Fundamentals and Applications of Supramolecular Chemistry

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Lecture 17

W4L17_Cation complexation in cryptands, spherands, Molecular Conformation

So, now let us continue the discussion. So, now we will, we have looked at the corands, we have also looked at the podands, and we have looked at crown ethers, which are very special cases of corands.

Now let us look at the other types of ligands for which host-guest complexation behavior has been studied. Now, once it was realized that a cyclic arrangement actually provides stability and encapsulates cations very efficiently, the next question was whether we could create a more rigid host and even further enhance the binding constant associated with host-guest processes.

So, in this regard, after Pedersen's work, there was a French scientist named Jean-Marie Lehn who was at the University of Strasbourg in France. He wanted to now synthesize and design three-dimensional host molecules that are of a bicyclic nature.

So, the crown ethers had just one cyclic loop. He wanted to further derivatize it and make bicyclic hosts and 3D host molecules that are more pre-organized and can effectively encapsulate the metal ion so that the metal ion is effectively hidden in the cavity created by this three-dimensional host.

So, instead of having a cyclic host, which is more like two-dimensional, you now have a three-dimensional host; the metal ion goes and sits inside, and it effectively encapsulates it so that it is hidden inside that particular cavity created by the host, and this process of the metal ion being hidden is referred to as Kryptos in Greek, and hence came the word cryptands.

So, the cryptands come from the Greek word kryptos, which essentially means hidden; whenever a complex takes place, the metal ion is effectively hidden inside the cavity created by the three-dimensional host.

The first cryptand synthesized by Jean Marie Lehn is referred to as the 2-2-2 cryptand, and this is a very, very important compound because this 2-2-2 cryptand is sold commercially under the name Cryptofix.

So, it has a commercial name associated with it, and it has also been observed that this particular cryptand, in comparison to the 18-crown-6, encapsulates the potassium ion much more efficiently, and it is approximately 10 to the power of 4 times greater for the cryptand compared to that of the crown ether when the experiments are done in methanol at 25 degrees centigrade.

So, when done in this particular solvent at room temperature, it has been observed that the potassium ion binding for the cryptand is 10 to the power of 4 times stronger than that of the corresponding 18-crown-6.

And that is what also gives it a remarkable property because a similar kind of ligand, which is akin to that of 18-crown-6 but has a bicyclic nature instead of a cyclic nature, can more effectively encapsulate the potassium ion with a stronger affinity towards it. So, the first thing was how the synthesis of these cryptands was achieved.

So, regarding the synthesis of the cryptands, let us look at the synthesis, which is very important because you need to synthesize these. So, it started with what we looked at in the last lecture, where we took this particular cyclic host, which has four oxygen atoms and two NH groups, and we had derivatized this NH through chemical modification of the side chain by replacing it with R.

So, now if we can again start from this cyclic ether and we can first treat it with this particular reagent, which is the dichloro compound, and then under the principle of high dilution, in 45 percent yield we get the corresponding compound.

The nitrogen lone pair reacts with the carbonyl group, and then the chloride goes away, minus 2 HCl is eliminated, and then you have this thing. This is the bottom part, and we can have the other one as well.

So, the nitrogen lone pair is there as well. So, you can see here that this is n. So, now we treat it with a reducing agent, diborane, and then do an aqueous workup; we get the corresponding cryptand in 95 percent yield because this carbonyl group is converted into the methylene group. And therefore, we now have the corresponding cryptand. Let us see the structure of the cryptand, and here we now have n.

So, we have this species present with us. This is the carbonyl group that has been reduced to methylene, and we have the spacer. Now, here you have got n equal to 2, 2 oxygen atoms. Here we have got n equal to 2, 2 oxygen atoms. We can now have a case where n is equal to 1.

So, it is referred to as a 2, 2, 1 cryptand, and if n is equal to 2, it is referred to as a 2, 2, 2 cryptand. Thus, we have two different cryptands, depending on whether n is equal to 1 or

2. So, you can see that in this cryptand, it now has a very, very rigid host. And it's a bicyclic host. You have two different cyclic rings.

You have one here, and you have another one here, and the number of donor atoms is also greater. In this case, the number of donor atoms is 5; in this case, the number of donor atoms is 6.

So, keeping this in mind, this discovery by Lehn was very interesting, and many other cryptands have been synthesized using different techniques, and complexation behavior has also been examined in these as well.

The next class of ligands is now that we see Pedersen had discovered the crown ethers, Jean-Marie Lehn had discovered the cryptands, and then came Donald Cram, who discovered spherands. And all three of these people got the Nobel Prize in Chemistry in 1987 for this tremendous development in the field of supramolecular chemistry.

So, Pedersen, Lehn, and Cram all received the Nobel Prize because each of them discovered a new class of chemical entities, a new class of host complexes that can effectively encapsulate guests, and later on we will see that there are many applications of this phenomenon.

So, what was the hypothesis now proposed by Donald Cram? What he wanted to do was further rigidification of the host. In addition to the chelate effect, macrocyclic effect, and macrobicyclic effect, we wanted to see whether further rigidification of the host can be obtained such that the donor atoms converge towards the central binding pocket, even before the addition of the metal.

This is because keeping in mind that before the complexation takes place, the lone pairs have a certain orientation, and after the complexation takes place, the lone pairs are forced to adopt converging binding sites. So, there is an energy penalty involved.

So, what Donald Kram thought was that if we can further rigidify the host by converging the donor sites even before the metal ion has started to complex, then it will display excellent activities or affinities for certain metal ions only.

For example, we have realized until now that sodium ions have been encapsulated by sodium, potassium ions have been encapsulated, but what about a small cation like lithium cation?

It is very difficult to encapsulate lithium cation because the size of the lithium cation is very small, and you need a host that has very strong converging binding sites such that once it effectively encapsulates lithium, it tightly holds on to it and does not release it, and this particular binding is preserved.

So, what he thought was that he needed to modify the host in such a way that there are converging binding sites which are already pre-organized before the metal ion complexation takes place or before the metal ion has been added. To keep that in mind, he designed a spherand. Let us now see the structure of a spherand here.

So, we have this. This is a hexaphenyl host, but now we will see what the changes are here. So, we will have this, and this one will be above, and this one will be below. Again, this one will be 1, 2, 3, 4, 5, 6; we have got 1, 2, 3, 4, 5, 6, and we will have this one, have this one, will have this one, and we will have this one.

So, then this one is a bit difficult to draw, but what I would like to show you here is that we have got this hexa phenyl host; you will see here that these three oxygen atoms are here, here, and here.

I need to draw it; this one got rubbed off. So, these three oxygen atoms you see are above the plane. So naturally, when these three oxygen atoms come above the plane, the corresponding methyl groups go below the plane. So, this is the exposure to the three -OMe groups, and then the Me groups are below. These ones here are below the plane.

So, there are 3 oxygen atoms below the plane, 3 oxygen atoms above the plane, and the corresponding methyl groups are opposite. So, the lithium ion can now come and sit here and form a nice octahedral arrangement.

So, the lithium ion is now coordinated by the six oxygen atoms, and we know that the lithium ion has a strong affinity for oxygens. So, lithium ion is effectively encapsulated so that you have 3 oxygens above the plane, coming from one side, and 3 oxygens from below the plane.

And what also happens is that when this encapsulation takes place, the outer part is lipophilic, or you can say hydrophobic; it is either lipophilic, or it is hydrophobic.

So, now you see that when you have the solvent, this particular lipophilic part will expose itself to the solvent, and what can happen is that small-sized cations like lithium can very effectively get encapsulated into this particular host.

And you can see that the overall shape of this host is like a sphere; the overall shape of this host resembles a sphere, and that is why this is referred to as a spherand, and this is also very, very specific to lithium.

This is the interesting thing and a very important property about this host: you can see here that, as proposed by Donald Cram, he wanted to create converging binding sites towards the central binding pocket.

So, already in this hexa-host-related compound, three oxygens are already pre-organized. They have the converging binding sites, and the three oxygen atoms at the bottom are already rigidly pre-organized.

All that has to be done is for the metal to simply come and sit there and encapsulate itself very, very tightly. So, it is very, very specific for lithium. The overall shape is spherical in nature, and this is referred to as a spherand; it was found to display an extremely strong affinity towards lithium ions.

So, we need to have excellent activity and selectivity for certain metal ions. So, in this regard, lithium ion displays the maximum selectivity for this particular spherand-like arrangement.

Larger cations like potassium and sodium ions are not able to fit into this small size created by this highly pre-organized host and therefore do not undergo host-guest complexation.

So, this class of ligands is referred to as the spherands, and what was observed is that if you replace this oxygen. So, when you replace the oxygen with fluorine, it now becomes a carbon-fluorine bond; then the complexation with the corresponding cations drops.

So, it is very, very specific to this particular lithium ion that this activity takes place. Now, let us go and look at some other properties of the crown ether complexes.

Overall, after looking at podands, corands, cryptands, and spherands, and the fact that the Nobel Prize was given to all the people who were associated with this work, what emerged was that crown ethers are a very interesting class of compounds, and people were interested in examining the properties and applications of crown ethers.

We did look at some of these aspects in the previous lecture. Now, we would like to go a bit deeper into the applications of crown ether ligands. So, to start with the crown ethers, these are soluble in a wide range of solvents, from water to alkanes, and they have the right balance of lipophilicity and hydrophilicity.

So, the polar content and the non-polar content have the right balance, and you know the partition coefficient, which is measured in the octanol-water system, is 0.

That means it has a perfect balance between lipophilicity and hydrophilicity. That means it represents a very balanced polar and non-polar surface for any solvent with which it is going to interact.

So, because we know that solvation plays a very important role in host-guest complexation, it is essential to know the conformation of this particular crown ether in different solvents. We can have polar solvents and non-polar solvents.

Like we can have hydrocarbons, or we can have polar solvents like chloroform, ethanol, and methanol, is the conformation of the crown ether the same or different in different solvents? It has been observed that crown ether is flexible in nature.

Although it is a cyclic ligand, it is flexible in nature. Let us see what the different conformations it adopts in different kinds of solvents are. So, this is my 18-crown-6, 18-crown-6 ether, so 1, 2, 3, 4, 5, 6, and we have got the 12 carbon atoms, so a total of 18, and you can see here that in this case, it is the non-polar part that is exposed.

And the polar part, the polar part is in the interior, and the exterior is the hydrophobic part. Or you can also say the lipophilic part, which is the exterior.

So, if you were to actually dissolve this compound, for example, in a non-polar solvent like oil or in some hydrocarbon, then this is the conformation in which the 18-crown-6 will exist, and this is something similar to a drop of water in oil. So, because oil is a non-polar medium, it has a balance of hydrophilicity and lipophilicity.

So, naturally, the lipophilic part will present itself to the medium oil that is in its vicinity, and that is what will be exposed in oil. However, the polar part is in the interior. So, it will represent a polar environment, which is simply like having a small amount of the polar environment compared to a non-polar environment, something we can say resembles a drop of water in oil.

On the other hand, if you look in polar solvents, it now presents a hydrophilic exterior. So how does it present that? Let us see the conformation now. Here we can see the lone pairs. The lone pairs are now exposed. This is the hydrophilic exterior and the lipophilic interior.

The hydrocarbon part, or the non-polar part, is now pushed inwards, such that the lone pair parts, the more polar parts, are now exposed, and this is called the hydrophilic exterior, which has a lipophilic interior, and this is something similar to a drop of oil in water.

So, water is definitely the much more polar environment, and therefore, this particular molecule will only expose the polar parts. So, there are nice hydrogen bonds between the polar solvent and the oxygen lone pairs, and this particular crown ether 6 is extensively solvated and stabilized in the polar solvent.

So, you see that there exists an equilibrium between these two conformations depending on the polarity of the medium. If you have a highly polar medium, then this particular conformation is stabilized; if you have a non-polar medium, then this particular conformation is present in abundance.

So, the conformation that is available for cation complexation is this particular cyclic conformation with the hydrophobic or lipophilic exterior that is available for complexation. In this case, the oxygen atoms are exposed outwards and therefore, they are not available for complexation.

So, it is important to keep in mind that when we are going to study the host-guest complexation behavior, the correct conformation is now available for binding. So, most people would like to exploit this conformation where the oxygen lone pairs are directed inwards, and the exterior is hydrophobic. So, now let us look at the applications of crown ethers as phase transfer catalysts.

This is a case of nucleophilic substitution and Table 1 where A can be acetate, or it can be a chloro compound, and this reaction is done in the presence of added crown ether. What has been observed is the following: the reaction half-life in hours.

So, when we have the crown ether, it is 685 hours. That depends on the type of crown ether. When we have none, it is 695 hours; when it is 18-crown-6, the time drops to 3.5 hours; when it is dibenzo-18-crown-6, it becomes 9.5 hours; and when it is dicyclohexyl-18-crown-6, the time is 1.5 hours.

So, we can see here that the reaction time is dramatically affected by the presence of crown ethers. So, in the next class, we will look at the mechanism of this phase transfer catalyst and how the presence of the crown ether modifies the reaction environment such that the reaction proceeds at extremely fast rates.

Thank you.