# Essentials of Biomolecules: Nucleic Acids, Peptides and Carbohydrates

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## Lecture-33
## Chemistry of Carbohydrates

Hello, everybody and welcome back so, today we will be on module 10 in the last module that was module 9, I have mainly discussed on the bio molecular probes, the basically the constructions of artificially synthesized molecules that you can use to study what is going on inside the cells. In other words that will be giving you reports back to you so detection purpose to see the live cell imaging or where you your biomolecules are actually going.

And what is happening those in order to know that we have synthesized or nowadays a lot of different kinds of artificially synthesized molecular probes have been used. So I had tried to give you kind of 1 or 2 important ones of them such as PNA and LNA along with SiRNA which can act as biomolecules especially for research purpose. So today we will be talking about a different topic and that is chemistry of carbohydrates.

So carbohydrate is of course you know, that it is a one of the very important biomolecule that is present in our body in our cells, carbohydrates constitute a major part of our body constructions and it is also a major source of our cellular energy. So, there are different kinds of carbohydrates that are present in animal body, in plants in microorganisms. Such as if you talk about the plants the stems of many different plants such as bamboo, straw, wheat.

Majorly 2 of them are basically constructed of carbohydrates and the small carbohydrate molecules, the small molecules containing the sugars and other kinds of carbohydrates are the major source of the energy in plants. Similarly, in our animals in higher organisms, also cellular membranes are constructed of glycol lipids. So it is a basically a combination of lipids and carbohydrate. Also, there are other parts of the body that are that have carbohydrates in it, and carbohydrate metabolism is obviously a major source of our energy microorganisms also have the same things.

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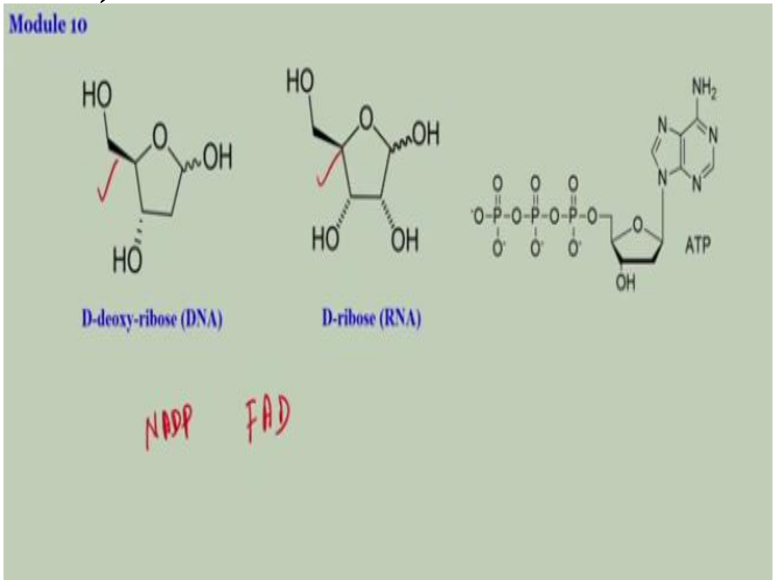

And apart from those, there are other kinds of small molecules of course they are also biomolecules and they are present in our body in higher organisms as well as lower organisms and that have carbohydrate part in it or sugars part in it, such as we have seen before, to a large extent, our DNA that is constructed of the deoxy ribose sugar RNA that is constructed of D-ribose sugar so, these are the constructions of DNA and RNA on large biological macromolecules.

Small molecules includes ATP, adenosine triphosphate, adenosine diphosphate they are the source of energy in our body, the cells and obviously along with that, you know, there are many coenzymes there are many enzymes that have like glyosidic part in it. They are many coenzymes such as NADP, nicotinamide adenine dinucleotide, phosphate, FAD, Flavin adenine dinucleotide and so on. There are many others and all of these coenzymes have sugar you need to attach to it most of the times its ribose or the deoxyribose. So, these are the smaller organic molecules or smaller biomolecules that contain the carbohydrates.

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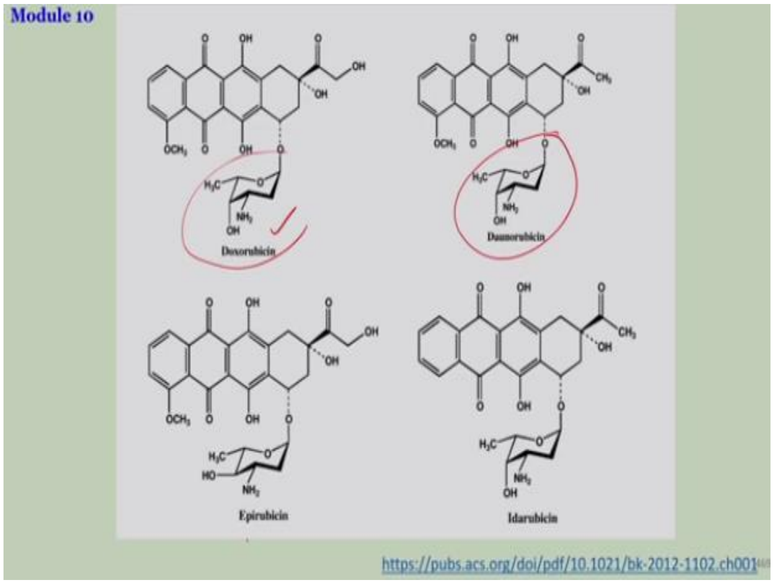

Module 10

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Here if you see a lot of drugs, some of them are natural products, you can isolate it from natural sources. Some of them are synthesized also but they are very popular, very well-known drugs and these are mostly the anti-tumor agents. Doxorubicin is a very famous chemotherapeutic agent which is used in many different types of cancers. It has a glyosidic bond and that has a carbohydrate or the sugar moiety which is little bit modified of course here.

Doxorubicin was initially synthesized from Daunaubicin, Daunaubicin is a naturally occurring molecule or is a natural product. So, this has a diamond group and this is very close similarity with the doxorubicin structure. This is a Epirubicin, this is Idarubicin. So many of them are available as drugs in the market and they content, the carbohydrates.

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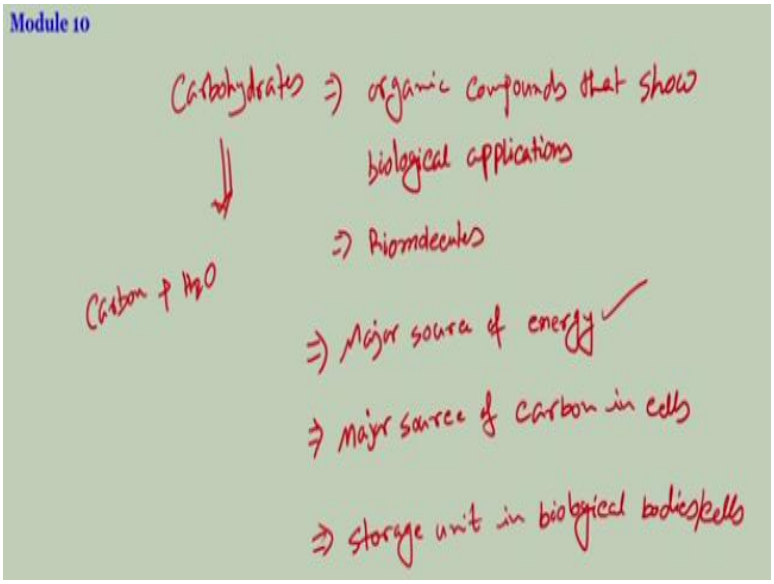

Module 10

Carbohydrates ⇒ organic compounds that show biological applications

⇒ Biomolecules

Carbon + $H_2O$

⇒ Major source of energy ✓

⇒ major source of carbon in cells

⇒ storage unit in biological bodies/cells

So, in general carbohydrates, basically the organic molecules or organic compounds that show biological applications not only that, they are themselves are biomolecules. The molecules that are abundant in the biological system as I have said, they are the major source of energy. Also, carbohydrate is the major source of the carbon that are needed in the various cellular activities to synthesize with various molecules in the cells carbon containing molecules.

It is a major source of carbon in cells obviously most of the smaller molecules that are present in cells have carbons in it and many of those molecules or the biomolecules are actually derivitized or actually synthesized back from carbohydrates. So it is a major source of carbons in the cells also, they also serve as a storage unit in biological bodies or biological cells. The name carbohydrate basically means that if you charge a molecule, what you get is carbon and hydrates means water.

So that is where the name came from carbohydrates means it produces carbon plus water when you make it to undergo massive oxidations. So it is a major source of energy because that is due to the metabolism effect, which basically means the oxidation of the carbohydrates that produces the energy now, carbohydrates can be divided into many different kinds.

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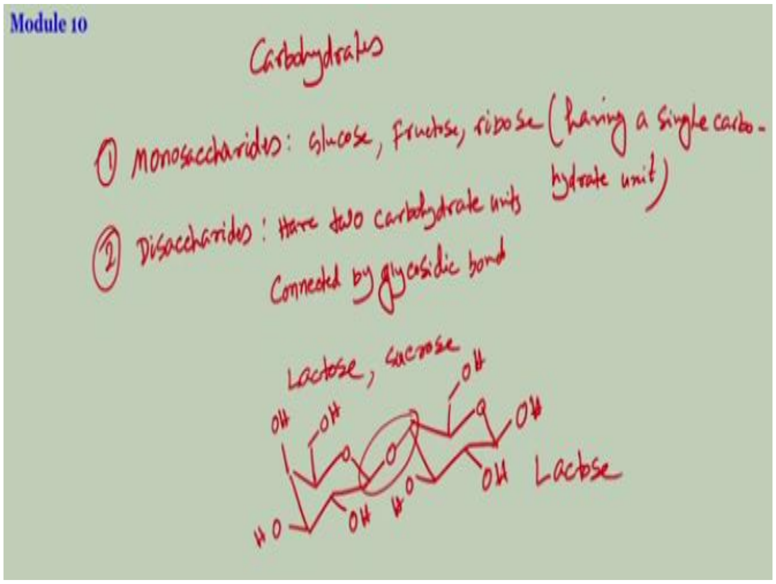

Module 10

Carbohydrates

① Monosaccharides: Glucose, Fructose, ribose (having a single carbo-hydrate unit)

② Disaccharides: Have two carbohydrate units Connected by glycosidic bond

Lactose, sucrose

So carbohydrates have the types of carbohydrates many different types 1 is of course, we call it monosaccharides. Carbohydrates are also known as saccharides. Monosaccharides are the carbohydrates which has a single carbohydrate unit such as glucose, fructose, ribose of course all sorts of smaller structures, which has a single carbohydrate unit is called monosaccharide of course I think most of these things that I will be around the carbohydrates.

And they are structures when they are utilities most of those things you already know of for the sake of the course I think I will go through them again so monosaccharides second division is called the disaccharides. Disaccharides are the one of the molecule so, having a single carbohydrate unit disaccharides have 2 carbohydrates units and those are connected by glycosidic bonds a single glycosidic bond would be there so it is a bond.

The example of such the disaccharides can be lactose, sucrose and shown I will show you the structure of lactose for example to draw the chair conformation, this is O CH 2 OH OH this is the equatorial has hydrogen in it and here the beta enamor down the plane this is off the plane wage. Now this is the glycosidic bond O and there is another one that can be developed from here. So, is this O, this is the other one here is your hydroxyl group this is OH OH and beta OH. So you have a single glycosidic bond here and this is the structure of lactose which has to have the carbohydrates units so it is a disaccharides.

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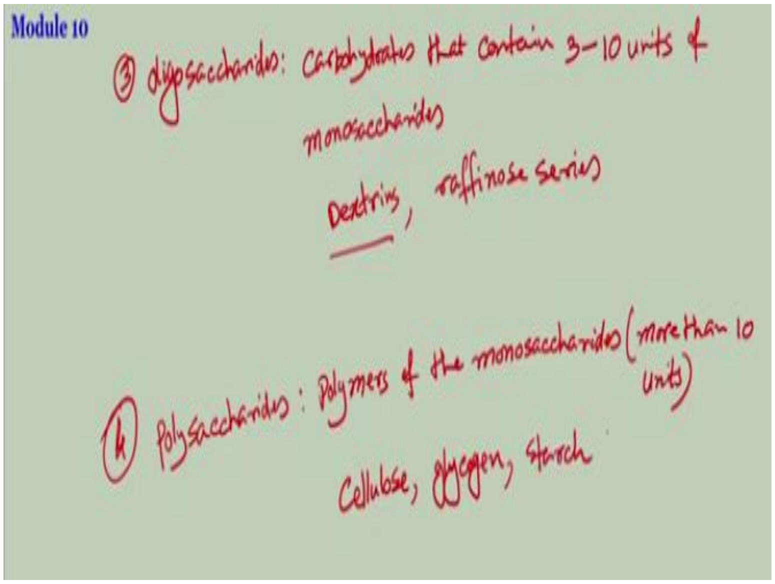

Module 10

③ oligosaccharides: Carbohydrates that contain 3-10 units of monosaccharides

Dextrins, raffinose series

④ Polysaccharides : Polymers of the monosaccharides (more than 10 units)

Cellulose, glycogen, starch

The third one is called oligosaccharides, oligosaccharides that name itself represents that it should have multiple number of or more than 2 number of carbohydrate units. So in this case, typically, the oligosaccharides are the carbohydrates that contain around 3 to 10 units of monosaccharides so, typical examples are dextrins. Dextrins are an important class of oligosaccharides they have lot of use in pharmaceutical industry, in textile industries, in other industries as well.

So, a lot of industrial applications from dextrins. Other one is the raffin series, raffinoses series of molecules they contain multiple number of less than 10 number of monosaccharide units attached via glycosidic bonds together that is called oligosaccharides and the fourth one which you will know a lot of examples of are called polysaccharides, Polysaccharides are basically the polymers of the monosaccharides.

Polymers of the mono saccharides more than 10 units connected together while other glycosidic bonds and this monosaccharides can be different, different means in the same polysaccharide there can be multiple kinds of monosaccharides multiple number of course is there along with that multiple kinds of monosaccharides can be connected together to give you the polysaccharides cellulose present in many plants is a major material.

That is obtained from plants, glycogen, starch these are all part of the polysaccharides they have different kinds of units that are connected together to give you the polymeric structure and that is why they have very long structures, very tough structures sometimes. So, I will give you a table regarding the division of these sugars and then we will move on to the chemical part.

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Module 10

| class | Subgroup | Components |
|---|---|---|
| Sugar (1/2) | Monosaccharides | Glucose, galactose, fructose, xylose |
| | Disaccharides | sucrose, lactose, trehalose, maltose |
| | Polyols | sorbitor, mannitol |
| oligosaccharides (3-10) | 3-10 | maltodextrins, Fructo-oligosaccharide |
| Polysaccharides $>10$ | Starch | Amylose, amylopectin |
| | Non-starch | Glycogen, Cellulose, Pectins |

So, if you make a table so, this is the class what kind of sugar this is subgroup. This is the components or the what materials are present in them. Sugar can be monosaccharide examples are glucose, galactose, fructose, xylose I will show you all the structures also just a little bit later and then you have the disaccharide as we have talked examples of the disaccharide are sucrose, lactose, trehalose.

Trehalose is a very important carbohydrate or a very important sugar containing molecule which has a lot of biological applications maltose and then polyols such as very well-known sorbitor, mannitol. So first class sugar means which has 1 unit of monosaccharides or 2 units of monosaccharides disaccharides and then comes the oligosaccharides. It is the first, second is oligosaccharides the example I have seen, given is dextrin, it can be in general maltodextrins.

Oligosaccharides would be between 3 to 9 numbers of monosaccharide units. Then fructo-oligosaccharide is also there and the reference in the last one is, so this is basically 3 to 10 units. Then comes the polysaccharides, polysaccharides are more than 10. So more than 10 units of sugars, they can be divided into 2 parts. One is the starch containing amylose and then amylopectin and then non-starch such as glycogen, cellulose off course pectins and so on.

There are other examples also so, these are briefly the division that you can make or the different classes of carbohydrates. Now, coming to the chemical structures so most of them, is it kind of have been evolved from the basic unit which is glyceraldehydes. So, structural similarity or the is from the glyceraldehydes.

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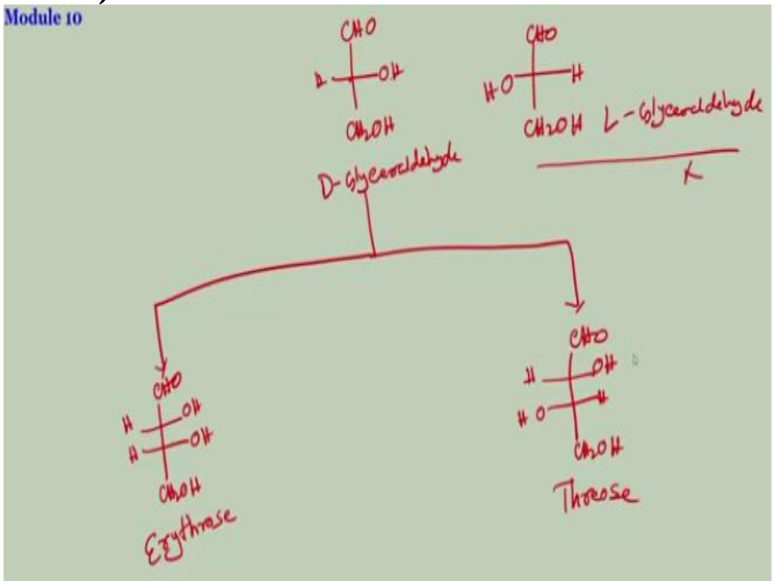

Glyceraldehydes has this structure OH these CH 2 OH this is glyceraldehydes and according to the nomenclature, glyceraldehydes has a Kidal center here because all 4 groups attach us to the carbon are different so it is a Kidal Center, which is optically active. And therefore, it should have 2 isomers one is this other one is this I have drawn the free surf projection this here H CH 2 OH, this is also glyceraldehydes so according to nomenclature, this is D-glyceraldehydes.

Because the OH is on the right hand side dextro so D-glyceraldehydes so now, here in this class I will talk about only the monosaccharides and all those monosaccharides are mostly of the configurations. So and this is L- glyceraldehydes, so I will not talk about the L-isomer will mostly talk about the D-isomer. For D-glyceraldehydes, if you go one carbon up from here, then what to synthesize what to get is 2 here, 2 optical centers or 2 carbons Carroll centers.

CHO this one remain as it is D because that is what the name is coming from. Now, here the next one can have the same or this remains D. Here this can be the opposite OH H CH 2 OH. If you have multiple carbon centers did you hear the name erythrose and threose. So, same side and the opposite side this is known as it basically erythrose and threose the concept basically came from the sugars this is called erythrose 4 carbon units, both the hydroxyl groups on the same side. This is called threose, where the hydroxyl groups are on opposite sides so this is the 4 carbon units.

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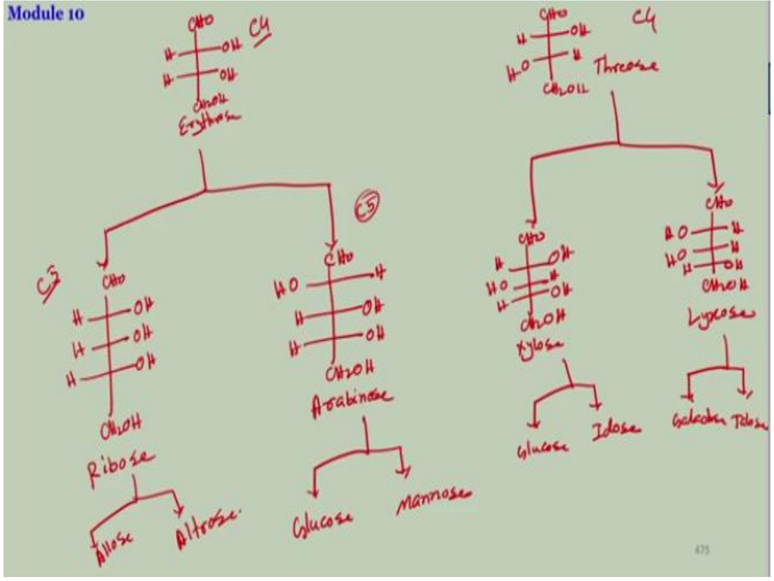

And now moving on erythrose this is your threose if you move to one carbon of again. So, here is basically C-3, 3 carbon center this basically becomes C-4, 4 carbon centers C 4 C 4 and from here 1 step of ascending series 5 carbon CHO OH H OH H so, this should be CH 2 OH. Now the new one can be OH in this direction this is your arrivals, so the differences in the new one CHO this can be the other way around H OH remains same so, we are adding up.

So, this is what is the new addition right from here the new carbon is joining here. So, this should change the other should remain intact this is your ribose, this is your arabinose. Similarly, from threose you can draw 2 so, this is your C-5 C 5 that is evolving from erythrose from threose is CHO this is the new one. So, it can be OH H H OH OH H CH 2 OH that is your xylose and H OH H OH OH H this is your lyxose so, ribose is a sugar that is abundant for DNA and RNA.

Similarly, if you move half, I am not drawing them you will have altrose and allose that is the 6 membereing with the 6 carbon and from arabinose that I will draw the next page what you will have is because these are the most well-known one glucose and mannose. From xylose you can have again glucose also and idose. Lycose you will have galactose and talose those are for the 6 carbons so structure of glucose is very important.

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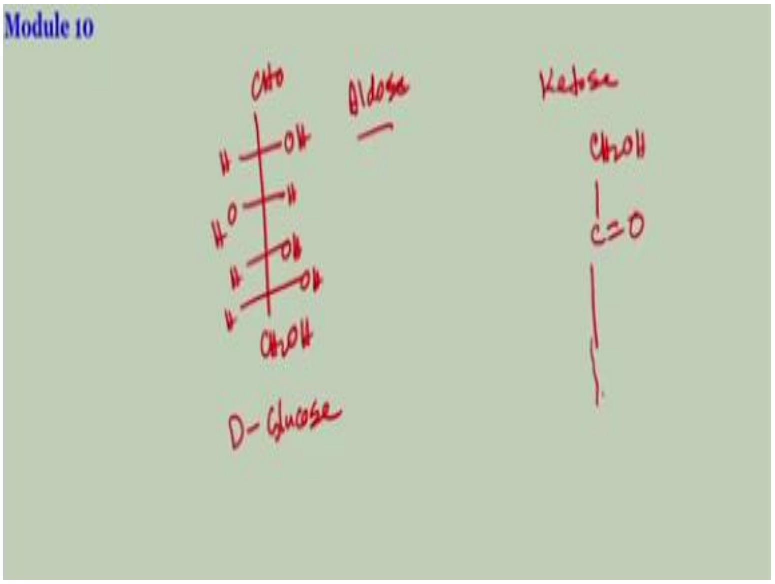

So these are all aldose sugars I will draw the structure of glucose CH OH H OH H OH H OH H CH 2 OH this is your D-glucose basic sugar is a source of energy. So, it is a purely optical active molecule which shows the specific optical rotations and this is aldose sugar. So, monosaccharides can be of 2 different kinds one is aldose means which has an aldehyde group here and other one is ketose such as the fructose.

So as we move on, I will show you the structure of fructose, aldose and that would be ketose because that has, it has the general structure of the ketones is the first one will have the CH 2 OH and then you will have the ketone and then the other way around, it will move on. When you form a disaccharide then you need to form a glycosidic bond right. So, I will show you first a reaction through which our glycosidic bond can be formed in a synthetic way.

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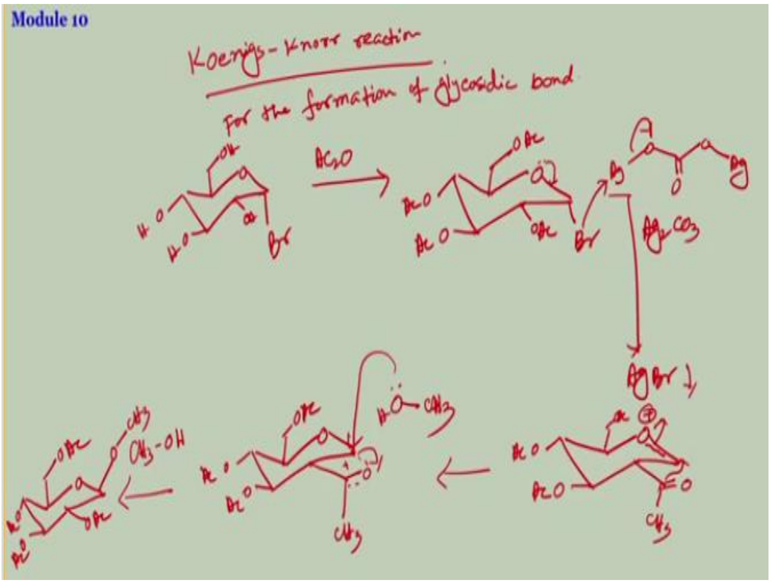

The name reaction is Koenigs-Knorr reaction actually k o loud as German pronunciation if you write in English, you will find this most this spelling in book Koenigs Knorr reaction for the formation of glycosidic bond. In this case if you start for example, if you take the chair conformation, you start with the halide alpha one bromo you have here CH 2 OH this is OH, this is OH and this is alpha OH.

So, first thing you have to do the production of all the hydroxyl groups otherwise it will react and that can be done very well. That you know already we have done some sugar chemistry during DNA synthesis, acidic and hydride if you add then or acetic acid also, then this will protect all the hydroxyl groups bromin so this will be converted into O Ac. This would be O Ac O Acited CH2 OAc.

So you have to form our glycosidic bond over here it is usually done by using Ag 2 CO 3 a mile reagent actually silver carbonate, what it does is it will precipitate it, one molecule of Ag Br, Ag Br would be forming and that will precipitate out that is the driving force for the reaction. So it will drag the Br. I will show you the structure in a structural orientation these O O Ag this is the structure of Ag 2 Co 3 Br minus goes there.

It will take up this will become a kind of a minus since the Br minus is getting out, this will create a positive charge on this carbon that will be to some extent compensated by that lone pair of oxygen and we will form plus this complex O Ac O Ac O Ac now you have acited and that has double bond oxygen. So, this will attack here, open this up that will give you a better complex or better intermediate energetically more favorable intermediate.

So, basically O here it will form a complexation and this will be delta plus of course CH 3 this will be positive charge over here O Ac O Ac O Ac. So that blocks the down the plane and now you have to form the glycosidic bond you reacted with just for example, you treat it with methanol. So, your first reaction is basically treatment of this compound with acetic anhydride Ag 2 Co3 and methanol.

So, what this will do, this will come attack this carbon this will open up but this attack has to come from the top position here because the down is blocked by the acited so that triggers the stereochemistry. So, it will be up the plane O CH 3 up the plane and then rest will come as it is, O Ac back O Ac this is O Ac CH 2 O Ac and for extra hydrolysis you can cleave the acetate and get back your hydroxyls back so, this is the formation of the glycosidic bond.

So, one of the reactions which you can use to form the glycosidic bond, as I had shown that from glyceraldehydes, you can approach or you can synthesize all the higher orders of the monosaccharides. So, I will show you a couple of reactions, which are methods which are used some pretty old reactions actually many of you already know of all this reactions. Those are used to increase the number of carbons on the glyceraldehydes or on the sugars so one of them.

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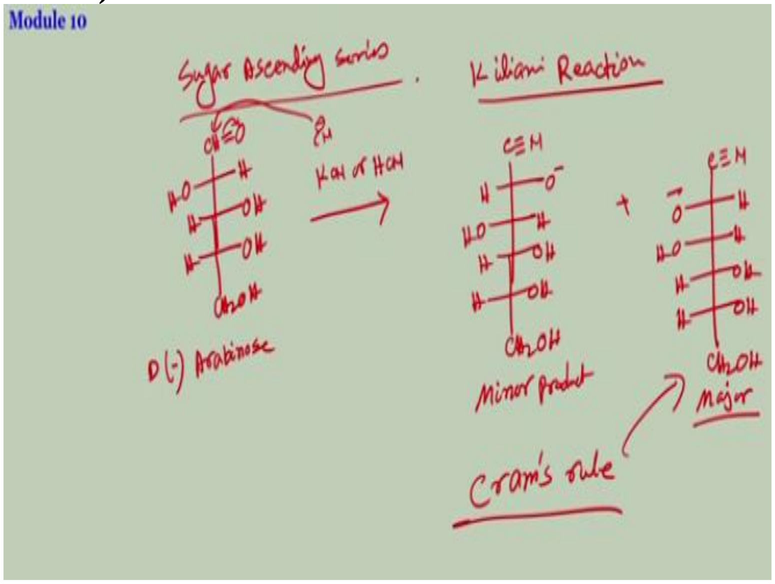

So this is called ascending series alcohol sugar ascending series so if you start from, let us say arabinose and you want to get synthesis, glucose from there this is the structure 1,2,3 so D This is D means the minus actually this comes from your experiment D arabinose. The question is how can you increase the 1 carbon here. So the reaction is called as Kiliani reaction very well-known reaction, it is an AMD reaction very old reaction.

The way to do is to add up one cyanide over here, because cyanide it is a source of carbon. So if you treat this with KCN or HCN not a nice reaction. Because cyanide are very harmful all of you know, but in a controlled way. Now, you can bypass these regions in a little bit modern regions, but still so this is how I am talking about the old method the actual reaction that people have used.

So, if you have cyanide, if you use cyanide, what it will do? This will cyanide is basically CN minus nucleophilic addition on the aldehyde. So you will have CN here, CN and this becomes O minus CH OH, it can be this way it can be the other way around also and rest will be as it is H OH OH H OH H CH 2 OH plus you will have the other one, this is H this is O minus H OH OH H OH H CH 2 OH it turns out that this is actually the minor product.

And this is actually your major product this is according to cramps rule, if you remember, this is a very famous carbonyl compound reactions of which way the incoming nucleophile will come depends, that is governed by a rule called known as the Cramps rule or write it here. So according to Cramps rule, this should be the major product and obviously O minus would become OH so, what you basically have now.

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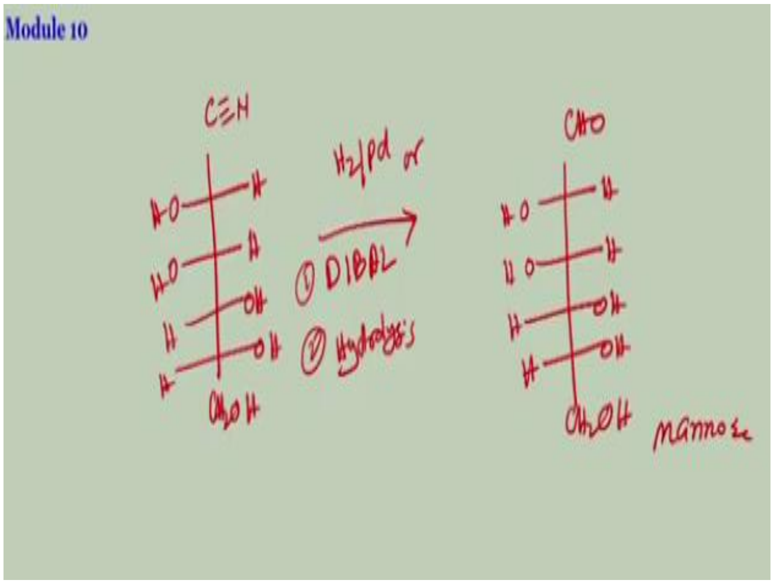

This as a major product, you have a cyanide and you have H OH H OH OH H OH H CH 2 OH. Now you have to convert this into an aldehyde you can use it using the catalytic hydrogen palladium or if you do on electron you can also use DIBAL salaminium reagent, di isopropylbutyl, di isobutylaluminium chloride. So, that will give you the basically CH2 NH2 and this for further hydrolysis.

So, this is number 1 number 2 would be for the hydrolysis that will move it to the aldehyde, H OH H OH OH H OH H CH 2 OH this becomes your H OH H OH this is actually your mannose and from the other one. If you do this minor product, this will give you your glucose. So if you want to have your glucose I think you have to start with ribose. As a major product if you want glucose as the major product, you have to start with the ribose not arabinose so this is one reaction for increasing the carbon in the sugar.

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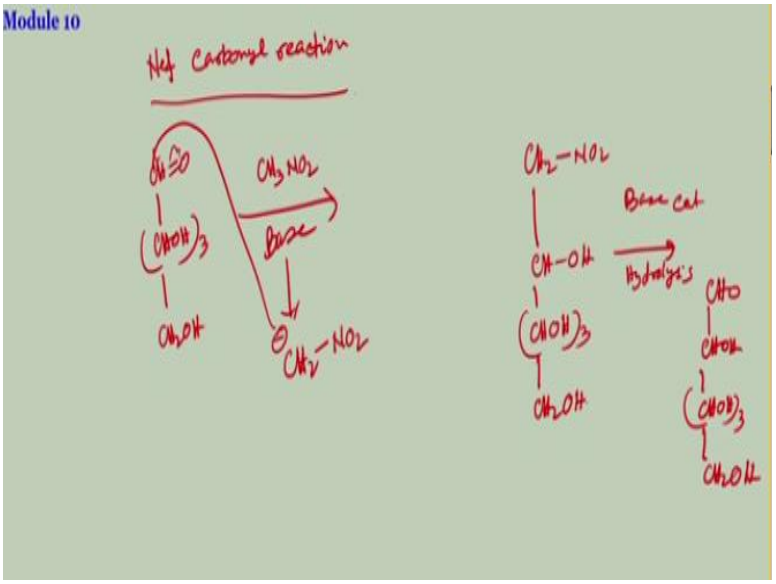

Another reaction is Nef carbonyl reaction so in general, you have a CHO I am not writing the stereochemistry anymore. Just taking a general example CH3 CH 2 OH, if you treat these with a nitro compound, so the idea is you have to create a carbon and that will act as a nucleophile to attack on the aldehyde. So you have to use a base H minus condoning or I will simply base it can be many different kinds of bases can be used.

So base that will actually produce a carbonine CH 2 NO 2 this carbonine because of the presence of an NO 2, which has strong electron the ability is quite stable, and it is a good chemistry actually with karbonn chemistry. So this will react here so, you have CH 2 NO 2 in the next phase you have CH OH and other CHOH so, you have created a new CH 2 OH. And then on base catalyzed hydrolysis this you can convert it into the aldehyde CHO CHOH CHOH CH 2 OH so you have now, one carbon up.

So, these are some of the very well-known techniques to all organic chemistry methods that we use in the laboratory to vary the number of carbons. So to in this case I have talked about the ascending series, you know means the addition of one carbon, they are now coming to descending series.

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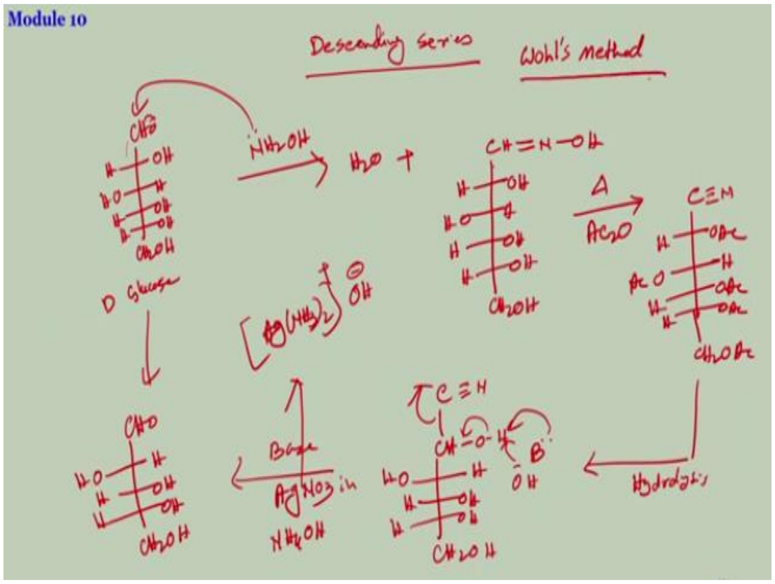

So, starting with higher order, how can you reduce one? For example, you start with glucose 1, 2, 3, 4, 5, 6. So, this is your D glucose if you treat these with hydroxyl amine, then what do you get this act as a nucleophile this comes back. So you will have CH and then it basically liberates water one molecule it is the condensation reaction right carbonyl with amine condensation is pretty popular.

So this will have your CH double bond in OH H H OH OH H CH 2 OH, if you hit this up ideally this can remove another molecule of water. But this does not happen like that. It works best if you use a little bit of acetic anhydride. So, that will basically eliminate another molecule of water and this will create your cyanide CN. At the same time, since you have used acetic anhydride it will rotate all the hydroxyl groups as well.

So, you will have now OAc H CH 2 OAc. Now hydrolysis Ester hydrolysis basically to deprotect all this that will create CH O H and all the rest of it I am writing this because I need this H OH OH H OH H CH 2 OH. If you treat these with the base what happens base will take up this it will go and your cyanide will be eliminated because cyanide is also a good living group so, that will expose the CH one CHO here and this one carbon would be gone.

So, you will have CH O and then the rest of it one carbon down H OH OH OH OH H CH 2 OH so, you have descended 1 carbon here. Now this base is actually you should not use a very strong base because this is kind of a numeric one, so it is very level you need a mild base and the reagent is we use silver nitrate in is called ammonical silver nitrate in ammonium hydroxide which is known as the ammonical silver nitrate.

This basically generates ammonia complex plus OH minus some mild base. So, you have free OH minus that will act as the base here. So, this is basically the OH minus that will take up the proton will do this chemistry and this reaction is known as the Wohl's method to reduce sugar, to reduce a carbon.

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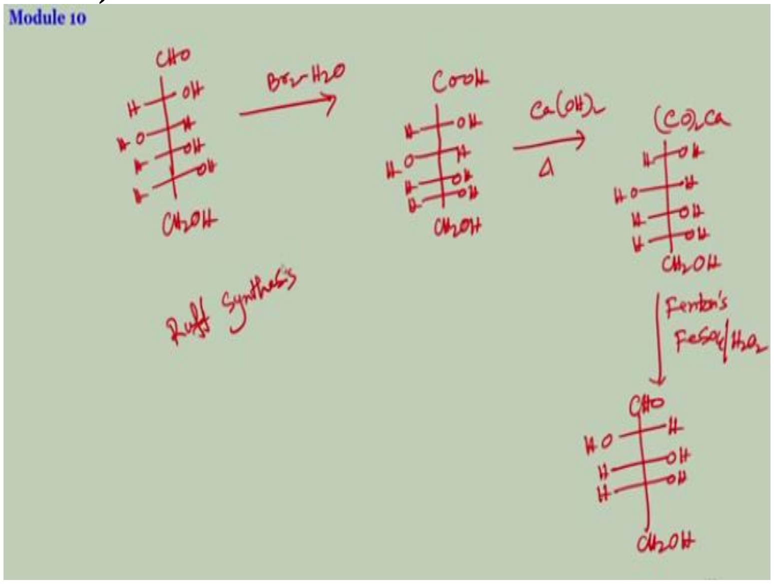

Second reaction is if I start with the same glucose OH H H OH CH 2 OH glucose again and then you treat this with bromine water. Bromine water is used to oxidize aldehyde to carboxylic acid. So you will have a carboxylic acid and all the rest of it then treat this with calcium hydroxide and heat it off it will form CO whole 2 CA CH 2 OH this if you treat it with Fentons reagent. Fentons reagent is basically your FeSo 4 for in hydrogen peroxide.

Then you get elimination of carbon dioxide and this will be, next carbon would be exposed. So, this will become CHO and you have this OH H OH H CH 2 OH. This is another method through which you can reduce one carbon on the sugar and this reaction is known as Ruff synthesis or Ruff reaction. Another very interesting thing is a very important reaction that a sugar undergoes and that is for the formation of osazone is called the Amadori rearrangement.

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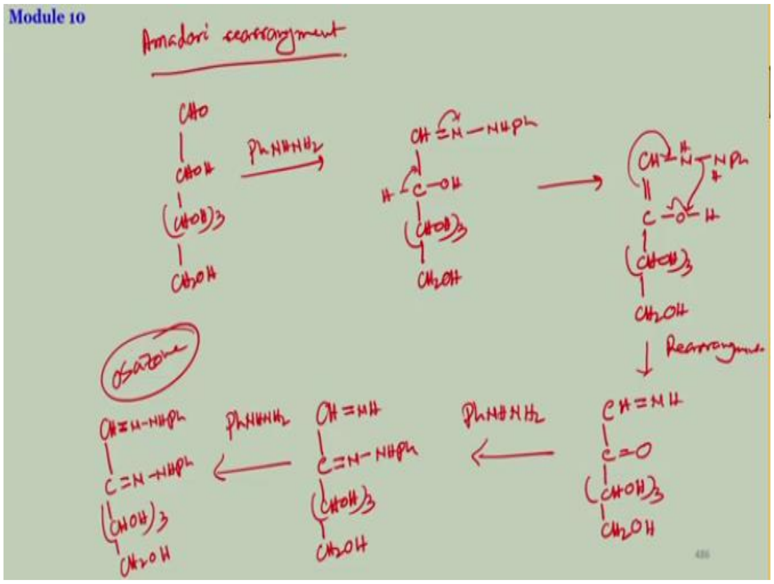

If you take either allose or ketose and if you treat it with phenol hydrogen you will get the formation of ozone, people have used that chemistry for various other aspects also. So I will show you that amadori rearrangement first and then we can maybe use it later aldo hexose, it will start with 6 carbon with aldehyde is called aldose hexose, phenol hydrogen NHNH 2 phenol hydrogen reacts with a carbonyl compound.

To give you phenol hydro zone minus water condensation reaction it is very well known in NHPH. This now, this can happen and you can use a little bit of base also NH PH. This will create this OH CHOH whole 3 OH. Now, this is the driving force this will come and this will take up the proton and this will open up. This is basically the amadori rearrangement this is the rearrangement. So, you will remain with CH double bond so this will be here NH.

And you will form a keto all 3 CH 2 OH. So I will basically write it here this, this is coming here it will take up go there and you exposed now another ketone, if you treat this with another molecule of phenol hydrogen that will again condense with the keto NH C double bond N NHPH whole 3 CH 2 OH another molecule of phenol hydrogen we will hydrolyze these and we will replace these by the same compound.

In N NHPH N NHPH CH whole 3 CH 2 OH this would be formed and this is known as osazone formation. This actually is used some of this chemistry has been used for in the next one I will show you the AP modernization if you want to change the stereochemistry of the anabolic carbon. This is one of the way to do it even from allose to ketose conversion, you can also do using this kind of chemistry. Thank you.