Course on Stereochemistry
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Module No 01
Lecture 01: Constitution and Configuration

Ok, welcome to this course on Stereochemistry. This is a basic subject branch of the of chemistry and it primarily focuses on the fundamental aspects of this topic. Now stereochemistry like any other branch of subdisciplines, this shall also emerged from a historical perspective. This is a very interesting concept in the subject of chemistry which is applicable to not only to chemistry, higher-level get history but also to various other branches of sciences like biology and medicine in particular.

Why the subject is so important? Because of many reasons for the primary reason is that the world that we are living in today, is a chiral world. What does it mean? That means it is made up of systems which have a handedness. Handedness means that if I see the 2 hands, these 2 hands, one is the, is they look almost the same but they are not same. You cannot really you cannot say that they are the same hands because you cannot superimpose one hand on top of each other.

And that is primarily because of their geometry and the way the fingers are aligned. Similar things happen in the molecular world. And as I said, we live in a chiral world and that means that all the living systems that are there, they are made up of molecules which exhibit this type of handedness. The stereochemistry is a subject which deals with the property of the molecule in three-dimensional space.

Chemistry 1st of all developed as the function and reactivity and structure of molecules but purely on a two-dimensional plane that is the chemistry what was known earlier. In earlier days was two-dimensional chemistry. That means, we looked at molecules from a two-dimensional aspect.

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But since since this is the 1st class of stereochemistry so I thought that I will 1st show you that I will introduce the course instructor which is myself, Professor Amit Basak and my teaching assistants, you can see the names, Arundhati Mandal, Eshani Das, and Monisha Singha. And they will help in answering your queries and your and they will also upload the questions and the other teaching materials and finally they will also try to dispel any doubt that you have while going through this course.

The problem of stereochemistry lies with the visualisation of molecules in three-dimensional space because you do not have the luxury of having a molecular module in your hand when you see it in an examination hall. What you have to do if you have a problem? You have to visualise it in the three-dimensional and then try to figure out that what would be the perfect geometry, how does it interact with other systems?

So that was the most difficult part of stereochemistry, that is the visualisation of molecules in three-dimensional space. What is the difference between this two-dimensional chemistry I was talking about?

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That is okay before that let me show you what are the different modules that are there in this course. These are already put in the way when I think you can go through these 8 modules that are orchestrated in such a fashion that slowly you would learn how to draw the three-dimensional structure and then try to analyse the, analyse the their interrelationship and then finally we will come to the reactivity of these molecules and the reactions evolving with these molecules.

So basically this is a very fundamental underaged course at the 1st year, 2nd-year BSc level and I hope that initially there may be some difficulties in visualisation and conceptualisation of this 3-D 3-D molecules but later on, I am confident that if you go through this course, you will also feel confident like me in in answering order in conceptualising the reactivity of molecules which can exhibit three-dimensional geometry.

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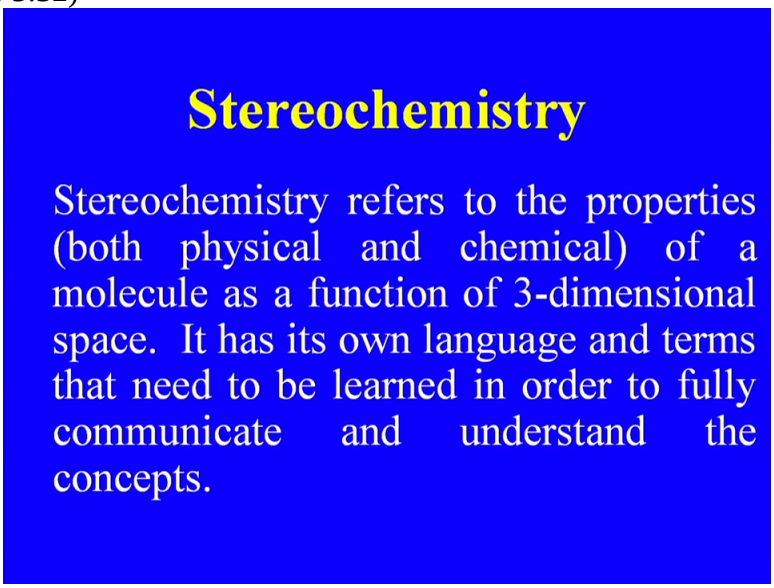

So what is the again I come back to the definition of stereochemistry. That means it is what I am telling that is a function, it is a function of, three-dimensional, a function of a molecule in three-dimensional space. I can clarify it little bit. They decide that if you take benzyle dehyde vs ortho methoxyl benzyle dehyde, you know that this carbonyl group is susceptible to nucleophilic addition because of the electrophilicity of this carbon.

But this is, these 2 molecules although they react with a nucleaophile, like X - but their reactivity is little bit different, their rate of reaction will be different because of not, because of the electronic effect of this methoxy group vs the hydrogen. What are these electronic effects? That is the - I and + R. So here the reactivity difference comes from the electronic effects and not in a state of chemical effect.

That means what I am saying is not that the methoxy is pointing in this direction and that is the cause of difference in the activity of this carbonyl vs the other carbonyl. While if you take the completely reduced system of of these 2 molecules especially this one, so if you reduce it, all the double bonds are reduced. So you get what is called as cyclo hexile system. And when you reduce, you have a you have a very interesting situation that this aldehyde may be aligned on the same face as the methoxy group or the aldehyde may be aligned in the opposite face of the methoxy group.

And because of this relationship, geometrical relationship, now the reactivity of these carbonyls will be different. And this difference now comes from the as a result of the different geometrical relationship between these methoxy and the aldehyde. In aldehyde case, again I repeat, these methoxy is exerting electronic effects compared to the hydrogen and that is the reason for their difference in reactivity.

So the activity of this aldehyde, now is dependent on the steric disposition, that means the three-dimensional disposition of the methoxy group in space, its relation to the aldehyde. So that is a very simplified way of describing what is stereochemistry. Now this subject did not evolve from a very rational approach like many other subjects. In medicine, what happens? Many of the medicines have discovered by chance and then people know how these medicines worker and then developed newer medicines.

Similarly stereochemistry also developed all it has developed by chance by trial and error, by serendipitous discovery. And then people finally come out and explain what was happening that what was the serendipitous observation, why is it happening.

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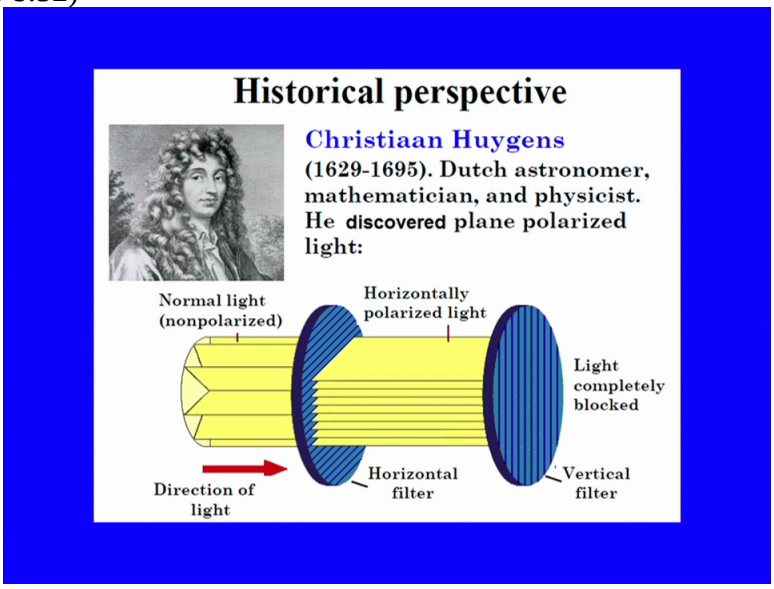

So I will tell you their historical perspective of the development of the subject. Now it all started with the property of light which we know that it is electromagnetic it is an electromagnetic wave. So there are 2 vectors, electrical vector, electrical waves and a magnetic vector, a magnetic wave

and both are perpendicular to each other. Now if you consider only the electric vector, so what happens, in normal light the the vibrations, the electrical wave vibrations are taking place in all directions, in all directions that is possible around a point.

That means if I take this, this is the light the light passing from here to there. Then the wave actually the wave is taking place in in every possible place in every possible direction. So basically it encompasses the whole 360 degree around this axis of migration of the light. That is the normal light. Now in in the 17th century, this Dutch astronomer, Huygens, he discovered what is called plane polarised light.

Means that means what I was telling earlier that the wave was vibrating in all possible directions. That is the normal light. But when it passes through a special type of glass which is made up of some crystals, what happens? It allows only the vibrations which is occurring in a particular plane and then the light that comes out, all the objections are taking place in a particular plane and that is what is called plane polarised light.

In this case because I am showing it is in the horizontal direction, so that will be called horizontally polarised. But actually these are what are called either linearly polarised light or for you as a beginner, you should call it as plane polarised light. And the plane in which the vibrations are taking place is called the plane of polarisation okay? As I said again, this is what is the the plate, the kind of a crystal.

It is made up of a crystal like crystal of calcium carbonate which is known as calcite, they have this special property. Not all crystals will do this. So this plane polarised light if you take another crystal which allows, which will also can can produce this plane polarised light but what happens? If you now have these crystals or this plate aligned in such a direction that it is it will it will have the plane of polarisation perpendicular to the plane of polarisation that this crystal is is generating.

So in that case what happens? This will completely block the propagation of the light on the right site. On the other hand if you rotate this and ultimately by 90 degree, then what happens? The axis of polarisation will become aligned to the axis of polarisation of these plate and then the

light will come out. So by these 2 plates, you can actually analyse whether if you put a molecule here, in between these, the light going from here to there, then what happens?

If you think that the plane of polarisation is rotated then the way to do it that whether there is any rotation or not, then you have to rotate this plate and then find out whether light is coming out or not.

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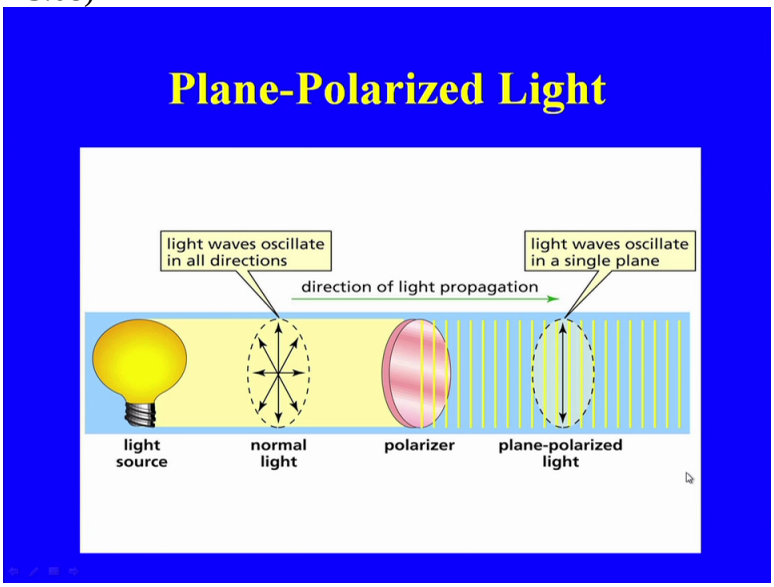

And so it all started with the planar polarisation, plane polarised light but then people are interested in seeing that what how the molecules behave when plane polarised light passes through the molecule in a solution or in a liquid state. And very interestingly, they found that that suppose this is your, a solution containing a Sample X, a molecule X and you produce plane polarised light by shining a bulb and putting a polariser.

This is by the way is called a polariser. So it will produce the plane polarised light and suppose the vibrations are taking place in a vertical direction. So now when it goes through the solution, if the solution does not change the plane of polarisation, so the plane of polarisation remains vertical. And if you put the other plate here which is now called an analyser because you are analysing whether there is any perturbation in the plane of polarisation of this light.

So by the analysis, by this analyser, you can now check whether there is any rotation in the plane of solar radiation while passing through the solution of the Sample X. So people started doing all

sorts of experiments like with using different types of molecules. And what they found that there are some molecules which rotate this plane of polarisation either clockwise or in anticlockwise fashion and there are some molecules which do not.

So if it rotates, suppose this is an example where the plane of polarisation is getting rotated in a clockwise direction and how do we know it? You rotate the analyser so that the axis becomes aligned to the rotated plane of polarisation. Now you can see the light coming out from this. So by the amount of rotation that is needed to see the light coming out, that will be the amount of rotation that has occurred while like is going through the solution ok.

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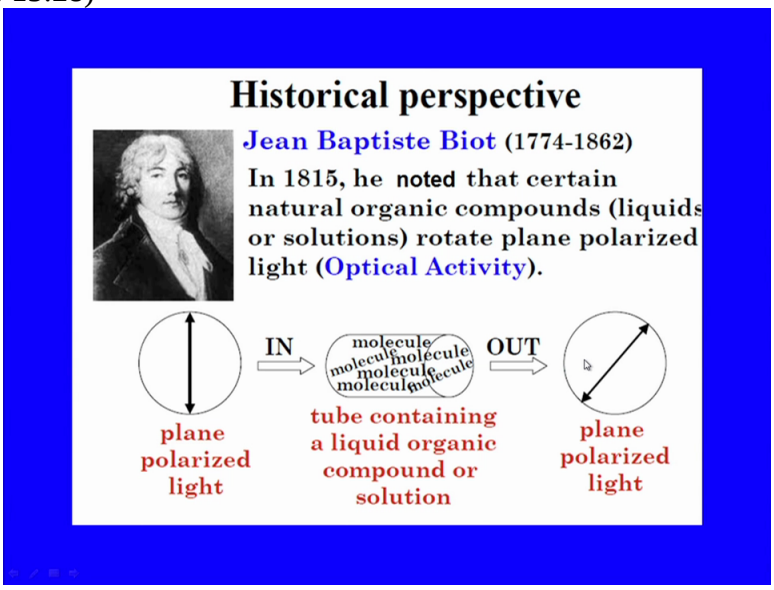

So this was this was known or this was shown by by Biot, by a French scientist who discovered this phenomen that there are some molecules where if you if you pass the plane polarised light that undergoes rotation that means the planar polar radiation undergoes rotation and then you can see the amount of rotation and that is characteristic of the Sample. But as I told you, this does not happen with all compounds.

There are some particular compounds which has this typical property and he called this rotation of this plane polarised light as the molecules are showing optical activity and these molecules he called optically active molecules. The reason for this rotation of plane of polarisation was not known at that time. Then what happened?

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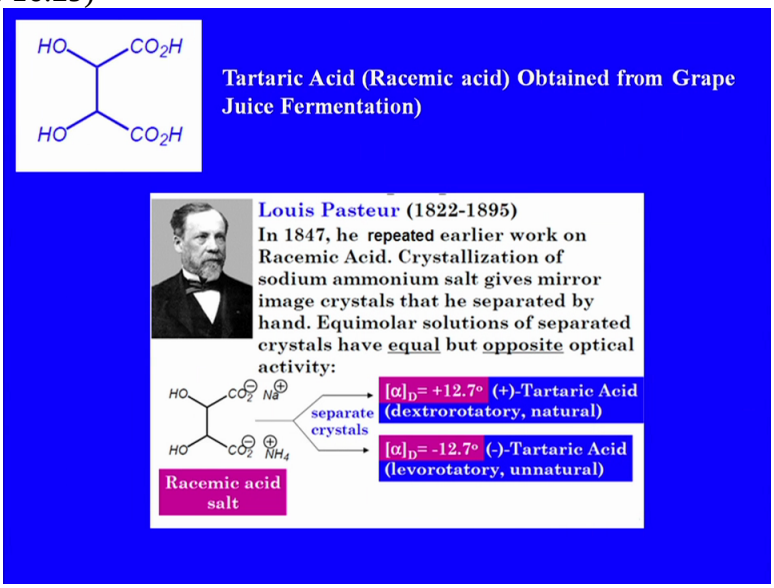

After this event, the Louis Pasteur, the famous again French chemist, he came into the picture. So what he did? See at that time, this molecule was known. This was called tartaric acid. It was obtained from from various sources like it can be obtained from fermentation of grape juice. So this tartaric acid, he he collected and then he did a crystallisation of this tartaric acid which was called at that time, racemic acid.

This tartaric acid plane from grape juice fermentation was called Racemic acid. And this Racemic acid, he crystallised it as the sodium ammonium salt because it is a dicarboxylic acid. So one is sodium, one hydrogen is replaced by sodium and the other sort is the ammonium. So it is a sodium ammonium salt. And then he crystallised it and what he noticed that there are 2 kinds of crystals that were obtained.

And he using using a microscope, he could separate these 2 kinds of crystals. And then he could find that this one set of crystals is the perfect mirror image of the other crystal. And then with the separated crystals, he analysed them that what is the effect on the plane polarised light when it passes through these crystals but the crystals are in solution now.

So basically Racemic tartaric acid was divided into 2 sets of crystals, these crystals were mirror images of each other and then when light passes through these crystals, he found that one set of

crystals is rotating the light in a clockwise direction, the other set of crystals which are in solution, they are rotating the light in the other, in the anticlockwise direction okay?

So that formed the the basis that okay, so basically you have the same molecule, tartaric acid. St two-dimensional chemistry, this looked to be only one compound but because they have different rotation power, rotate the power, so they cannot be the same molecule. So the same, the molecule which looks the same in two-dimensional geometry, Pasteur has shown that actually they can be consisting of 2 different sets of molecules.

So that actually is the beginning of the three-dimensional chemistry which is called now the stereochemistry. So this is the, he laid the foundation of stereochemistry.

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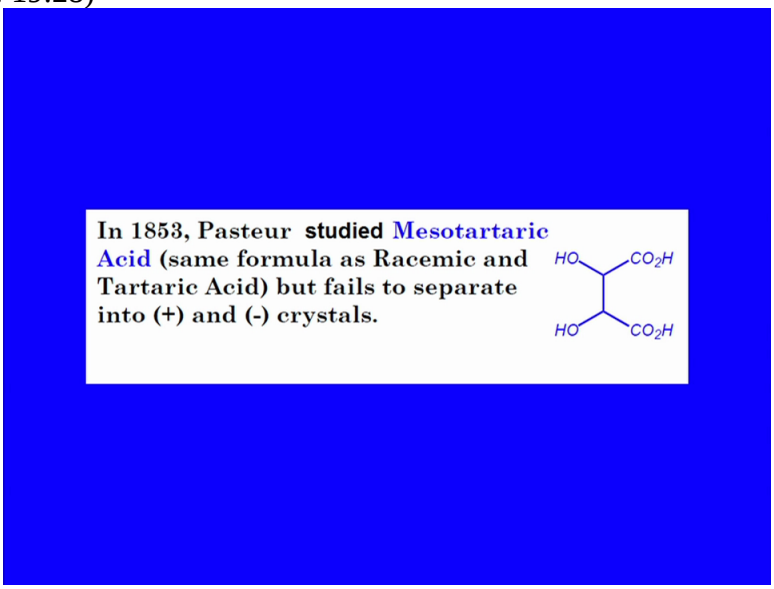

But the question is why? How can you really explain this type of phenomena that where you have the same formula, molecular formula, same type of connectivity but you can have 2 systems generated out of that okay? But before that, Pasteur actually did another experiment. See, apart from Racemic acid which can be separated into 2 sets of crystals, he also studied another form of tartaric acid.

He found another form of tartaric acid, the same molecule formula, same constitution. That means, same type of atoms attached to the similar type of atoms. And then he found that this tartaric acid which was called mesotartaric acid, he could not, he failed to separate it into 2

isomers and then he found that this is, this does not also rotate the plane of plane polarised light. So this is again different from the earlier Racemic acid that he used that he obtained from the grapefruit juice.

So now we have 3 types of tartaric acid, one is this mesotartaric acid which does not which cannot be separated into any any different crystalline forms, that means it is basically it is a one compound, single compound. And on the other hand, you have this tartaric acid which was obtained from grapefruit juice, at that time it was called Racemic acid. It consists of 2 types of tartaric acid, one was called because one was rotating in the clockwise direction, so that was called dextro tartaric acid and the other one is the livo tartaric acid because it was rotating the light in the other direction, that means counterclockwise or anticlockwise direction.

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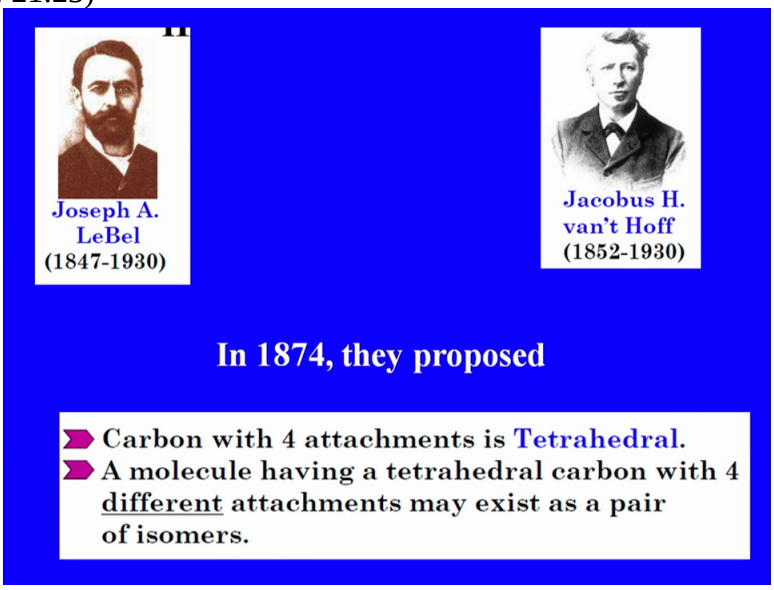

However, Pasteur could not explain why this phenomena is happening. That means, the molecule having the same molecular formula, same constitution but how can it exist in 3 different forms? In 1874, Vant Hoff and Lebel, they proposed that this is because of the existence of carbon in tartaric acid where the carbon is attached to 4 different groups.

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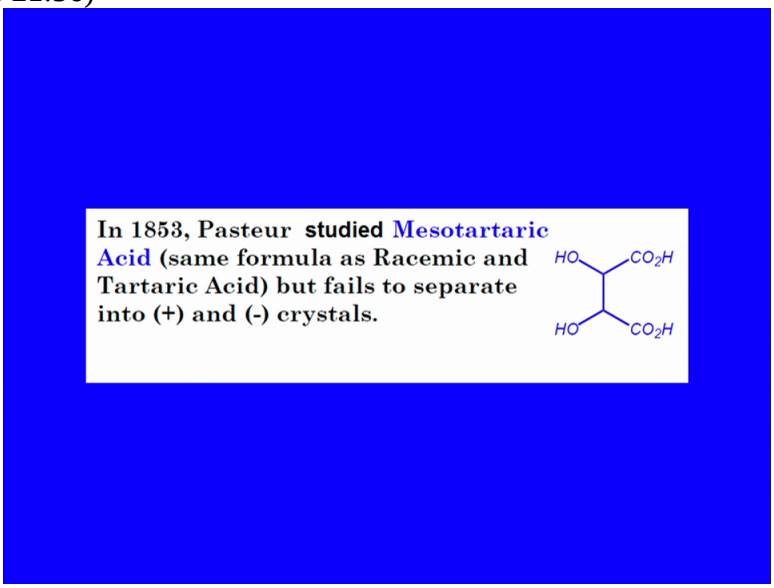

Again I just go back to the previous light, if you consider the tartaric acid structure, you see that there is a carbon. Usually we do not put the hydrogen which is attached to the carbon. So that is why, the hydrogen is missing. So the carbon has a hydrogen, has a carboxylic acid, has OH and this whole group. That means 4 different groups are attached to this carbon and these 4 different groups are attached according to Vant Hoff and Lebel, they said that they are attached in a tetrahedral fashion.

And because of this tetrahedral arrangement, they said that if a carbon has this 4 different groups attached to it, then you can generate 2 molecules out of it and one will be the mirror image of the other. And they can exist as a pair of isomers. So that is the breakthrough concept. Remember, it is only 1874. At that time, the tetrahedral geometry of carbon by SP3 hybridisation was not known.

So it was a pure speculation or a brilliance from these 2 scientists who could who could propose propose the tetrahedral geometry of carbon because they knew that if the carbon is flat, square planar, then you cannot generate these type of systems out of it. So just from geometric concept, they developed this tetrahedral geometry of carbon.

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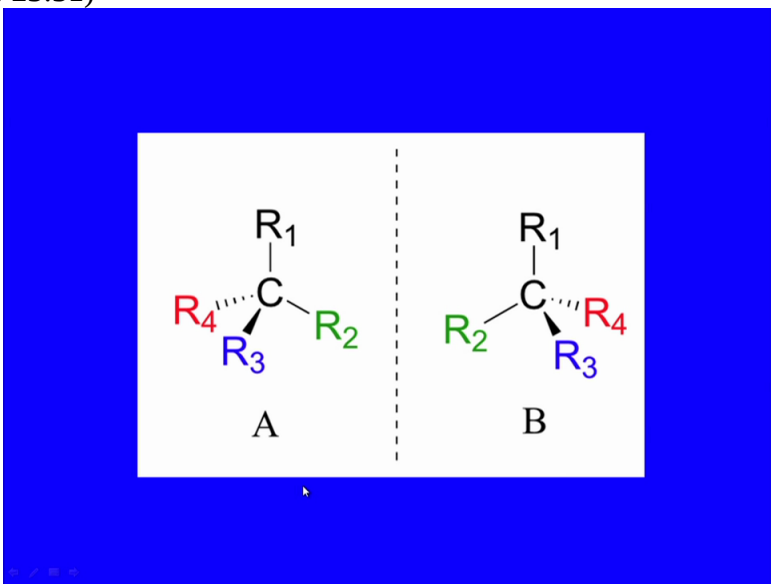

So what is the ultimate? So 1st it was the development of plane polarised light. Then the observation that some molecules rotate the plane of plane polarised light. The 3rd is tartaric acid. So it all started with tartaric acid. And the tartaric acid exists in sub-tartaric acid in 3 different forms and finally Vant Hoff and Lebel, they they postulated that this is because of the existence of a carbon with 4 different groups and you can generate 2 different molecules out of this. So that takes care of the slides. Now I will show you, I will start from Vant Hoff and Lebel, what they said I will show you in a model.

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See, if you look at this, this system, that there is a carbon, there is a green atom, there is a blue atom, there is a white atom and a red atom. So this is a tetrahedral carbon with 4 different groups and if you take a mirror image of this and I can take a mirror image of this, I can build up this particle. So they are, they are not mirror images I think you have to rotate it little bit, yes. And now, you can see that they are mirror images other.

But if you would now want to see whether they are identical or not, you try to what is called the principle of superposition. So you want to put one on top of each other and then see whether they are superimposable, that means all the green atoms or blue atoms or red atoms or the white atoms, they match or they fall on top of one another or not. So that is what is called superimposition.

So you apply that superimposition principle. Now whatever you do, if you try to match the green and the blue, you see there is a mismatch between the red and the white. Here also, there is a mismatch between the red and the white. If you want to match the red ones and the green ones, now what happens, you see there is a mismatch between the blue and the between the blue and the white.

So basically you cannot superimpose these 2 molecules. So they are mirror images, they are different. So that is the starting point as I said. So they are now isomers because you know what are isomers? Isomers are molecules with the same molecular formula but having different properties. That means a different molecule with same molecular formula are called isomers, okay.

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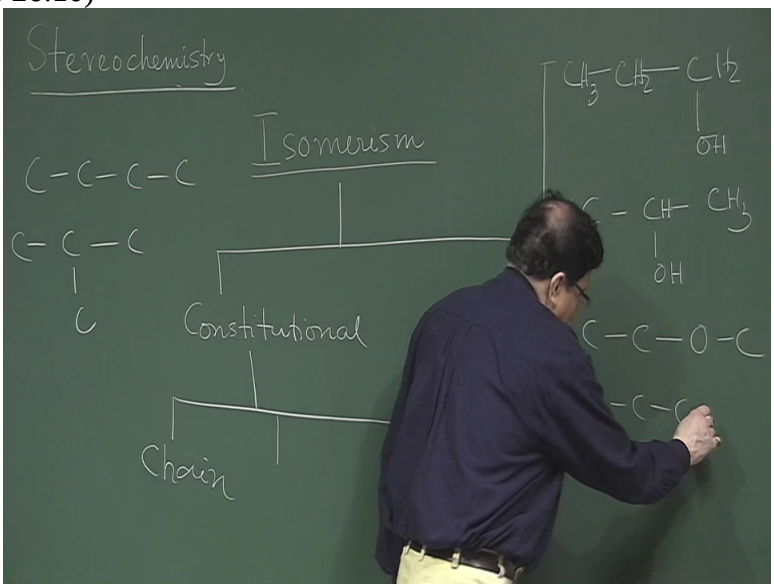

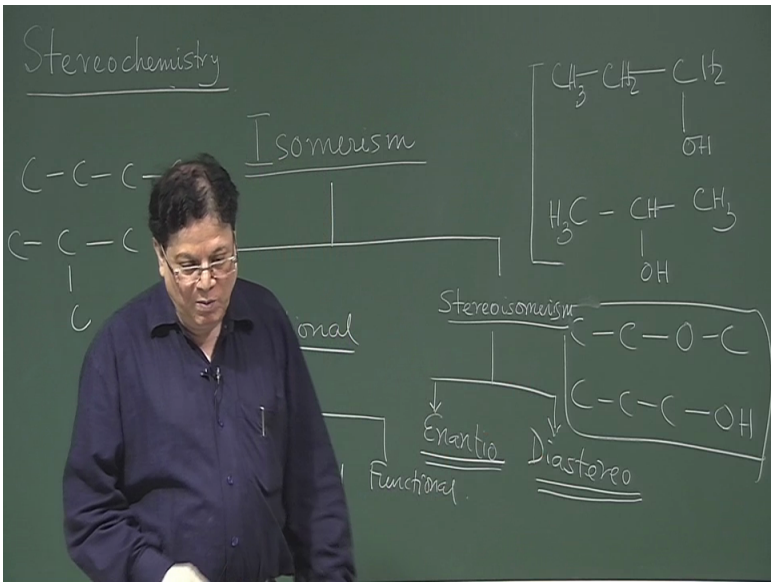

So let us start with these. Isomerism is a very important concept in, not only in stereochemistry but also in two-dimensional chemistry we know. And we can now subdivide this isomerism into into 2 classes, one was based on two-dimensional chemistry and that is called the kind of isomerism that you are exposed to, is called constitutional isomerism.

Now what is that? What is constitution? Constitution is nothing but what is called the connectivity. That means if I have a carbon C, another carbon, such 3 carbon system and then if I have OH here vs again the 3 carbon system, if I have OH here, I am not putting the high Trojans.

If you put the hydrogens now, methyl, this is hydrogen, this is methyl and that is CH 2 CH 2 and CH 3. Now what is the difference between these 2 molecules?

The difference is in the connectivity. Here, the terminal carbon is connected to OH, here the middle carbon is connected to OH. So that is what, that means they have different constitution. Constitution means the connectivity. So this is also isomerism but that will be called constitutional isomerism. So you have a set of constitutional isomerism.

Similar is, in constitutional isomerism, you have different branches, you have different subdivisions. These are all known. Like one is called chain isomerism where the carbon chain is different. So if you have 4 carbon system, you can grow this 4 carbon system in this fashion also. So again the Constitution is different. This is N butane and this is 2 methyl butane.

They are different molecules because their Constitution is different. So but that is called chain isomerism. Then you have you have positional isomerism like this example, positional isomerism, the hydroxy group changes position from here to there. So that is called positional isomerism. And another class of constitutional isomerism is what is called functional group isomerism.

I am not again putting the hydrogens. So this is the ether molecule. So you this is ethyl methyl ether. You can draw another molecule with the same molecular formula but that will be called propanol, one propanol. So that is what is called functional group isomerism. So you have 3 types, chain isomerism, then positional isomerism and you have functional group isomerism.

But this is two-dimensional chemistry, again I repeat. The more important one which is relevant to our subject is this, is the other part where the Constitution is same. But the molecules are different and that is called stereo isomerism. So is the Constitution is different, that means connectivity, atom connectivity is different. Then if they fall into the class of constitutional isomerism.

If the connectivity is same but the molecules are still different like tartaric acid as I showed where where the connectivities are all same but you have 3 different types of tartaric acid. So then the concept of stereo isomerism comes. So what are stereo isomers then? Molecules with

same molecular formula, with same functional groups, with same Constitution, so what the difference?

The difference is the arrangement of the groups in the three-dimensional space such that is, they are the stereoisomers. Now in stereo isomerism you have again two different types of stereo isomerism, one is called Enantiomerism and the other is called Diastereo isomerism. Okay? We will discuss, we will start from this stereo isomerism, Enantio and Diastereo from now on, okay.

Enantiomers are molecules which are mirror images, non-superimposable mirror images of each other. Like what I showed about the Racemic tartaric acid which was resolved into 2 sets of crystals, one crystal was mirror image of the other crystal but they are not superimposable. They are different.

Similarly molecules, if you look at the molecular level, molecules which are stereoisomers and mirror images, non-superimposable mirror images of each other, they are called Enantiomers whereas molecules which have same Constitution, same functional groups, same connectivity, but they are not mirror images of each other and they are called diastereomers or you can say the molecules are exhibiting Diastereo isomerism okay?

Okay, let us wipe this out now. Let us concentrate on the 1st on the Enantiomerism. So Enantiomers are what? Enantiomers again I repeat, are molecules which are non-superimposable, are stereo isomers which are non-superimposable on each other, which are non-superimposable mirror images of each other. They are called Enantiomers and they have the typical property of rotating the plane of plane polarised light.

So Enantiomer is always a pair, Enantiomeric there. So one is the mirror image of the other. So if I have a A, I have a mirror image of A. If this has got a + rotation, so I can have a mirror image which will have a - rotation. So they are a pair of Enantiomers okay. So Enantiomerism is directly connected to optical activity. So if you take just one Enantiomer and pass the light, this light will be rotated clockwise or anticlockwise direction.

One thing one should remember that this rotation when we tell, we have to view the the rotation from against the propagation of the light. So if light moves from here to there, the Observer is here, the Observer I should be here and then he will see whether it is rotating clockwise or

anticlockwise. This is very important because if you look from this side then the clockwise becomes anticlockwise and the anticlockwise becomes clockwise.

So basically what when the chemists measure the optical rotation of a molecule, what is the optical rotation? That means the degree of rotation that what the molecule does onto the plane of plane polarised light. So we have to view against the propagation of the light. Then you can say that whether it is clockwise rotation or it is anticlockwise rotation.

Now by the way, clockwise rotation is also called dextro as I already mentioned, dextro rotate any molecule, if the molecule rotates the plane of the plane polarised light in the clockwise direction, that is called dextro rotatory molecule and the other one, will be called liver rotatory molecule means liver rotatory molecule. Rotate the plane of plane polarised light into the left side.

The question is, we know that they form superimposable mirror image, a non-superimposable mirror images sorry, they form a non-superimposable mirror image system. But what makes it what is the cause of this rotation? What is the genesis of this optical activity? Okay? Now by the way, another terminology is there that molecules which can rotate the plane of plane polarised light, they are, earlier I said, they are optically active compounds, they are also called chiral molecules okay?

Chiral molecules, like these 2 hands, one hand is the mirror image of the other. So but they are not superimposable as I said and this is hand. So if I consider this as a molecule, so if light passes through this, the light will suffer rotation. If light passes through this, that will also suffer rotation but the 2 rotations will be just opposite to each other okay? This is earlier it used to be called handedness but the same thing is, the modern day we call it chirality.

So now we can summarise little better that what we have learnt is that there are molecules which have the same molecule formula, same connectivity, same functional group but they can be different. They are called stereo isomerism and that stereo isomerism is arising because of the disposition, different disposition of groups in the three-dimensional space. Then we have seen that there are 2 sets of stereo isomers, one is called Enantiomers and the other set is called

Diastereomers. Enantiomers have non-superimposable mirror images and Diastereomers are, they are not mirror images of each other but they are stereoisomers okay?

Then Enantiomers have the property of rotating the plane of plane polarised light. I have not concentrate in we will back to the Diastereomel later on but let us 1st concentrate on the Enantiomer that Enantiomers have the capability. Because they are chiral, they have the capability of rotating the plane of plane polarised light. Now comes the bigger issue that why this molecules which have non-resolvable or which have non-superimposable mirror images, why do they rotate the plane of plane polarised light, okay? So that will be the next half an hour we will discuss the genesis of this optical activity.