Concepts of Chemistry for Engineering
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Lecture 72
Enantiomers and Diastereomers

Hello, everyone. Welcome to the module on stereochemistry. We are still continuing to discuss the arrangement of atoms in space in a molecule, and what are the consequences are the properties thereof. So, we will continue this discussion in this lecture. And in this lecture we will look at a bit more closely what are called as an enantiomers and diastereomers, the different properties and possible applications.

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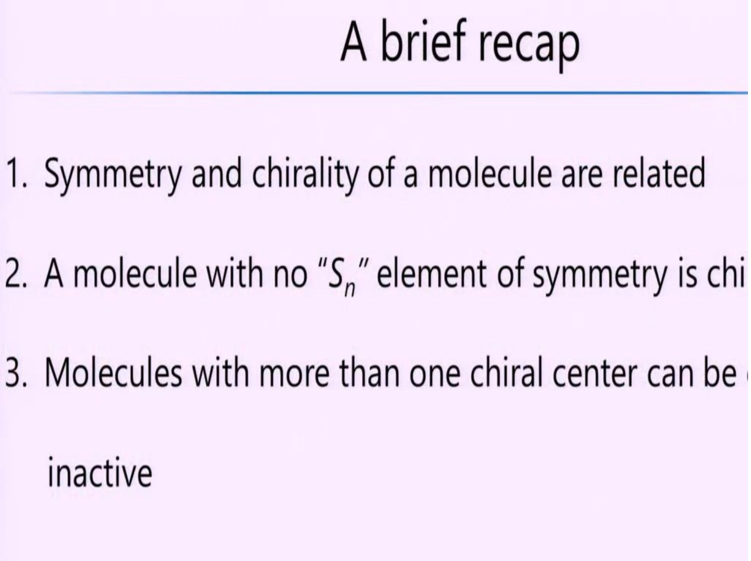

A brief recap

1. Symmetry and chirality of a molecule are related
2. A molecule with no "S_n" element of symmetry is chi
3. Molecules with more than one chiral center can be

   inactive

Before we get into enantiomers and diastereomers, let us just first briefly recap what we discussed in the last lecture. In the last lecture, we said that symmetry and chirality of a molecule are related to each other, and a molecule is said to be chiral when there is no improper axis of symmetry, that is, S n in a given molecule.

So just to reiterate, we, if we take a molecule, the earlier definition or the earlier proposition, what we had discussed was if a molecule is attached to four different carbon atoms, we call it a chiral center, which is indeed not in correct, but not fully correct either. So, to have a complete definition or a definition which captures a large class of molecules, what has been done is to look at the relation between symmetry and chirality of a system.

And it is concluded that molecule or a system which lacks improper axis of symmetry that is S n, is said to be chiral. And we looked at some examples of this in the previous lecture. And a consequence of this is that I could have a molecule, for example, tartaric acid or the one we discussed in the previous lecture, that is 1, 2 dichloro dibromoethane, where you have more than one individual chiral centers, but the molecule as a whole the or the molecule in totality is optically inactive.

So, this is a consequence of the relation between symmetry and chirality. So, this is a very key distinction which one needs to keep in mind. With this, now let us get into looking at what are called as an enantiomers and diastereomers.

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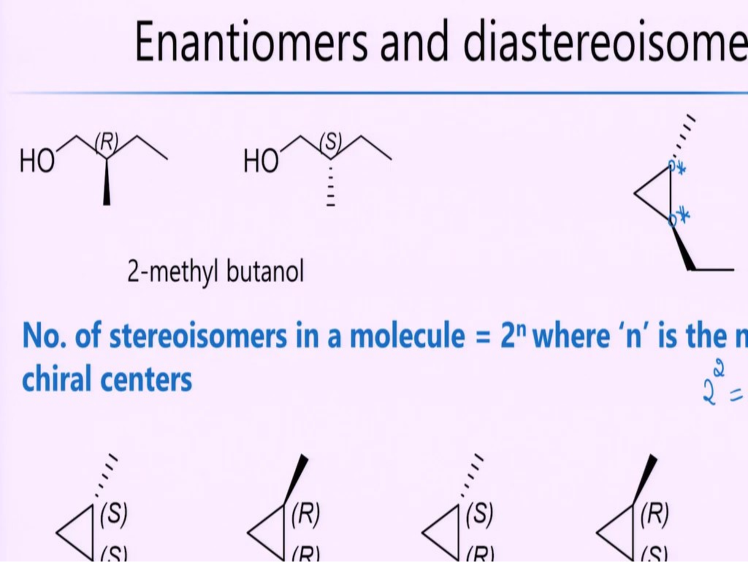

Enantiomers and diastereoisome

2-methyl butanol

No. of stereoisomers in a molecule = 2^n where 'n' is the n
chiral centers

$2^2 =$

So, we again go back and try to look at this example of 2-methyl butanol, which we looked at in the previous class. So, here what we have is one carbon atom, which is the one which the pointer is showing now, it is connected to four different atoms, and it also lacks the S n improper axis of symmetry. As a result, this is a chiral molecule, both of these are.

And the relationship between them is that they are non superimposable mirror image of one another. I will repeat again, these are non superimposable mirror image of each other similar to our hands.

So as a result, we call these two sets of molecules that is R 2-mehtyl butanol and S 2 methyl butanol as enantiomers. And they always come in pairs. Like you can see here, if I have a carbon atom, which has a methyl group, which is coming up. Counter part of that would be the methyl group, which goes into the plane of the board, of the screen, and that would lead me to the S enantiomer.

So, this is a very simple case of when we have one atom or one carbon atom, which has four different substitutes, or which lacks a symmetry. Now, what happens if I go to a system which has more than one chiral center.

Now let us take the example of this 1, 1-ethyl 2-methyl cyclopropane, and look at it in a little more detail. So, here, what I have is I have two carbon atoms which are chiral. So, I am just going to mark them with an asterisks, that is this particular carbon and this particular carbon. So, rule of thumb is that if I had just one stereo center, then I got two, two stereoisomers, which way, which we call them as enantiomers, in the case of 2-methyl butanol, like for example here.

However, now we have two chiral atoms, two chiral centers in this particular example. So, in such a case, what is known is that the number of possible stereo isomers is given by this formula of 2 to the power n, where n is the number of chiral centers. As a consequence, you could easily say that if I have 2 to the power n, so then it would be 2 to the power 2, so it would be, I would expect four stereo isomers of this.

So now let us look at what are the different possible stereo isomers. So, I have drawn here the four possible stereo isomers of this molecule. So, let us go one by one and look at them. So, if we start with the one on the left, that is the molecule S S, what you see is that the methyl is first actually pointing into the plane of the screen, and the ethyl is actually coming out.

And what you can, what is done in the molecule to is exactly the opposite. That is, you have the methyl going into the plane and the, sorry, the methyl is actually coming out of the plane and ethyl goes into the plane. And so on and so forth, we can just vary the disposition of this methyl and ethyl. And we would end up in these four combinations.

And so now we have four set of stereo isomers. So, now let us go ahead and try to visualize them and try to understand from this what are di, enantiomers, which we have partly understood, and also look into what are diastereoisomers.

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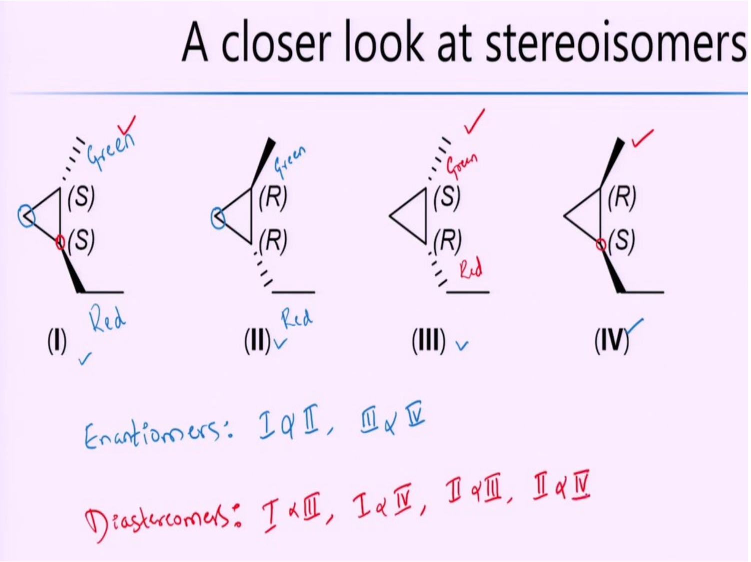

A closer look at stereoisomers

Enantiomers: I & II, III & IV

Diastereomers: I & III, I & IV, II & III, II & IV

To do that, what I would do is I would again, go back to our molecular models and take the help of molecular models. So, here, I have constructed a molecular model of a particular system here, which I would begin by showing it to you. So, this is the cyclopropane system, is what I have constructed. So, this is a, I am trying to show it as a structure 1, the one on the extreme left.

And what you see here it is that I have a C H 2 group, which is exactly the same as this particular C H 2. So, that is the, this C H 2 is what I am trying to show here, on this left, this is the carbon which is the C H 2. And then I have this carbon, which has a CH which is coming towards me. And a methyl group, I am showing the methyl group by a red ball here. So, this could be any substituent. And this is the one which is actually going down. So, let us call this the green.

And if I actually now come down, then I have the ethyl group, which I am showing it by the red ball here, and the red ball is actually coming towards me. So, I would call this red just to keep track of the colors. So, I have this particular enantiomer or this particular stereoisomer, which I have made a model of. And I hope everyone can see this from this particular model.

And now what I will do is, I will go to the second one, where I am again holding it in the same kind of same kind of position as that of 2, structure 2. And you can see that the C H 2 is here, which is the one, which you can see here, the C H 2. And now the green ball, which is actually the one which was actually going down is now coming up, that is in accordance with what is drawn on this board. So, it is actually coming up if I hold it like this, and C H is going into the plane of the board.

So now this is the green is, actually now I have put the green as coming towards me or away, or out of the plane of the screen. And if we now go and look at the ethyl, which is the red one, so this is actually now going into the plane of the board. And that is in accordance with the structure 2. So, I am just going to draw this as red.

So, I will just hold these two again. So, I have just these, the same two structures. I am just holding it again here to show you from two different perspective. This is structure 2 on my left hand and the, on my right hand is the structure 2. So, to look at the relation between the two, what I would do is I would just hold them like this, and I am just holding it and just a different confirmation on my hand. I am holding it like this and I am gonna just flip this guy.

And I hope you can see that the one on the right, the molecule on the on my hand is actually a mirror image of the molecule on my left hand. If I, if you draw a mirror plane just in between these two, then you would see that these two are actually mirror image of each other. I hope everyone sees that, because you have the, the green balls, which are actually kind of mirror images, the reds are mirror image, and if you have the hydrogen are also mirror image for both of this.

So, once you have the mirror image, what we need to now next look at is try to see if these are superimposable. So, let us, let me try and put one on top of each other now. So, I am trying to put one on top of each other. So, here, what I have been able to do is in this sort of matched geometry, I have been able to put the red ones together, I have the red atoms are actually coincide with each other. But you can see that the green is now on top of the on top of the white. And similarly, here, the white is on top of the green.

So that means these are actually non superimposable mirror image of each other, 1 and 2. So, what that means is that the structures 1 and 2 are enantiomers. So, I again, reiterate structures 1 and 2 are an enantiomers. So, let me just write here enantiomers, 1, and 2. So, this is one pair.

And you can do a similar exercise for let us say, molecule 3 and 4, where I hope you can see that the absolute configuration is exactly opposite in this case. Like the carbon bearing the methyl has an S in 3, whereas it has a configuration of R in the 4. And similarly, it is R in the case of 3 and it becomes S in the case of 4. So, that means these are again a pair of enantiomers, similar to molecule 1 and 2.

You can again convince this yourself by making a model like this and then trying to superimpose them or look at the mirror images. I will, just for the sake of convenience, I will write here that both three and four are also a pair of enantiomers.

So now we looked at two sets, that is, 1 and 2, 1 and 2, and we also looked at the relation between 3 and 4. So, now the question is what happens if I look at with respect to 1 and 3, or 1 and 4, or between 2 and 3 or 2 and 4. So, that is the interesting bit. So, let us try and do that now. So, let us try to compare 1 and 3. So, now I am going to compare the structure 1 with the structure 3.

So, I go back to my first structure here, that is, the C H 2 is intact, and the green or the methyl is actually going into the plane and the red or the ethyl is actually coming out. So, I keep the structure intact. And in order to make the, in order to make the other structure, that is, the structure 3, I am going to just tweak around this a bit. So, this is, this was actually my 2, I would like to make this into 3. So, for that I have to just juggle a bit.

So now I hope you guys can see this now. The, the model, which I am showing you is the model of structure 3. So, here you have now the green, which is again pointing into the plane of the screen, and you have the red which is the ethyl which is also pointing into the plane of the screen, like in this particular case here. This is green, and this is red. So, both are actually going into the plane in this particular, particular example.

So now what I what I have is, I go back to this molecule, that is, molecule 1, and I have molecule 3. I am just going to hold them back here like this, similar to what I did with molecule 1 and 2. So, now what you see is that if I actually play, or if I try to play around with this, if I try to, let us say, do a similar trick, if I rotate it, actually these are not mirror images.

If you carefully look at them, you see that the red items are in accordance with what would one expect, but the green atoms, or the green substituents are actually not. So, as a result what you see is that the 1 and 3 are actually not mirror images of each other. I hope this is visible because you can see the red balls are actually in correct relation what you would expect, but the green ones are actually off. So, what this means is that structure 1 and 3 are non mirror images.

And now let us look at if they are super impossible. So, I am going to just put them one on top of each other. And, so what you see here is that I have the white or the C H 2s I am able to match, which is this particular carbon to the left whereas, the carbon which has the red and the green balls are actually not on the, exactly the same, they are actually offset. So, what this tells you is that these structures are non superimposable and also non mirror image of each other.

So, I again reiterate that structure 1 and 3 are non mirror image, that is the first point and they are also not super imposable on each other. So, what these kinds of structures are what are called as diastereomers. So, I am just going to write down here. So, structure 1 and structure 3 is a pair of diastereomers. So, that together constitutes one pair.

You can do this exercise similarly, and what you would see is that the structure 1 and the structure 4 is also a pair of diastereomer because here you see that the, on this particular, on structure 1, this is S configuration and here on this structure 4, it is S configuration, but if you go to the other carbon it is S whereas here it is R. As a result, I will write down them as 1 and 4 also form a pair of diastereomers.

With the same set of arguments, you can do the, you can compare now, 2, with respect to 3 and 4. And what you would see is that 2 and 3 are again, a pair of diastereomers because both the stereo centers on each of them are not exactly same, that they are, they are not exactly opposite. As a result, they are not enantiomers but they are diastereomers. So, you would have 2 and 3 as a set of diastereomers.

And you would, if you go and compare 2 and 4, you will again see the same relationship, that is, they are non mirror image non superimposable one on top of each other. So, that would mean that 2 and 4 are also a pair of diastereomers.

So, I hope till now it is at least a bit clear that what do we mean by enantiomers, and what do we mean by diastereomers. I will again reiterate. Enantiomers are mirror image of each other, but they are not superimposable one on top of each other. Whereas, diastereomers are non mirror image and also non superimposable on top of each other. So, that is the key but a subtle distinction between an enantiomers and diastereomers.

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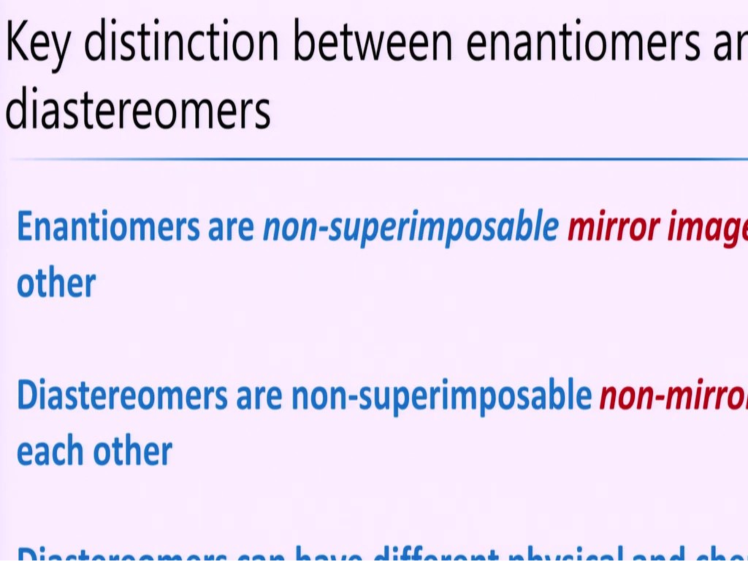

Key distinction between enantiomers ar diastereomers

Enantiomers are *non-superimposable* ***mirror imag*** other

Diastereomers are non-superimposable ***non-mirro*** each other

Diastereomers can have different physical and che

So let us try to concretize this distinction between enantiomers and diastereomers. So, the first one is that, as I told you, enantiomers are non superimposable mirror image of each other whereas, diastereomers are non superimposable non mirror image of each other. So, they are also not mirror image of each other.

And another important distinction is that in the case of enantiomers we have what is, we have what is called as both the, both the systems have opposite chirality. That is, if we if we took two systems, the chiral centers at each of the points are actually of opposite configurations. Whereas, in case of diastereomers, not all stereo centers be of opposite configuration. There can only be some which are of opposite configuration. That is also very key distinction between an enantiomers and diastereomers, like we saw in the previous slide.

And finally, a consequence of that is we know that enantiomers, typically, are having almost exactly the same physical and chemical properties except the way they rotate the plane polarized light, that is the rotate to the, to the right or to the left. However, once it comes to diastereomers the properties of diastereomers can be distinct. That is, they can have different melting point, different boiling point, and so on and so forth. So, that is a very, very key attribute of diastereomers.

So, this all looks nice and very, sort of, academic and textbook kind of stuff. So, then some of you might be wondering, is there any application to this? Or is this of any use? So let us go ahead and briefly look at one of the application of these concepts.

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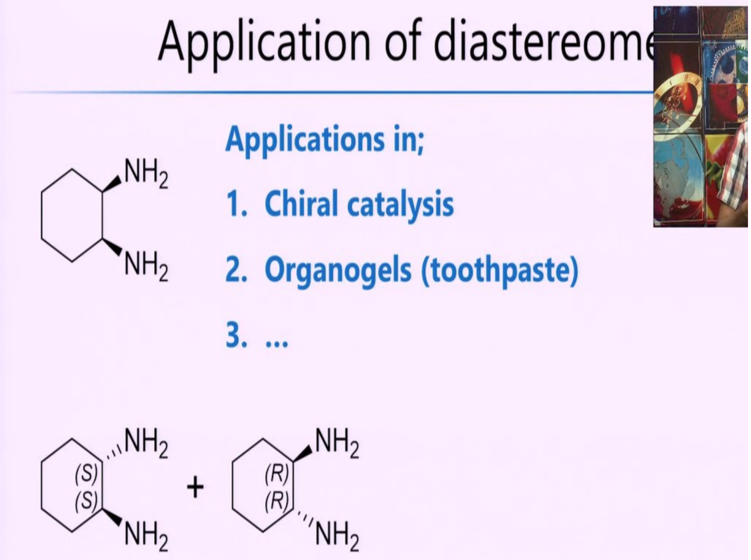

Application of diastereom

Applications in;

1. Chiral catalysis
2. Organogels (toothpaste)
3. ...

So here what I have tried to do is I have tried to show you 1, 2 diamino cyclohexane system. This is a particular one is cis, but you can also get a trans. Then you will have both enantiomers possible. What is known is that these kinds of molecules are actually, have a wide range of applications like in chiral catalysis.

That is, the drugs which you take, nowadays, for example, for COVID or for any other ailments, these drugs are invariably having only one of the configuration, that is R or S of a particular studio center. And it is very, very important to have it in a high purity, that is, the R should be in extremely high purity, which is also called as enantiomeric excess.

So, there is a huge field in which people are interested in making a given enantiomer or diastereomer of a molecule with almost exclusive, exclusive purity, so that you do not have other diastereomers or enantiomers and that is important for the ultimate biological activity. So, in this context, what is known is that these kinds of molecules are actually very good catalyst to synthesize a given, a small part of a drug. That is one of the application.

And another important application is something called as an organogel. If you have not come across them, you can visualize them or think of them as a toothpaste which we all use in the morning. So, these are actually very soft materials, which can have various kinds of applications. So, these materials are also useful as organogels and various other applications.

So now, where comes the problem? So, the problem is as follows, that if you want to use this as, these particular molecules as either chiral catalyst or as organogels, one should be able to have them in very high enantiomeric purities, that is, I should be able to have exclusively S S or exclusively R R derivatives. However, commercially obtaining them is actually a bit expensive.

Whereas, if you really look at commercially the 1 is to 1 mixture is very, very easy to get because that is more easily available and it is very hard or it is economically not viable to separate a mixture of enantiomers into their separate components, that is, two enantiomers. So, it is in this context or this problem of separating the two enantiomers from a racemic mixture, or also called as optical resolution is where diastereomers can be of extreme utility.

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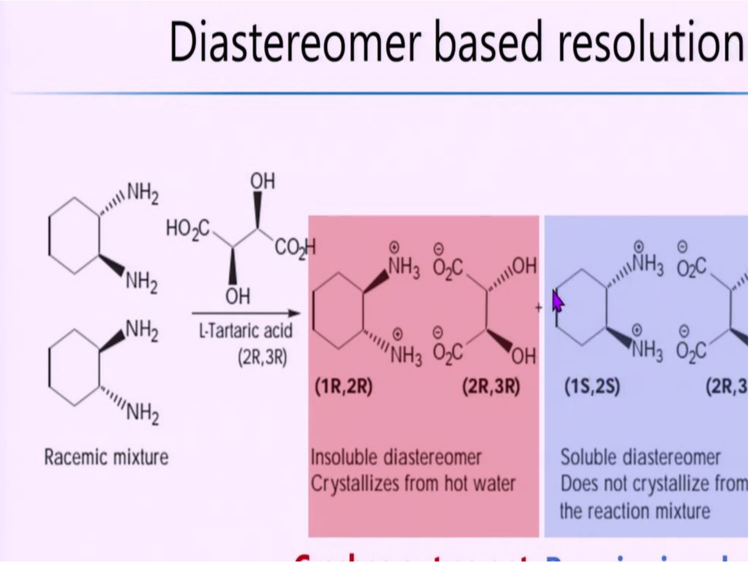

Diastereomer based resolution

And let us see how they can be a futility. So, here is an, a very simple idea, which actually was published in, about two decades ago. So, here what the authors have done is on the left, I have a mixture of both the enantiomers, that is, I have a racemic mixture. And to this racemic mixture, they add L-tartaric acid, that is, a 2 R, 3 R derivative, which is also commercially easily available. And once you add this, they observed two kinds of products.

So, what happened is the 1 R 2 R derivative of the cyclohexane actually goes and complexes with the 2 R 3 R tartaric acid, and this interaction between the cyclohexane and tartaric acid is very strong because they have a matching chirality. If you look at the chirality here, the cyclohexane is a 1 R 2 R and the tartaric acid also as a 2 R 3 R.

As a result, they have a very favorable configuration to interact with one another. Thus they interact strongly. And once they interact strongly they can, they form a precipitate and then the solubility product diminishes and the crash out of the solution, or they are insoluble.

However, on the other hand, if the 1 S 2 S derivative of the cyclohexane actually does not interact so strongly with the 2 R 3 R, just because of the way in which the groups are arranged spatially. That would be evident if you build a space filling or if you build a molecule a model like this.

So, a consequence of this lose interaction between the cyclohexane 1 S 2 S derivative and the tartaric acid is that they still remain in solution as a weak complex. So, the solubility of the pro, solubility product of this complex does not overcome and it does not crash out.

So thus, what I mean is that this particular product, which is the 1 R 2 R, complex with the tartaric acid actually crashes out as precipitate or as a, as a lumps, whereas, the other enantiomer actually still remains in the solution. So, once you have this, then all you need to do is to go back to lab and just filter this out, then, you are now left with a pure 1 R 2 R complex with the tartaric acid which can be further easily de-complex to get a pure derivative of 1 R 2 R, 1 R 2 R diamino cyclohexane.

So, with this simple experiment, what we are trying to say is that these diastereomeric complex is, that is, the interaction between the diamino cyclohexane and the tartaric acid, it is a diastereomeric interaction. And similarly, here between the 1 S 2 S and the tartaric acid is diastereomeric interaction. And this diastereomeric interaction is what ultimately governs their solubility product and also the way in which we can actually resolve them.

I hope this has given you at least an idea of how the idea of diastereomers can be used for optical resolution as one of the applications. With this, we will stop here. And thank you for listening.