you have the thymine if we use the in enolate form so your idea is that to increase the nucleophilicity on this nitrogen NH.

Now if you treat this with a cylon compound TMS chloride trimethylsilyl chloride which is basically this methyl methyl methyl and this is silicon choloride, trimethylsilyl chloride silicon compounds are very, very, very useful for organics and synthesis and they have nowadays in modern organic reactions they are their use is in plenty in numbers. So, what this will do is silicon reacts very easily with oxygen with the double wound maybe single bond oxygen or double bond oxygen does not matter it.

Gives you eliminated reaction same thing will happen here and that will give you since if this comes here this will has to go to make the saturation. So, it basically allows you O Si Me3 similarly this will also happen here and this methyl, so this is basically the enolate form. Enolate form of thymine it is quite stable compound. Now then how can you do this chemistry?

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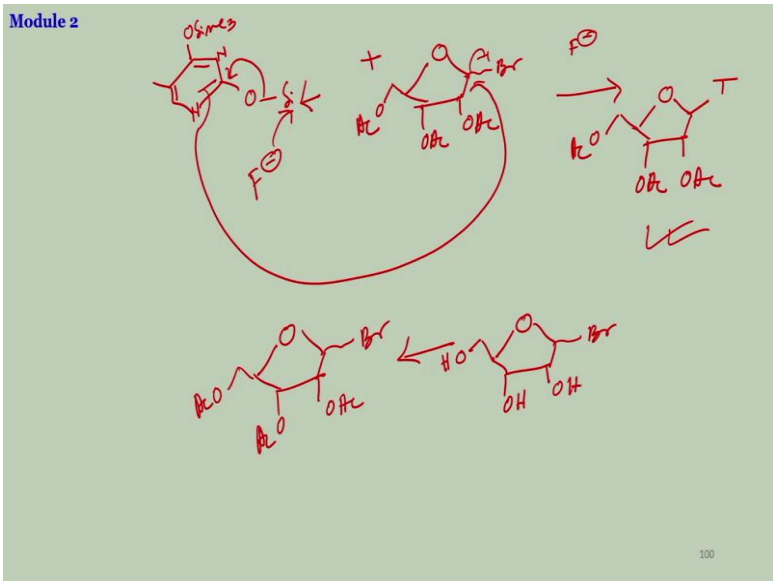

The chemistry is yes I am just writing N Me3 note the structure again you already know the structure and this, so you have the sugar with the bromine protected once. Now if you use it is very easy to break this kind of bond also salile compounds are very easy to break also. Just a little bit treatment with water or even better is if you have fluoride f- in your solution if you use a tiny bit of f- then that reacts with salile it breaks this bond back and it comes back here which creates a negative charge that will immediately react.

So, it this becomes a much better nucleophile when you treat this reaction mixture with a little bit of fluoride or even with water. Same thing will happen here it will be dehydrogenated and it will be hydrolyzed giving back the thymine. So, you will get your timing back here OAC. So, the enolate form of the pyramidion nucleobases you can do it with purine also with purine nucleus is for example thymine or cytosine since you can treat that with trimethylsilyl chloride and get this enolate form and then react it with the sugar protected sugar that will give you a very easy or the more amount of much facile synthesis of the nucleoside.

So, now the question is the same thing you can do with the cytosine. When you look at the sugar I have started with this bromide and of course all the protected ones. And this has of course come the protected ones of course come from its original one with OH bromine and then OH here OH there OH there. So, this can be converted into this as we have seen, now how to get this C here.

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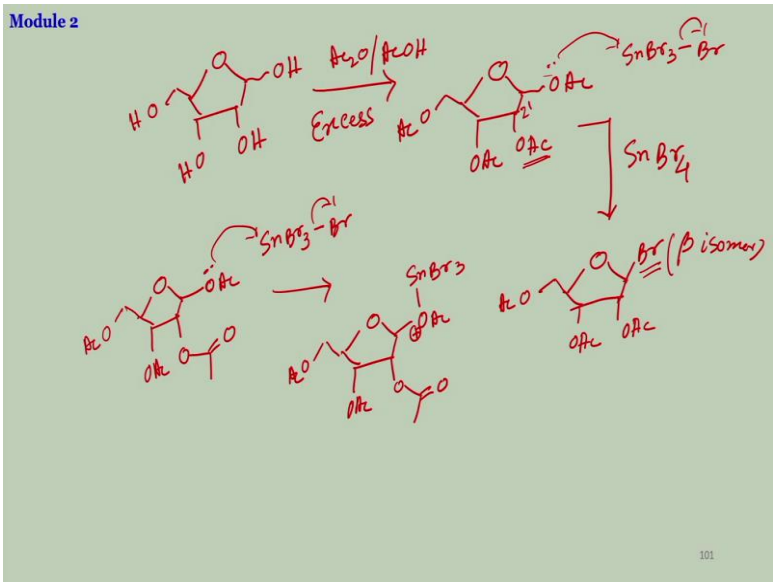

So, this you can actually get very easily if you start with all protected for example if you have the free form here OH and you randomly protect all of them treat it with acetic anhydride. Acetic anhydride is now banned in India. So similarly you can treat it with acetic acid also a little bit of high heat reflux then excess of this material excess of the acetic acid or acetic anhydride then everything will be protected.

This will be OAC this will be OAC everything would become acetate because you have used not Excel excess. Now this if you use treat it with tin bromide or tin chloride if used in chloride you get you are going to get chlorine here if you are treating with the tin bromide it is in Br4

then you are going to get bromine here. so, if you treat it with Br4 then you are going to get a reaction which will happen only here and it will give you Br.

The Br will mostly come at the beta position the up plane Br, here OAC OAC OAC the reaction goes this way if you have Br4, Br4 is basically BR 3 + BR tin is a kind of a Lewis acid. So, the lone pair of electrons will go there eliminating Br- in this Br- reacts here. So, ideally if the acetate is up the plane in the beta position then as a nucleophilic substitution rule your Br- should have come from the opposite side but it does not happen.

Independent no matter what if we was there the stereochemistry here be it Beta Beta Alpha you always get a beta isomer of this compound and this comes from the rule which is known as the Baker rule.

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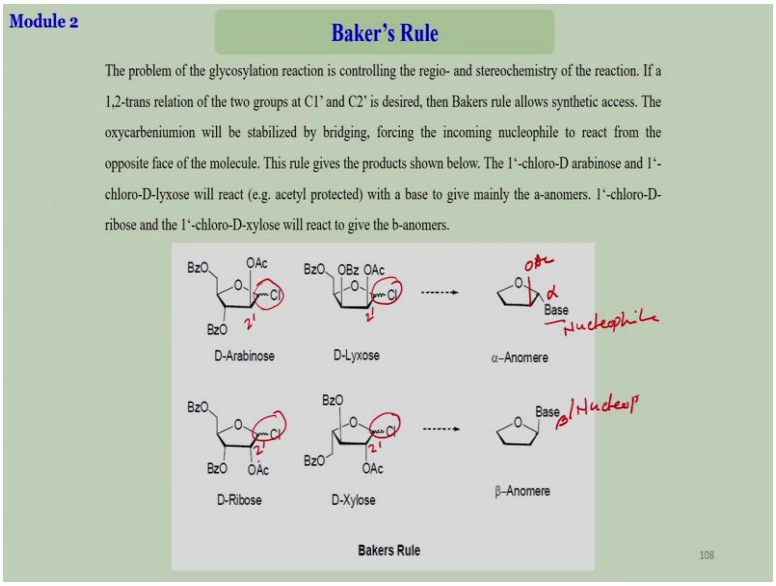

This is what the Baker rule is it basically states that if you use sugar compounds like this have start it can have different the geometry if it is Arabinose D arabinose I am not now talking in general sugar chemistry D arabinose will have the acetate if you have a acetate this should be the 2 prime position would be up the plane beta position. If this is a weak source then 2 and 3 both are up the plane.

If you have ribose then both are down the plane and we are using ribose so both are down the plane for our case. If you have xylose then 2 prime is down the plane 3 prime is up the plane and this is the 5 prime or 4 prime is also down the plane but in all cases whatever

stereochemistry you use of the C 1 prime be it a beta be it alpha when you do the reaction when you do a nucleophilic substitution reactions their stereochemistry does not matter.

What matters is what is the stereochemistry at the C2 prime position if the 2 prime position is up the plane 2 prime position is up the plane then your nucleophilic substitution this can be a base this can be any nucleophile. The nucleophile will come down the plane in the final product. So, if 2 prime position is up the plane 2 prime position is up the plane then the nucleophile at the C 1 prime position will come opposite side of it down the plane.

So in this case 2 prime position is I am just writing OAC up the plane then the nucleophile will come down the plane alpha alpha anomer alpha anomer is going to be your major product. Similarly here if your 2 prime position is down the flame 2 prime position down the plane here 2 prime position down the plane here does not matter what is the stereochemistry of the other positions not even the C1 prime then you will have the beta anomer your nucleophile is going to come from the up the plane. So, that is what the bakers rule is.

That the stereochemistry when you do when you are trying to do a reaction at the anomeric position the C1 prime is known as the anomeric position when you are trying to do the nucleophilic reaction or a substitution reaction at the anomeric position then the stereochemistry of the final product will depend not on the anomeric atom or anomeric living group but will depend what is the stereochemistry of the 2 prime position and it is always the opposite of that geometry.

If 2 prime position is up the plane or in beta position then you are going to have the alpha anomer. If they are down the plane you are going to have the beta anomer. So, there is a reason for this also why so same thing is happening here if you look if you come back that it does not matter what is the stereochemistry of OAC here since this is ribose sugar we are using so as 2 prime position is down the plane since this is down the plane your bromine or the chlorine or the nucleobase if you do it is going to come from up the plane and the beta anomer is going to be your preferred confirmations.

Now there is a reason for it also why is that so if you look OAC here since this is involved I am going to draw this structure so always your 2 prime position is dictating what should be the stereochemistry at the 1 prime. Now if you treat it with Sn Br4 Br3 and Br then this is going out

which means you are going to have a transient intermediate O AC and this is going to be your Sn Br3 this is going to be your plus and Br- there OAC OAC.

Now since you have a positive charge here it is going to leave and immediately this is going to attack. The oxygen or the double bonded oxygen of the acetate is going to attack immediately to the C1 prime position because you are having a positive charge here which is leaving.

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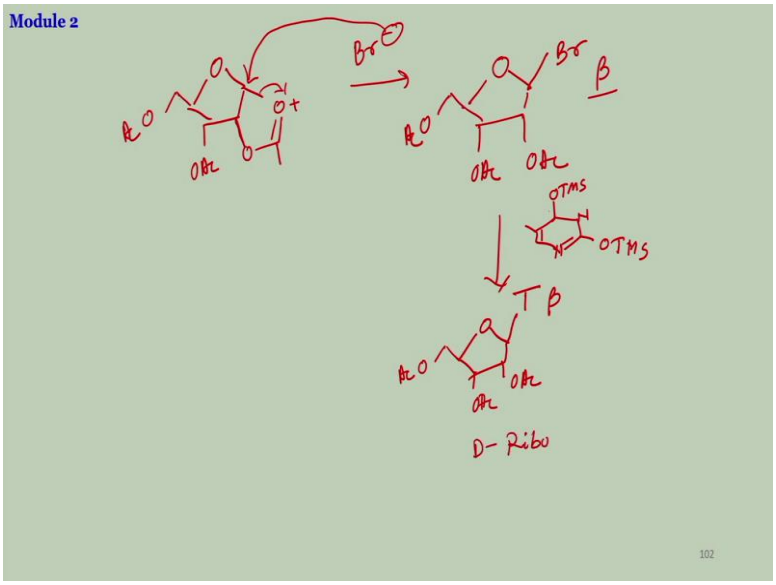

So, that is giving you an intermediate which is this positive charge OAC OAC this kind of intermediate is going to come. So, it is intramolecular nucleophilic substitution reaction because the acetate group of the same molecule is attacking as a nucleophile. So, if you see here the acetate group is attacking as a nucleophile and this is your living room so internal nucleophilic reactions or we call it NGP neighbouring group participation. Because of neighbouring group participation it forms this kind of intermediate.

So whole of the intermediate that would be forming is down the plane. Now the Br minus that you had from which side it will come you are down the plane is block so only available position is up the plane. So, Br minus has to attack from up the plane because down the plane is blocked by the intermediate formation intra molecular intermediate formation. So, therefore this is going to attack and it is good it is going to come back because it is an intermediate it is not very stable you are going to get back your OAC where OAC here and then your bromine has to come from up the plane so, beta anomer.

So, that is what the Baker's rule basically states. So, similarly when you are treating this with a thymine or any other nucleobase if I use the OTMS the salile related OTMS then this is going to attack again the same thing will happen Br minus will be eliminated OAC will attack from backside it will create an intermediate in the down the plane so your thymine has to come from up the plane will give you always thymine as the beta anomer.

This is going to be your product. So, now that is for the sugars so far we have taken is the ribose sugar. So, this is D and ribose sugar right for RNA molecules.

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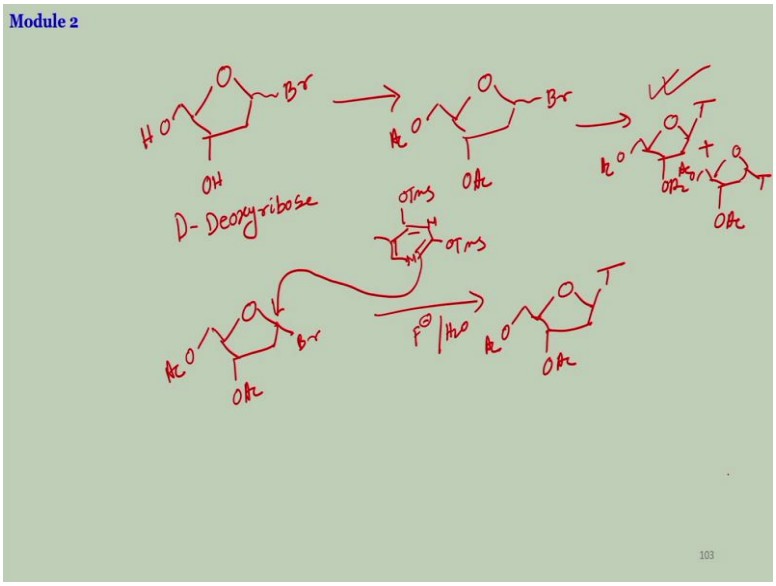

Now if you want to synthesize that DNA what you have to start with you have to start with the deoxyribose for example bromine here nothing here OH OH and of course so this is for the D deoxyribose sugar we can start with the bromine version bromide added and of course you can convert it into a OAC and do the rest of the reactions like thymine and adenine addition the same way. But here there is a problem now if you start with any geometry here you are not going to get the same beta anomer that we have seen for the ribose cases.

The reason is for ribose cases you had substitutions in this position which was down the plane and that was dictating the stereochemistry of the incoming nucleophile. In this case for the DNA case you have nothing here. So, there is nothing to dictate the stereochemistry of the nucleophilic reaction over this position so if you want to get the desired beta anomer of the nucleoside there is no other alternative but to start with a specific stereochemistry at the beginning.

So if you want to have the desired beta anomer then you are going to start with the specific alpha anomer alpha substituted bromine of this position and then you treat it with the thymine just giving the example OTMS OTMS and these same conditions then you have little bit of fluoride or water either of them you can use then it is going to be pure Sn2 kind of reactions where your nucleophile will attack.

Since this is down the plane your nucleophile will attack on the opposite part that is the up the plane you are going to get the thymine of the plane but only when you are starting with a specific stereochemistry in this position. If you start with a random geometry here you are going to get a random geometry. So, you will get a mixture of Alpha and the beta product if you use this then you are going to get beta plus alpha thymine a mixture of these 2 which is not desired what you want is you are looking for this a beta that exists in DNA.

Here also most of the times even if you start with the alpha anomer it is restricting the stereochemistry and here is little bit difficult you still get a little to some extent mixture of the other isomer also but mostly this. So, for DNA cases; keeping the stereochemistry intact is a challenge and that you have to keep it in mind. So, that is how you can synthesize the nucleosides which mean the nucleobases plus the sugar for DNA as well as for RNA versions.

The next step is of course how you can synthesize the whole the chain of that deoxyribose nucleic acid or the DNA or the RNA that we usually do it in a there is a protocol for it, it is little bit advance chemistry that I will explain i n the next lecture that is called the phosphoramidite chemistry or we use we even call it solid-state phosphoramidite chemistry that is usually done in a machine in a DNA synthesizer we call.

That I will explain in the next lecture but before that I would like to just mention a little bit of the sugar chemistry.

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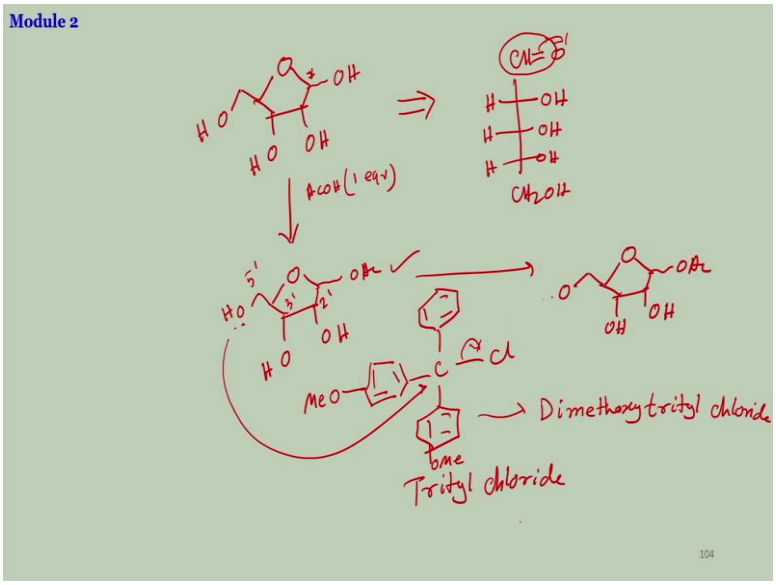

So, since we are doing with the DNA and RNA I will restrict myself to the ribose sugar. For DNA it will be deoxyribose, so I am making it more general so that we can handle it. Now the question is we have seen in the entire synthesis that sometimes you need to protect this and sometimes you need to protect this or you are converting this into the bromide as a living room other times we are protecting the other ones.

So, selective protections and the protections are very important for super chemistry. Now in this will try to do how to selectively protect one individually of all these positions. So, first is C1 and C1 is very easy because the reactivity of C1 is very different than that of the others why if you remember how the cyclic form is coming from this cyclic from is actually coming from the a cyclic sugar which is basically this it has a CHO aldehyde the open chain form this is the closed chain cyclic form the open chain form is this 1, 2, 3.

So, this is the open chain form which has the aldehyde group here and of course carbonyl compounds are much more reactive because they have electron deficient carbons because of carbonyl group this is double bond O. So, because of this electron withdrawing nature of this this carbon is little bit more electron deficient. So, therefore C1 position this is a little bit more reactive compared to the other positions and you can easily do chemistry here keeping intact all the other ones.

So here if you want to do for example if you want to protect this hydroxyl with an acetate all you have to do is to treat it with acetic acid or acetic anhydride in a very mild condition and you can use pretty much one equivalent. The others will not react under this condition. Y ou will get

a acetate here keeping intact all others. When you use a drastic condition little bit drastic condition of acetic anhydride or acetic acid and excess of death then only you are going to get all of these protections. Otherwise you know mostly the anomeric position we call this a anomeric position the C1 position this is going to be affected.

Similarly if you want to do it a bromide or chloride you just treat it with HCl or HBR when you are going to get the reactions only in the anomeric positions because of this aldehyde form that this is more reactive so this is C1 prime position is done. Now other position this is a secondary alcohol this is also in secondary alcohol so the reactivity of 2 prime and 3 prime are almost similar. On the other hand this alcohol is a primary alcohol at the 5 prime end and this is less crowded.

Number one is the primary alcohol so this is sterically less crowded these 2 are sterically more crowded. So, again doing chemistry of the 5 frame position is little bit easier than this 2 Prime and 3 prime. Now if I want to do selective protection of the 5 prime end all I have to do is if you is a large bulky group as the nucleophile sorry in this case it will be electrophilic reaction because the OAH is going to act as a lone pair of electrons through its lone pair of electrons OH OH these OH are going to act as a nucleophile when you do the protections.

So, your incoming group that you want to do the protection with should be large in size so, that that can only go to the 5 prime position and not here because these are crowded. So, one such reaction is if you use phenyl ring, 3 phenyl and a chloride this is known as trettel chloride we will use this molecule later also when we synthesize the solid-phase DNA chemistry. So, this is trettel chloride which has 3 bulky phenyl groups.

Or instead of trityl group we can use it little bit better that is called the O methxy trityl methoxy group at the para position here and a methoxy group at the para position here 2 of them have the methoxy group at the para position this compound is known as DMT chloride di methaxy trityl di methoxy trityl chloride we trityl chloride. so this is this molecule and this exists as a very good cation also. So, when you use this such kind of bulky group then this OH this OH cannot react because these 2 are sterically crowded.

Only the 5-prime will react and that will give you the protected 5 prime position. So, we have protected here with OAC leaving it with OH here living it with OH here, here you had the wage

now you had the MT which means this group so DMT is a good protection group specifically to the for the Phi prime position of the sugar, thank you.