Course on Stereochemistry
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Module No 03
Lecture 13: Chirality in Heteroatom Systems

Okay, welcome back to this course on stereochemistry. We have so far covered some of the basic concepts of chirality, stereoisomerism and then the assignment of absolute configuration, relative configuration and we started in the pro chiral faces, pro chiral centres and how to designate them and then finally we started last time the conformational analysis. But then I realised later on that we should discuss, so far we have discussed only the chirality involving the carbon centres.

We have not discussed any system where the chirality is originating from some other atom, other than carbon. So let us some concepts about molecules where chirality is exhibited by chirality is due to the presence of a noncarbon Centre.

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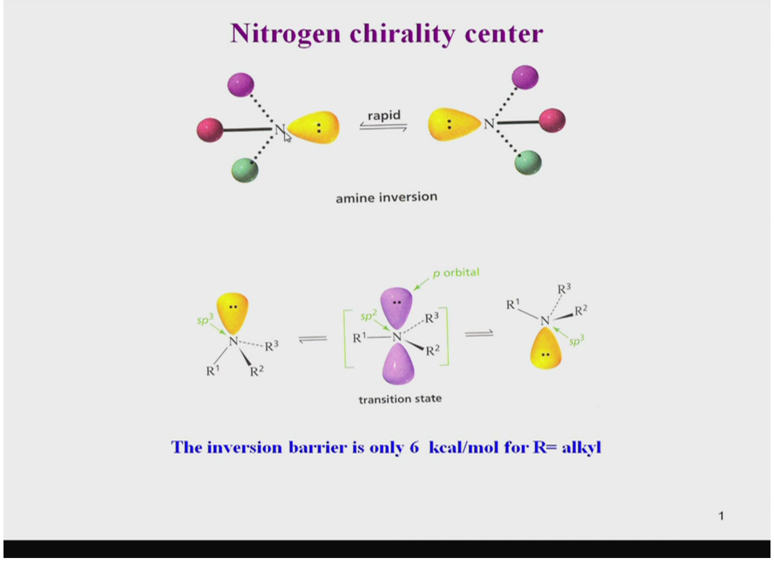

Nitrogen chirality center

The inversion barrier is only 6 kcal/mol for R= alkyl

So let us start with the atom nitrogen because the important thing is that that and that they will consider, the noncarbon atom that we will consider, should be tetrahedral, should have a tetrahedral geometry and then the concept of chirality only arises. So we will pick up atoms like nitrogen, Tetra co-ordinated nitrogen which is tetrahedral, that we know. And then we also have phosphorus, the the next atom in the same group of nitrogen.

So you can go down nitrogen, phosphorus, arsenic, antimony, bismuth and we can discuss the stereochemistry that is involved in all these in this series but just for this course will restrict our our description only to the case of nitrogen and phosphorus. So let us start by showing you the case of nitrogen. Now if you take nitrogen and trivalent nitrogen which is tetrahedral that we know, the geometric is is is a triagonal shape but the whole structure is tetrahedral because structure you have to consider the lone pair also.

So if you consider the lone pair as the 4th ligand, then you have the other 3 ligands. In ammonia, these 3 ligands are hydrogens and this is the lone pair. Now if these 3 ligands are not ammonia but derivatives of ammonia where the derivatives are such that these groups are different. I have here shown the difference by colour difference, so these 3 groups are different and lone pair is obviously another entity, different from the, from the ligands.

But the that is also considered, considered as a as a group or a ligand attached to the nitrogen. So lone pair is also here considered as a as a group attached to the nitrogen. Now if it is so there are 4 groups now basically there are 4 groups arranged in a tetrahedral fashion and all 4 groups are different. And so this nitrogen belongs to the class of a stereogenic Centre or the so-called chiral Centre in case of carbon.

And so this nitrogen is a chiral Centre. Okay? Because all 4 ligands are different okay? I again repeat, lone pair also it although it is not connected to any group, but here, for the sake of simplicity, you consider it as a as a 4th ligand. And so this is, this should be chiral and now, it s mirror image is drawn here. If you put a mirror here, then this will be the mirror image of this, of this molecule.

And they are not superimposable, exactly like the all the carbon system. Okay? However that is the problem here. If one tries to isolate one of these enantiomers, so they are basically Enantiomeric there. Now if you want to isolate these enantiomeric pair, it is not possible to do so because because there is a rapid interconversion between these enantiomers to this enantiomers and vice versa. Okay?

So they rapidly interconvert into one another and this interconversion is is what is called the nitrogen inversion phenomenon. What is nitrogen inversion phenomenona? That means the lone pair which was earlier pointing towards this direction, that now inverts its position, comes to the left side and these 2 groups which were towards the left-hand side, now goes to the right-hand side okay? So that is what is called the inversion in case of nitrogen. The same inversion we will come to phosphorus also happens in phosphorus. In nitrogen, this inversion is has a very low barrier.

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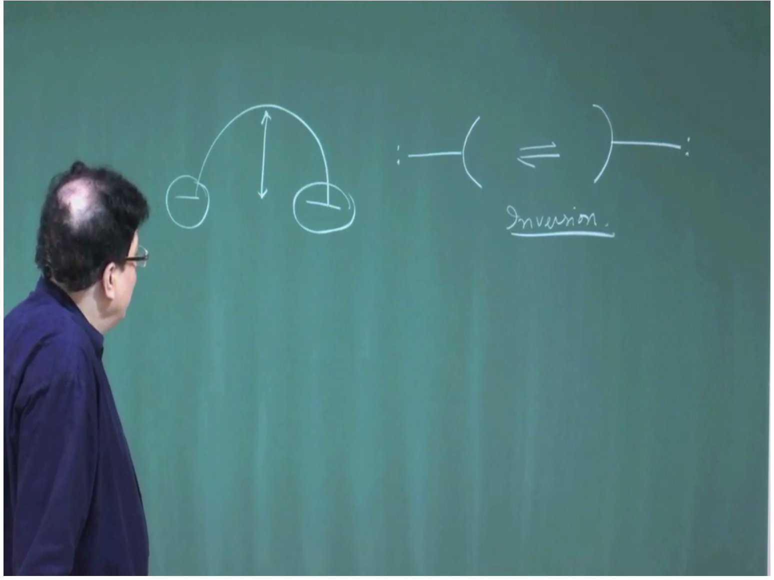

For any process, you know that there is a there is a barrier involved. Now in this case, these are enantiomers, so they will have the same energy. But there will be a barrier to this conversion process. Now this barrier is such in case of nitrogen that it happens at the room temperature. So if the barrier happens at, if the inversion happens at room temperature, that means one Enantiomer is converted to the other enantiomer at room temperature.

So it is not possible. The moment you try to isolate this, then that 50 percent of this will be converted to 50 percent of the other enantiomer. So it is not possible to isolate these enantiomers in case of nitrogen okay? Now that inversion can be described beautifully by by this diagram. Suppose you have an inverted umbrella like this and what happens in spin inversion is, that goes on to another inverted umbrella which will look like this okay?

So if this is the lone pair earlier, so now the lone pair is occupying this side okay? So this is the inversion process. So due to this inversion process, it is not possible to isolate the enantiomers in case of nitrogen. However there are ways to let us inspect this inversion process again through the slides.

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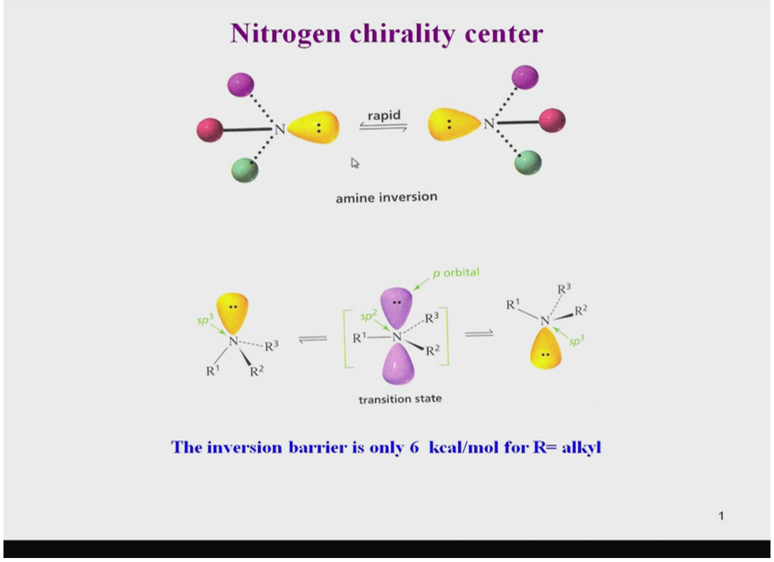

Nitrogen chirality center

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What happens here? Because this inversion cannot happen by by just that that jumps and go to the right side, that cannot happen. What happens here here the nitrogen is started as a SP3 hybridised nitrogen but during the inversion process, at the intermediate stage, it becomes SP2 where 3 groups, R1, R2, R3, here they are described by different colours. See now I am putting 3 different rooms, R1, R2, R3.

And this nitrogen was SP 3 to start with. The lone pair is at the top. Now what happens? As it tries to go to the bottom, it has to go through this intermediate where this is the nitrogen becomes SP2 hybridised and now this is a pure p orbital. So this is now brings the all the 3 groups in a planar orientation, in a planar orientation. That means now the nitrogen has lost the chirality in this configuration. It has lost chirality but it regains chirality by now again changing the hybridisation to SP 3 but in a but putting the lone pair in the different direction, just in the opposite direction.

So now the lone pair is occupying an orbital which is the bottom orbital. Earlier, it was at the top. The most important point is that this inversion process involves an intermediate where the nitrogen is SP2 hybridised and it has lost the chirality. So actually, you will know later on that to go from one enantiomer to another enantiomer, that means which is called inversion, you need to go through a planar planar molecule and then go to the non-planar molecule to bring back the chirality.

While going into the non-planar molecule, you have the option of either going to the starting point or going to a product point. So that what happens here. So the starting point is this nonplanar, is chiral. Then you go to a planar system which is achiral and then it had the option of going back or going farther to go to the opposite enantiomeric okay? So this process as I said happens at room temperature okay?

Because the barrier to, the inversion barrier is only 6 kilo calorie per mole, or R equal to alkyl. Because the inversion barrier depends on the size of definitely it will depend on the size of this different alkyl groups okay? So the inversion barrier may vary. So it is around roughly 6 kilo calorie per mole when R is equal to an alkyl group, a small alkyl group, say methyl. Okay? Now the question is that why the notion barrier in nitrogen is so low and which actually is inhibiting us to separate the 2 enantiomers of nitrogen?

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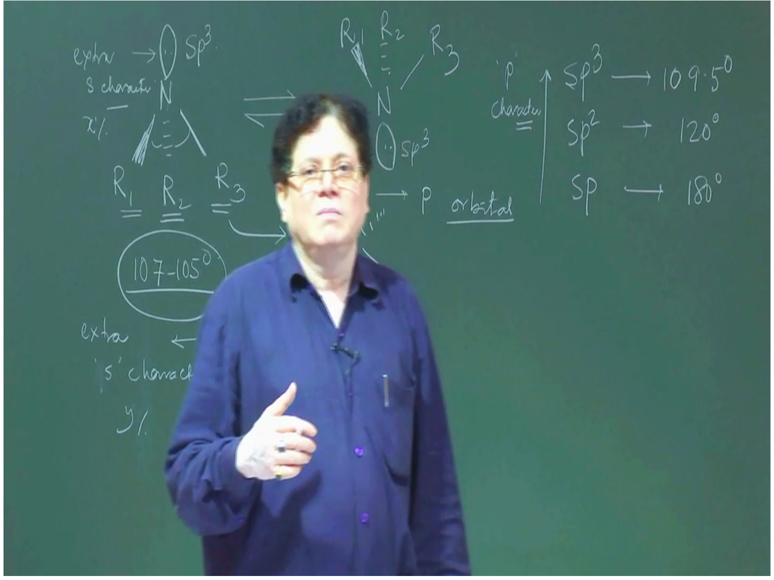

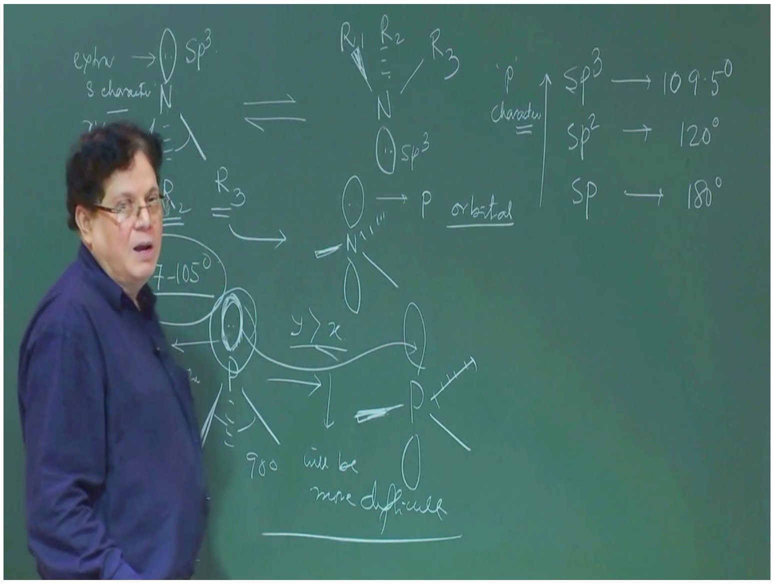

So let us draw that nitrogen compound, the tri-alkyl nitrogen compound and we have now come the very basic question that why is this inversion barrier so low in nitrogen? Just to mention that if you go to the next, next element in the periodic table along the nitrogen group, you will see phosphorus and in phosphorus, the inversion barrier is quite high and it is such an amount that allows the phosphorus compounds, the chiral phosphorus tri-alkyl compounds isolable at room temperature okay?

So the now the question is why is that? Why the inversion barrier is phosphorus high and nitrogen in nitrogen, it is low cost, so this is the the effect of inversion okay? So the lone pair was earlier up and now it is down. Now, one thing is clear that was shown earlier also. That while going from this to this, the nitrogen has to go through a pyramidal shape. That means the groups have to be pyramidal. And this orbital, the lone pair now assumes a pure P orbital. So this is P orbital.

And the nitrogen can call that it is assuming a triagonal bipyramid structure that includes the the lone pair. So the conversion is basically you have you have supposedly and SP 3 hybrid orbital and that goes to earlier it was up, now that goes to the down SP 3 orbital via the intermediacy of a P orbital okay? Nitrogen is 2P orbital okay? Now what happens? In nitrogen, you know that these angles are never maintained at 109 degree 28 minutes.

It is slightly less because of this lone pair, one pair repulsion is and they balance at a value when the angles are the the angles, these angles we are talking about is about 107 to 105 degree, varies with the nature of the alkyl group. So it is slightly less than the expected value of 109.5 degree. Now if you look at these different hybridisation states, SP 3, SP2 and SP, what happens? Here the bond angle, the correct bond angle, if it is your SP 3, is 109.5, here it is 120 and here it is 180.

So what we see that as the p character increases, the p character increases, the angle goes down. So that means, the nitrogen because the angle is less than 109 degree, 109.5 degrees is less than that, so the percentage of P character in these bonds, in these hybrid orbital is making the bonds, the percentage of P character will be more okay in not to lower this. Now that and how much will be the P character, X is P character, that depends on the how much deviation is from the actual bond angle okay?

So this has got, this has got your SP 3 now. So it will correspondingly has some extra S character but if you go to the phosphorus case, the inversion, plain inversions if you consider in the phosphorus, then what happens? These angles are close to 90 degree. And if it is close to 90 degree, that these these have got much more P character than the bonds which are making which are the trial nitrogen considering. Comparinging the nitrogen and phosphorus, this has got its more, this extra P character will be extra extra S character sorry S character.

Suppose this is X percent extra S character and this is Y percent so what you can say that Y is much greater than X. So this has got much more S character. Now the inversion means that it has to go from this orbital has to go from here to an SP2 orbital. So the orbital which has got already very high S character, for that orbital to go into the pure p orbital will be much more difficult than an orbital which has got, which is close to SP 3 hybrid orbital but S character is not way beyond SP 3 because the angle is only one 107 dollar 107 to 105 degree.

So again, I repeat the thing that because the S character of these of the orbital containing the lone pair in in trialkyl phosphine is much more than the expected SP 3 as compared to the nitrogen so this one for it to be converted to a pure P to convert the for this the intermediate, that is the intermediate, conversion of this to pure P will be more difficult will be more difficult and that is why you have a higher barrier to inversion and phosphorus than in comparison to nitrogen. Now this is one argument. There are other arguments you can also put forward and scientists also have done that.

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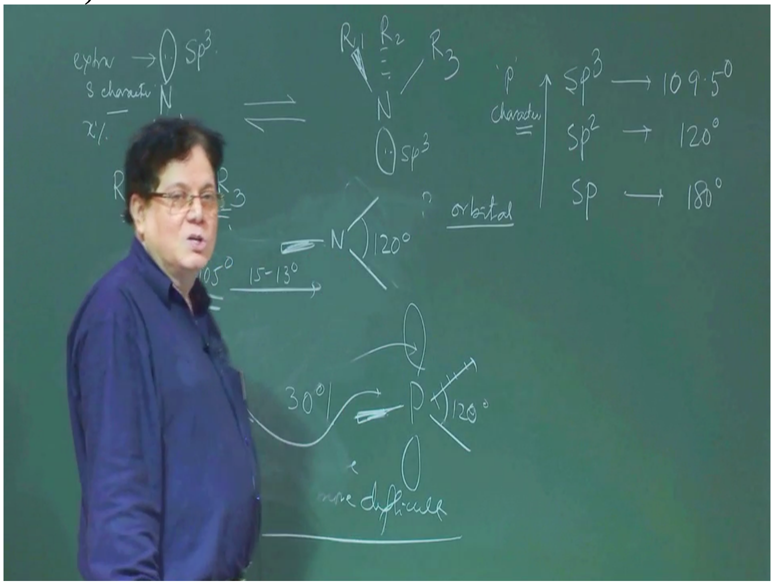

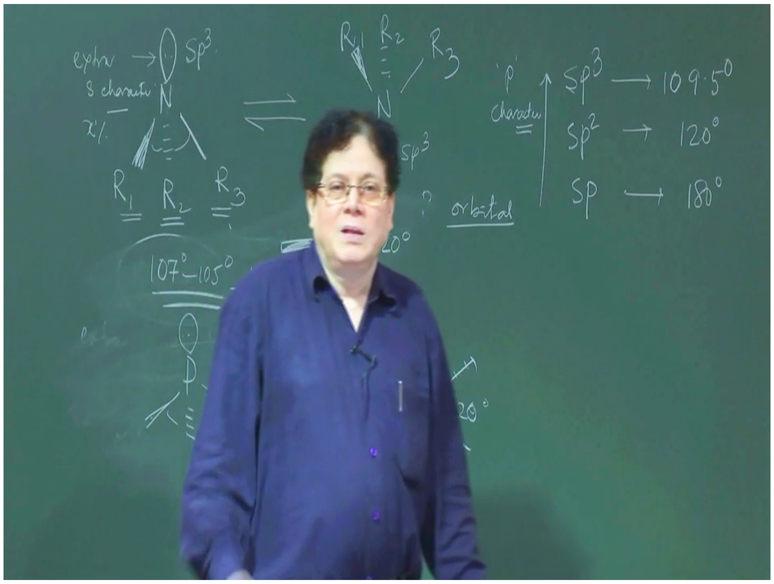

Another argument is is much easier, the argument is that in the intermediate stage, the angle between the alkyl groups is 120 degree. And in the nitrogen case, the earlier angle was about 107 to 105 degree. So now you have to increase the angle but in in increase is about 15 to 30 degrees to reach to 120.

In case of phosphorus, the angle is about 90. This is about 90 okay? So now from 90 to goes to 120, that means you have to increase the angle by about 30 degrees. So you need more energy to do this deformation. Okay? So you need more so you can explain as per the S character of the phosphorus lone pair or you can explain in terms of this angle concept that the angle was almost 90 earlier and you have to push it to 120 in the intermediate.

So it needs more energy than than that in case of nitrogen where the angle was about 107 to 105 degree and that is going to 120. So it is a much less amount of deformation in angle. So that is why, the inversion barrier in nitrogen is very low.

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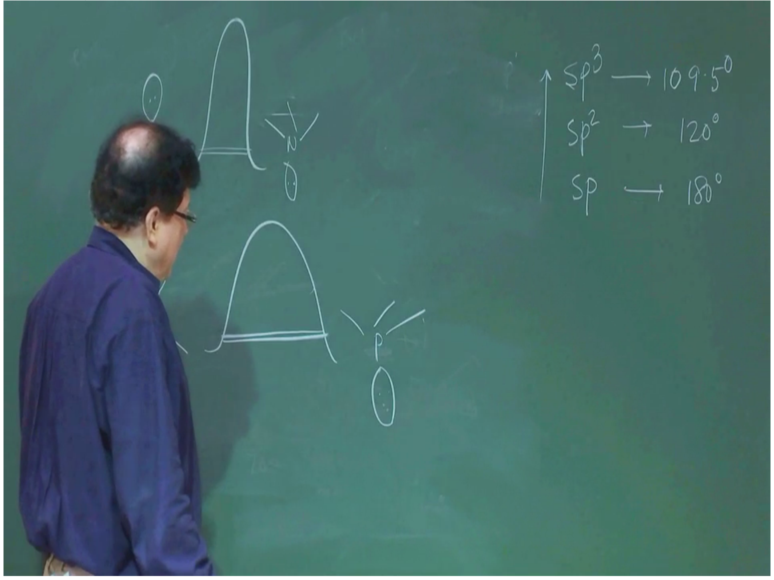

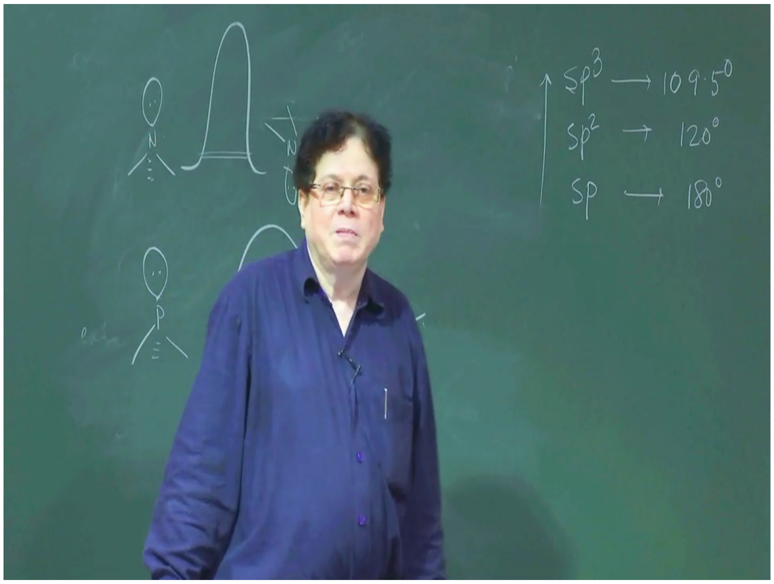

A 3rd argument which is based on quantum mechanical new concept which is little difficult, I can just simplify, I will not go into the details, what it says that the nitrogen energy barrier in going from one state to the other. One state means one one state is this one, the other state is the inverted one. So in going from this to that, the energy barrier is, has a much lower width than in case of phosphorus.

So in case of phosphorus, if you do the phosphorus chemistry, so if you do the same thing, the phosphorus energy barrier is, the width is very high okay? The width is very high. And there is an effect called tunnelling effect in quantum chemistry. That even if there is a very, some molecules can go from this side to that side by what is called the tunnelling. So then it is like physically physically you can think of a tunnel and this tunnel, the width of the tunnel is much less in case of nitrogen than in case of phosphorus.

So what it makes the tunnelling due to easy tunnelling effect in nitrogen as compared to the phosphorus because of the greater width of tunnel in case of phosphorus makes the nitrogen one nitrogen inversion much easier as compared to the phosphorus. Now this is entirely done by the quantum mechanical calculations okay? So these are the 3 explanations that are given.

Possibly this is this is the correct explanation but others are for organic chemist, I think the others are also quite okay because it fits to the general concept of organic chemistry which is based on hybridisation states of the atoms okay?

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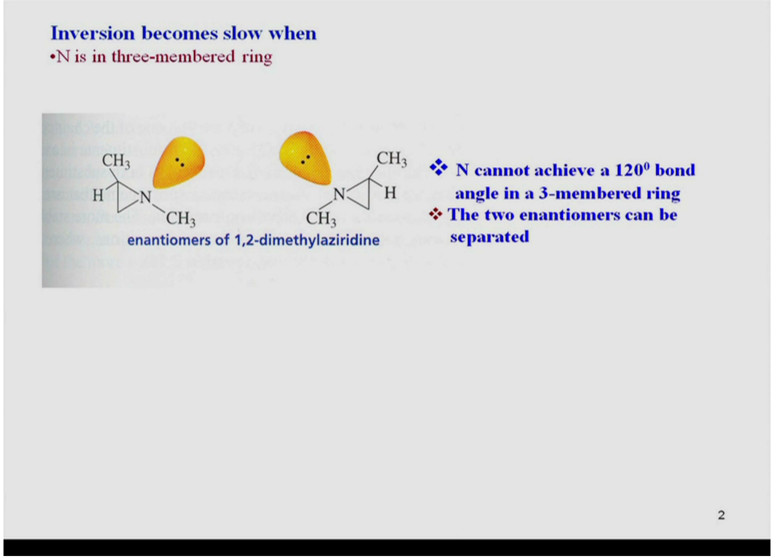
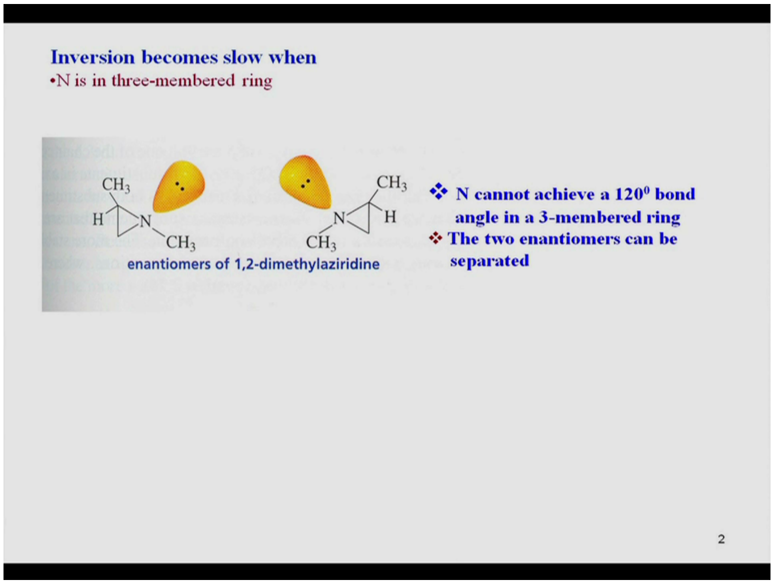


Inversion becomes slow when

•N is in three-membered ring

enantiomers of 1,2-dimethylaziridine

- ❖ N cannot achieve a 120⁰ bond angle in a 3-membered ring
- ❖ The two enantiomers can be separated



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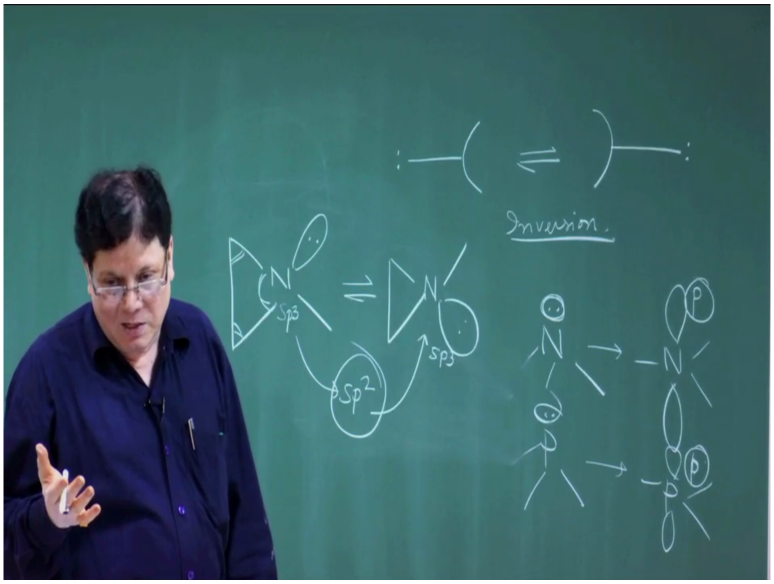

Now inversion becomes slow. How can you now isolate chiral nitrogen compounds? The only way to do it by slowing down the inversion by slowing down the inversion. That means increasing the inversion barrier. If you increase the inversion barrier, then you can do that. And in case of this Cyclo, this three-membered ring nitrogen which are by the way called aciditane, they in that case nitrogen is very difficult because it is a 3 membered ring and to convert nitrogen, to invert the lone pair from here to this position is is difficult actually this is written in in in particular form I can write it here, to show it in a better fashion that so this is the lone pair and this is the suppose this is methyl, so the inversion means this this is here and the lone pair is there.

This is what is the inversion okay? Now this inversion requires the nitrogen to be in the intermediate as I said, it requires the nitrogen to become from SP 3, then it goes to an SP2 nitrogen and then go to the SP 3 back because this is the intermediate, an SP2 hybridised nitrogen is the intermediate. So if that happens, if that is the requirement, then it will be very difficult to do it in a three-membered ring because three-membered ring already there is lot of angle, you will learn this, a lot of angle strain already is there.

But to make it when it is SP2, the angle has to be 120 and which increases the strain in the molecule. So virtually what you are doing then, you are slowing down this process. So here, the Enantio barrier is more. Why? Because to have a planar nitrogen here is very difficult in a 3 membered ring. And so the inversion barrier, you can conclude from here that as the ring size increases, inversion barrier decreases.

Okay? And ultimately, it will be very very fast at room temperature. Suppose you take, you take a 6 membered ring containing nitrogen, then the inversion barrier is very low and that will almost be similar to the SI click system where there are 3 alkyl groups attached to the nitrogen okay?

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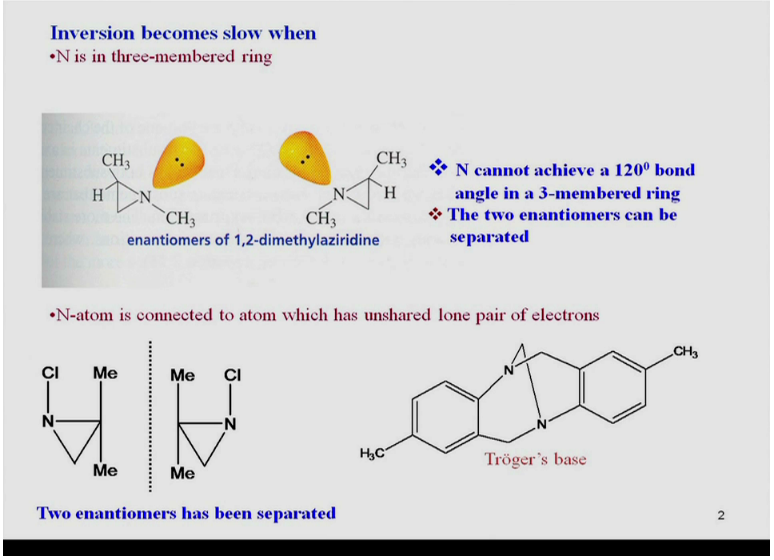

Inversion becomes slow when

- N is in three-membered ring

enantiomers of 1,2-dimethylaziridine

- ❖ N cannot achieve a 120⁰ bond angle in a 3-membered ring
- ❖ The two enantiomers can be separated

- N-atom is connected to atom which has unshared lone pair of electrons

Tröger's base

Two enantiomers has been separated

And in fact in this case, the Enantiomers can be separated and have been separated. Okay? There are other examples like this the same the aciridine I said, this actually works in case of 3 membered rings. It also works in rigid systems, bicyclic systems where the nitrogen also cannot adopt a planar configuration in the intermediate like this compound where the nitrogen is attached the 2 nitrogens are connected by a bridge, one carbon bridge.

These are what are called Troger's base. And the Troger's base, these 3 bonds, this is one born, this is the other bond and this is the 3rd bond and these 3 bonds you cannot actually it will be a tremendous trend that will be incorporated in the system if you want to bring these 3 items in the plane. So Troger's base, if they are properly substituted, they become chiral molecules okay? That that is the classical, the 1st I think the 1st nitrogen compounds which are which are isolated as chiral materials or as chiral compounds okay.

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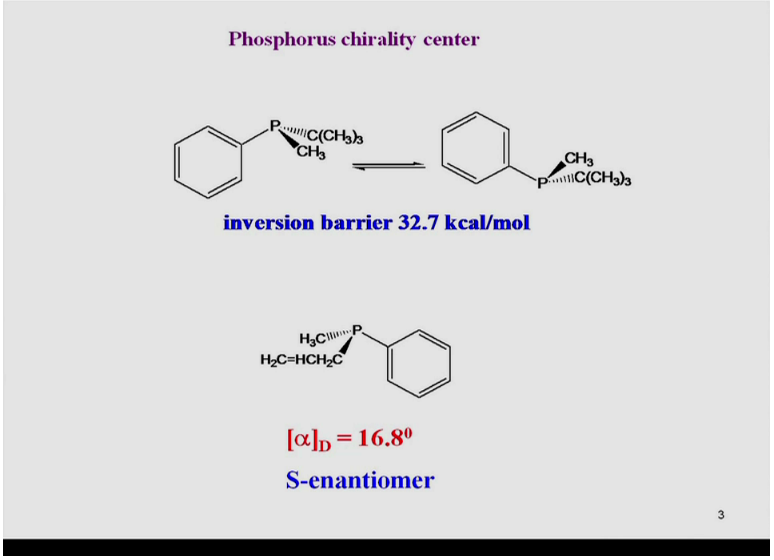

Phosphorus chirality center

inversion barrier 32.7 kcal/mol

$[\alpha]_D = 16.8^0$

S-enantiomer

In case of phosphorus, as I said, phosphorus the inversion barrier earlier it was 6 kilocalorie per mole, now the inversion barrier is 32 dollar 7 kilocalories per mole okay? And these compounds so there will be, you can easily separate them because the room temperature does not allow you that much of energy to invert. The phosphorus inversion case is not possible at room temperature so one can isolate these compounds and see this compound has isolated and it has got an alpha D.

Indeed they have shown that yes, they are chiral as predicted because what is the 4th ligand that is missing here? That should be the lone pair okay? And the lone pair here should be the should be at the bottom okay? And the relationship between these 2 will be enantiomers. So one of them have been isolated, one of them is not this one, a different compound, it is a it is an allyl group, a methyl group and a phenyl group and a phosphorus. And thes sign is not here. So possibly it is +. So +, the alpha D of this compound is is + 16 dollar 8 degree. So it is indeed, it was proven that the phosphorus compounds are chiral compounds okay?

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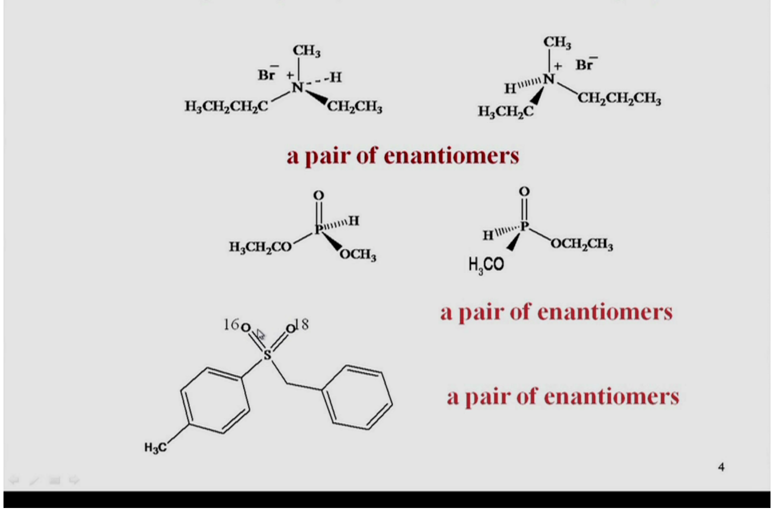

Nitrogen, Phosphorus, Sulfur attached to four different groups

a pair of enantiomers

a pair of enantiomers

a pair of enantiomers

Now you can have then there are 4 different groups attached, now unlike this, in the lone pair which can invert from one side to the other, or one face to the other face, if you have 4 different groups, then that possibility is gone. Okay? so then there is no inversion and you can make nitrogen compounds, phosphorus compounds or sulphur compounds that there are 4 different groups which are attached, 4 different groups so there is no question of inversion.

So you can isolate them they can exist as a pair of enantiomers and you can separate them like this, these are called quarternary ammonium salts. So quarternary ammonium salts where all the 4 groups are different. So you can have, they can exist as enantiomeric pair and it is possible to separate them. So that is the example of nitrogen. Phosphorus if you have this phosphonate where there is one oxygen no one attached to the hydrogen, another is OCH 3, another is OCH 2 CH 3, so these 2 groups are different as well as these 2 groups.

So then basically the phosphorus, this is tetrahedral in geometric and it can also exist as a pair of enantiomers, you can separate them okay? So the there is no question of inversion. So that is an example of phosphorus compound. And of course, phosphorus event trivalent, you can, I have shown that the inversion barrier is low, so trivalent you can separate also the Tetravalent obviously will be possible.

And in case of sulphur, say sulphone like this, these compounds are called sulphone where one oxygen is 18, O18, another oxygen is O16. So they are not the same, they are different. Although they are isotopes, but they are different okay? So they can also exist, the sulphur is again a tetrahedral sulphur, it is not planar because I told that in planar system, you cannot have this type of optical isomerism, this type of stereoisomerism means this enantiomerism. So this because the sulphur is tetrahedral and because there are 4 different groups, so it exists as a pair of enantiomers okay?

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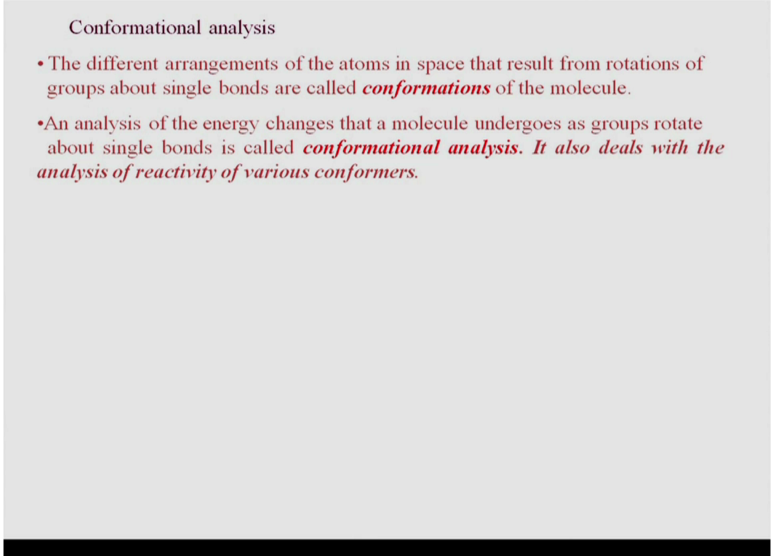

Conformational analysis

- The different arrangements of the atoms in space that result from rotations of groups about single bonds are called ***conformations*** of the molecule.
- An analysis of the energy changes that a molecule undergoes as groups rotate about single bonds is called ***conformational analysis. It also deals with the analysis of reactivity of various conformers.***

So that ends up the the case of non-carbon containing noncarbon the chirality of compounds where carbon is not the is the key cause for the for chirality, it is the other items like nitrogen, sulphur or phosphorus. Again I repeat, the most important, the most important point is that they should be in the tetrahedral configuration. They should have a tetrahedral configuration okay?

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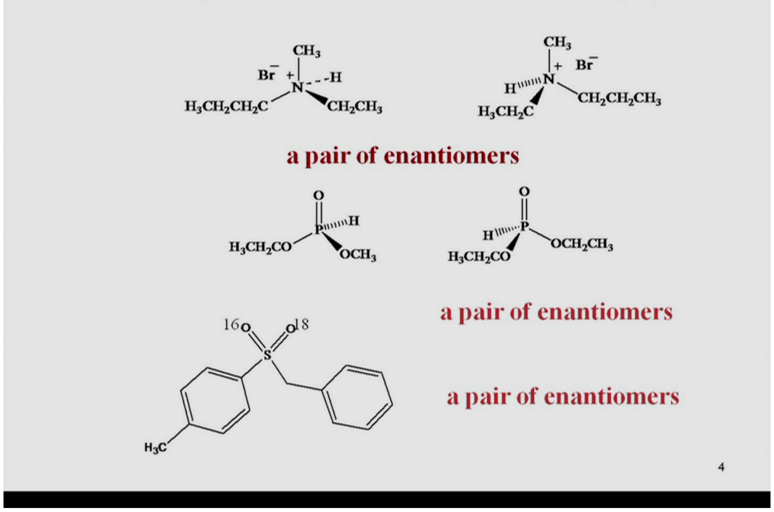

Nitrogen, Phosphorus, Sulfur attached to four different groups

a pair of enantiomers

a pair of enantiomers

a pair of enantiomers

Now just before we finish this part, let us see this compound because they are chiral, so they should have also optical activity. They should have optical activity and they should also have absolute configuration. What is absolute configuration? The exact arrangement of the groups in the space. And we have different notations? I explained the DL nomenclature system, capital D capital L and also the RS nomenclature system.

So how to assign RS2 these compounds? Just one example say in case of aciridine because I told you that in case of aciridine the compounds exhibit, the compounds can be separated. See any trivalent nitrogen where all the groups are different, they show optical isomerism but the problem is, you cannot separate, you cannot, you cannot prove them unless you go at very low temperature where the inversion cannot take place, then it is possible to separate them.

But to my knowledge, nobody has done that yet. So the only compounds that are chiral nitrogen compounds are the aciridines and the the quarternary ammonium salts okay? So suppose you want to assign the RS nomenclature system in this molecule in the to the nitrogen okay? To the nitrogen. Now in order to make these 2 groups different, you have to put something here okay?

Suppose I put a group R1 or a methyl here, now I ask that what is the configuration of these, of the nitrogen here.

What is the configuration of this nitrogen? So how do you do it? I think I gave you because these 2 are, one is below the plane, this is above the plane, this is in the plane and this is in the plane, so what you do? You stand here in an orthogonal position to the plane, extend your right hand and left-hand and if you do that, so the groups will be spread out. These groups are, this will look exactly like your Fisher projection formula what it should appear like.

So when you look from this side but standing this way, standing in an orthogonal position, so your right hand will be towards your right hand towards will be this. This will be to your horizontal direction to your hands and these 2, this will go down that will be towards the bottom and this will go up okay? So now the the priority sequence will be this will be one obviously because there are 2 carbons are attached to this carbon.

One is this carbon, another is this carbon. This will be 2 because there are 1 carbon attached, extra carbon attached to this carbon. This will be 3 because only hydrogens are attached and lone pair is 4. Lone pair is always the least paired group that told you after after hydrogen. So this is the scenario. So you you stand here, extend your hand, on the 2 hands, the 4th group is going to your right hand, the 3rd group is going to your left hand and on the top, number 1 and on the and the bottom number 2.

Now you do the RS nomenclature, you can bring the 4th group at the bottom if you wish or at the here also any of the vertical position that you can do or I said, that you can just check here and whatever you see, you can invert that. But let us do a exchange in a group of 3, so 4 comes here, 2 goes there, 3 goes there, 1 remains as such. So 4 here, 2 there, 3 here. So if you do that, now you do the RS. So it becomes S.

So whatever you see, that is the configuration of the nitrogen. So the nitrogen is now in the S configuration okay? I hope this is clear that how do you, we just stand orthogonal with your head on this side and then spread your hands. So the molecule will look exactly what it should look like before you draw the Fisher projection okay? So that is part of the configurational assignment of noncarbon systems okay. Thank You.