

Fundamentals and Applications of Supramolecular Chemistry
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W4L16_ Cation complexation in podands, corands and lariat ethers

So, hello, everybody. So, now let us continue our discussion further, and today we are going to cover, this week, the applications of host-guest chemistry to different classes of molecules. So, we are going to investigate the host-guest complexation behavior in podands, corands, and spherands to start with.

And this will be followed by looking at another class of molecules. For example, we will be looking at cyclodextrins and the host-guest behavior in this class of molecules as well. So, let us start first by looking at what a podand is to begin with.

So, to start with a podand, it is written in the following way, where n is the number of repeating units and d is the donor atom. The open chain conformation of this organic molecule is referred to as a podand and is characterized by an open chain conformation. Then we will look at other properties of podands, but let us also look at what corands are. Corands are the cyclic components of these open-chain molecules.

For example, we can now write that in the same set of donor atoms, we have these cyclic rings, and then n is the number of units that repeat. The donor atoms can be oxygen, NH, sulfur, and so on.

So, this constitutes what we call corands, and when the donor atom is oxygen, this constitutes a special class of molecules which we call crown ethers, and we will be looking at the properties of crown ethers in more detail. Now we have also realized that the pre-organization of the host is very important. So, in this regard, this is a cyclic system.

So, this is more pre-organized and more rigid compared to a podand, which has an open conformation, and if you want to pre-organize the host even more and make it more rigid, then we can access the bicyclic compounds, which are essentially three-dimensional in nature and which we call cryptands.

So, let us look at how the cryptands look. Here we have B; B is referred to as a bridging atom. D is the donor atom, and you can see that the two B's represent the bridged atoms. Between these two bridges, you can have one ring that goes like this, the other like this, and the other like this.

So, this gives it a three-dimensional nature, a pre-organized host, and n is the number of repeating units here, and this class of molecules is referred to as the cryptands. Let us take some specific examples of podands. As we see, a podand is characterized by an open chain conformation. We can now write. So, we can have this particular podand which we call the pentaethylene glycol dimethyl ether.

We have the ethylene glycol units. These are the ethylene glycol units that are repeating, and there are 1, 2, 3, 4, 5 such units. And you can see that the methyl groups are present at the terminal part. So, this is referred to as the corresponding pentaethylene glycol dimethyl ether, and this you can see has an open chain conformation.

So, now if you put in a guest molecule, say, if you add a potassium cation, we know that this conformation has to wrap itself around the potassium cation, and that is going to be entropically unfavorable because we have an open chain conformation, and now we are going to rigidify the host.

So, we have to restrict the conformation so that it can effectively encapsulate this potassium ion, and therefore, there is an entropy loss. There is also an enthalpy penalty here because this particular ligand is extensively solvated in aqueous solution, and now you will have to remove the solvent molecules, desolvate it, and only then will it undergo complexation with the potassium cation so that it can form this particular cyclic system.

So, this is how the podand encapsulates the potassium cation. It wraps itself around the potassium cation and forms this cyclic substrate. So this wrapping process takes place, and therefore there is a large entropy penalty as well as an enthalpy penalty you pay, because pre-organization has not taken place and we have a very open chain conformation; hence, the synthetic chemist now feels that we should modify the podand ligand to a certain extent.

So, we can rigidify the host to a certain extent, and this is done using the concept of end groups, where we essentially anchor a bulky group at the end of the pod and arm. So, at the end of the pod, particularly here we can replace methyl with much bulkier substituents.

So, we have these 1, 2, 3, 4, 5, 5 oxygen atoms, and now we can bring in a quinoline moiety that has a lot of steric bulk. So when you bring in this kind of quinoline moiety, the podand gets reorganized and rigid, and this will facilitate the encapsulation of different kinds of cations. For example, you can have a potassium ion; you can have a uranyl ion.

So, you start with uranyl nitrate salt, and you can dissolve it in a solvent or in an aqueous

solution, and it will form the uranyl ion, which can also now bind with this particular quinoline substrate.

So, this kind of preorganization using the end group concept is supposed to impart rigidity to the podand host, and we can also modify this further. For example, we can make benzoic acid-substituted podands as well, and this kind of species can also now effectively encapsulate cations because the hydrogens are acidic.

So, in the presence of a base, I can form the acetate anion, and the benzoate anion can now participate in cation complexation along with the oxygen atoms as well. So, you can now have effective encapsulation of this cation using the benzoate moiety as well as the three individual etheric oxygens.

So, with this background, we can now go and see the corresponding cyclic ethers, which are called corands. And in comparison, to the acyclic host, it is the cyclic ethers that belong to the corand class of compounds that have gained a lot of recognition and have very important applications.

And these are also referred to as crown ethers. Now, the crown ethers are a very interesting class of molecules, and the discovery of crown ethers was made in 1987, for which the Nobel Prize in Chemistry was awarded to Charles Pedersen. Charles Pedersen was a chemist who was working at that time in an American company called DuPont.

And he was synthesizing; he was trying to synthesize an organic molecule. We will look at it. And it was during the process of synthesizing a particular organic molecule that the accidental discovery of crown ethers took place.

So, this is referred to as serendipity in science, and serendipity in science plays a very important role because most of the notable discoveries have happened due to serendipity. So, what he was trying to do was the following: in the presence of sodium hydroxide and tertiary butanol, and then under the workup conditions, he was trying to synthesize this particular compound.

So, what happens is that this is a dihydroxy compound. One of the OH groups has been protected, and then in the presence of a base, you generate the nucleophile, which then goes and attacks the electrophilic center; the anion chloride ion goes away, and you form sodium chloride.

And then in the second step, you have the deprotection step, where you actually deprotect the pyran system to form the dihydroxy compound. But what happened was that the starting material actually contained trace amounts of catechol. And because catechol was present under these reaction conditions, it yielded this particular product.

So, it produced this particular product, which we call Dibenzo-18-crown-6. So, you can see that the number 18 signifies the size of the ring 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18. So, you can see it is an 18-membered ring that is formed here.

The number 6 here refers to the number of oxygen atoms that are part of the cyclic system 1, 2, 3, 4, 5, 6; there are 6 etheric oxygens, and there are 2 phenyl rings; that is why it is referred to as a dibenzo system. And this particular compound was obtained during the course of the synthesis by only 0.4 percent.

So, even less than 1 percent of the product was dibenzo-18-crown-6, and Pedersen had remarkable synthetic skills. So, he was able to isolate this dibenzo-18-crown-6 and then look at its properties.

So, this is how the serendipitous discovery of this class of molecules called crown ethers was made during the process of a chemical transformation where the target compound was to create this particular organic ligand because he wanted to complex it with the vanadyl ion and make metal complexes, but he ended up obtaining this particular dibenzo-18-crown-6 as well because the starting material had a small amount of impurity referred to as catechol.

So, even trace amounts of impurity can give you a side product that can have very interesting properties in addition to the ligand of interest. The next thing was to look at the physical properties of crown ethers.

The observations made by Pedersen are that the compound, namely dibenzo-18-crown-6, dissolved sparingly in methanol, but its solubility was highly enhanced when it was dissolved in alkali metal salts. This is one of the most important observations or one of the most important properties of 18 crown 6 that it is sparingly soluble, but the moment you put it in an alkali metal salt like potassium chloride or potassium permanganate, the solubility of the compound is enhanced manifold.

And so, this compound has a very unique property that it is able to dissolve to a high extent in alkali metal salts. And so, what he was thinking is that it is possible that the potassium cation has essentially fitted itself into the interior of the crown ether's cavity. So, we know that the crown ether has a cyclic structure.

It is a cyclic system; it has a cavity here, and possibly the potassium ion has gone and fallen into this cavity. He actually proposed this statement, saying that the potassium ion had actually fallen into the hole at the center of the molecule.

Eventually, this did turn out to be correct. Because when the crystal structure of the complex of the potassium ion with this ligand was determined, it was observed that the

potassium ion is complexed with the oxygen lone pairs. So, now you see that the oxygen lone pairs here are pointing towards the interior of the cavity.

Because we know that the prerequisites for binding are that the host molecule should have donor atoms that are of a converging nature and the guest molecule should have diverging binding sites. So, in order to maximize the cation-host interactions, the oxygen lone pairs point towards the interior of the cavity and are able to effectively encapsulate potassium.

Secondly, potassium is also the right size to sterically fit into the cavity created by this particular dibenzo-18-crown-6. So, it is very, very specific to the size of the cation. If the size of the cation changes, for example, if it becomes smaller, then it is not a very effective complexation process.

If it becomes larger, then the potassium ion will not be sitting in the center of the void. Most probably, if you have a larger size cation, then it will sit above the plane containing the six oxygen atoms. It will not be in the center.

So, this is a very nice example of a steric fit between the size of the cation and the void created by the ligand. Then what people did was make other crown ethers as well.

We can look at, for example, instead of the phenyl group, we can also have the dicyclohexyl group. So, you can see this is the cyclohexyl ring, and this is the 18-crown-6, and because this is more organized and more rigid due to the stereochemical restriction in the cyclohexane system.

So, it has to maintain the stereochemistry at these two carbon atoms; therefore, it is a more conformationally rigid system. And if you want to actually include larger size cations, then you have to increase the number of donor atoms in the particular host. So, then you can make larger-sized crown ethers; for example, we can make 1, 2, 3, 4, 5, 6, and we can make this 8-oxygen atom system, as well as a 7-oxygen atom system.

So, we can make these larger-sized crown ethers. So that we can accommodate larger-sized cations, for example, cesium and rubidium, etc. And you can also make smaller-sized crown ethers; for example, you can make a 15-membered ring with 5 oxygen atoms.

So, this is called the 15-crown-6, and this is more complementary to the sodium cation. So, the sodium cation being slightly smaller in size needs a slightly smaller void, and therefore, 15-crown-6 is able to provide the same efficiently.

And then it is also important to keep in mind that this particular host here exists in

different configurations. In principle, there are five different conformations in the dicyclohexyl system, which are referred to as cis-syn-cis, cis-anti-cis, trans-syn-trans, trans-anti-trans, and cis-trans.

So, these are the five independent conformations in which the dicyclohexyl moiety can exist. The next thing is to actually compare the binding constants now. So, we have looked at podands, and we have looked at the cyclic ethers, which we call corands.

And now we can actually compare that, given a metal cation, what the magnitude of the binding constant is, which follows. So, keeping this in mind, let us compare, for example, the magnitude of the binding constant between 18-crown-6, which is a cyclic ether, and the corresponding pentaethylene glycol unit, the PEG unit. So, we have this particular moiety, pentaethylene glycol, which has 1, 2, 3, 4, 5, 6 donor atoms, and we also have crown ether 6, which has 1, 2, 3, 4, 5, 6 donor atoms.

So, in both cases, we have 6 donor atoms, and we would like to compare the log K value. In this case, this is for the potassium ion; we would like to compare the log K value, which is 6.08 for the 18-crown-6, compared to only 2.3 for the corresponding open chain conformation.

So, right away this tells you that 18-crown-6 is very efficient in encapsulating the potassium cation compared to the polyethylene glycol variant. And this is because we have already studied this; it is because of the pre-organization of the ligand. The ligand is already effectively pre-organized, and it has the converging binding sites.

So, it can effectively encapsulate potassium and therefore result in a high magnitude of the binding constant with the potassium ion. And then what people have done is try to modify the ether further so that they can enhance the magnitude of the binding constant.

So, in this regard, people have synthesized a new class of molecules which we call lariat ether, where what is done is that to start with, we have a cyclic structure. So, we have this particular ligand, and this is the ether where we have 4 oxygen atoms and 2 nitrogen atoms or 2 NH groups, and the binding constant log K is 2.04 for the potassium cation.

So, then what the scientists thought is that we can enhance or increase the magnitude of the binding constant by modifying the NH group, and synthetically this is done by replacing the NH with NR, where R also has donor atoms. So, if you do a chemical modification, you now have increased the number of donor atoms by 2.

So, now you see the side chain; this side chain, or the side arm, has a ligand that is of a flexible nature but has two donor atoms, and this is referred to as a lariat ether. This comes from the word lasso, where essentially in a lasso we have a rope that is tied up at the end with a circular kind of loop. So, the circular loop represents this particular ring,

and the linear part represents this.

So, we have a lasso where the rope part is the sidearm and the circular part is this particular cyclic ring. And now what happens is that when you add a potassium cation here, this sidearm will change its conformation. So, if the sidearm is actually flexible, it is moving around. Now, the moment you add the potassium cation, the side arm changes its conformation and folds itself. And then stabilizes the potassium ion by additional binding provided by these two donor atoms.

So, we see what happens is that there is now a change in the conformation of the system such that you have a potassium ion that is stabilized by this nitrogen.

So, this represents the cyclic part, which already has how many donor atoms: 1, 2, 3, 4, 5, and 6. So, there are 5 here; this is 6, 7, and 8. So, now, there are a total of 8 donor atoms that bind with this potassium ion. So, this additional stability, this additional enthalpic stabilization provided by the two donor atoms that bind with the potassium cation, actually increases the magnitude of the $\log K$ to 4.8.

So, the magnitude of the equilibrium constant is now more than double, keeping in mind the effect of the modification of the NH group by the side chain. So, these kinds of modifications can be done that can actually enhance the magnitude of the binding constant.

And we can also further modify the side chain by even replacing this hydrogen with an R group as well, and those are referred to as bi-bracchial ethers; these are referred to as bi-bracchial lariats. So, the bibracchial lariat ethers have both the NH groups replaced by the R group.

So, with this, we come to the end of this lecture, and in the next lecture, we will look at the other class of ligands, which are the spherands as well as the crypands.

Thank you.