Fundamentals and Applications of Supramolecular Chemistry

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Week 09
Lecture 43

W9L43_Self Assembly in Helicates, Formation and Structure of DNA

Hello, everybody. So now let us continue our discussion on helicates. So, in the last lecture, we were looking at metal-based systems as supramolecular self-assembly methods.

We looked at ladders, we looked at molecular racks, and we saw how this specific composition of a set of ligands, along with a metal ion, can actually create a template that can lead to the formation of larger-sized species that are thermodynamically stable entities.

So, we appreciated the principles of self-assembly in rigor in the last couple of lectures. Today, we are going to discuss another class of self-assembly processes involving helicates.

In this case, what happens is that the coordination complex adopts a helical geometry to start with, and the molecular threads that give rise to the formation of helical complexes are called helicands.

So, these are the ligand-based backbones, or the ligand-based chemical entities that can give rise to the formation of helical complexes, and these ligands are called helicands, and the resulting complexes are called helicates.

So, to start with, let us look at one specific example of a simple helicand. So, to start with, the ligand has a backbone, geometry, or conformation that already has the helical twist associated with it; for example, we can consider a simple helicand.

Thus, we have this particular complex that can be formed when you have a metal ion Mn+ interacting with these four nitrogen atoms, so this is one binding domain, and this is another binding domain.

So, it is a ditopic ligand, and we can put bulky groups R here, where R can be equal to methyl or hydrogen. What has been observed is that in the presence of a metal ion in the +1 oxidation state, for example, copper +1, it can form either a 1:1 complex, or it can

form a 2:2 binuclear non-helical complex or helicate, and it can also form a double helical 2:2 complex, which has tetrahedral geometry at the metal center.

And the binding domain, as you can see, has a different number of donor atoms. So, the number of donor atoms is 4, the denticity is 4, but the topicity is 2 because there are two distinct binding sites here.

And these can create the necessary arrangement of the metal ions around the particular ligand, which is referred to as quarter pyridine. So, let us see how these look. You can have a 1:1 complex. For example, in this case, we can have a 1:1 copper ion and a quarter pyridine ligand forming this particular complex. That is the first case.

In the second case, this is my metal ion sitting here, and this is another metal ion sitting here. So, this is a binuclear 2:2 non-helical complex. You see that this is an individual strand here, and you have the metal ion, which can now form a tetrahedral complex at every particular site. And then we can have the third one, which is referred to as the double helical arrangement. So, we have this kind of encapsulation.

So, you can see these are my arms. So, if one coordination is happening from this side, the other happens from the other side. And then on the other end, we will have the opposite orientation. So top and bottom on one side will have the bottom and top on the other side. This kind of arrangement will take place.

So, we now have this ligand backbone. This is the ligand backbone, and here we are going to have the metal ion, which is formed in the tetrahedral complex. This is again a 2:2 complex, but it is of a double helical nature. So, each strand of the helix is important here, and this together constitutes the double helical structure. Now there are some properties of these helicates.

Let us look at the properties of these helicates or helical structures. Now, the first thing is that the two chiral single helices go back. So, each one is a chiral helix; this is also a chiral helix, okay. The two chiral single helices of the same handedness, that is either left, left or right, right, fit together to form a double helix. This is very important.

So, both of these helices, which are now forming this helicate-like structure, both of these chiral single helices are of the same handedness. So, if I say this is one hand, and I have the other hand like this, these are the mirror images of each other. Then the opposite chirality helices cannot form the double helical structure, okay. Because they will essentially, when you superimpose one on the other, come like this. But what I need is this kind of arrangement.

So, this kind of arrangement can happen only when I rotate the same helical structure of a given chirality and then allow it to superimpose from the opposite direction. So, we essentially have a rotation of this single chiral helix, which can rotate, and then it can form the tetrahedral geometry or the double-helicate structure. But if we have the opposite chirality, then essentially these are non-superimposable mirror images.

As you can see, when they are placed one on top of the other, they will not be able to form the double helical structure or the double helical geometry. So, only when you have both helices of the same chirality, same handedness—left or right—do they fit together to form a double helix.

So, number 2, as it can now be concluded, is that single helices of opposite chirality cannot form a double helix. So, this is what follows: when we have the opposite chirality, they cannot form a double helix. However, the double helicates, which we have now formed, consist of a chiral helical screw.

So, the double helicates are themselves chiral, and once you have the chiral arrangement, you can now draw the non-superimposable mirror image of this double helicate. So, these do exist as chiral entities; they exist as chiral helices of opposite handedness.

So, the double helicates consist of a chiral helical screw, which results in the occurrence of left-handed (M) and right-handed (P) forms. This is according to the Cram-Ingold-Prelog (CIP) nomenclature. So, we have the CIP, the Cram-Ingold-Prelog nomenclature; according to that, we have now got the left-handed [M(-)] and the right-handed [P(+)] helices.

So, these are some of the most important properties of the helical structures. Another very important property is that both single and double helices can exist as enantiomeric pairs.

So, they can both exist as enantiomeric pairs, whether it is a single helix or a double-helical structure. But, unlike the conventional combination of two chiral fragments, the double helix does not exist as two diastereoisomers, because the heterochiral combination of two helices or two single helices does not give rise to a double helix.

This is also another very important property of the helices: although the single and double helices can exist as enantiomeric pairs, the double helix is made up of two single-chain helices of the same chirality; therefore, they are of the same chirality. So, we now have two chiral fragments. Whenever we have more than one chiral fragment in an organic molecule, we know that it can lead to the existence of diastereoisomers.

But unlike that of organic molecules, here the double helix does not exist as

diastereoisomers because the double helix itself is formed from single helices of the same chirality. If they were of the opposite chirality, then they could have given rise to diastereomers.

So, the heterochiral combination of two single helices does not give rise to a double helix, and therefore there is no scope for existence as diastereoisomers. Because what gives a double helical structure is the chirality of the helix, which is of the same type, heterochiral combinations do not give a double helix. So, now that you have a helical ligand, we can do some interesting electrochemistry with these metal complexes.

Now, given a metal ion, that can form both octahedral and tetrahedral complexes. So, now you can have a metal ion that can exist in different coordination environments, depending on the oxidation state of the metal ion. It will result in the formation of different kinds of helices, and this information is again encoded in the system, depending upon the coordination preferences of the metal ions. So, let us take one specific ligand here now.

And then we can have this one here.

So, now you can see this is having 6 nitrogen atoms. Now, you have two possibilities here. If you have a copper ion, it has a tendency to form octahedral complexes. Then we need a coordination number of 6; there will be two distinct binding domains. This will be one particular binding domain, and this will be another binding domain.

So, here the copper ion can now interact, and it will form a [6 + 6]–Cu^{2+} complex. Or, if you have other metal ions, like Fe^{2+}, Co^{2+}, and Cd^{2+}, they can form a [6+6] double helicate structure. So, if we have a metal ion in the d10 system, for example, in the plus one oxidation state, it can form tetrahedral complexes. Then we will have three distinct binding domains, and the topicity will be three.

It will be a tritopic ligand. In the case of octahedral complexes, it will be a ditopic ligand, and then because we are now going to have a [4+4+4] Cu^{+} helical structure, we can get a [4+4+4] double-stranded helix. And we can actually now do an oxidation of the Cu+1 center to Cu+2, and it will change from a [4 + 4 + 4] to a [6 + 6] helicate, depending upon whether you have done an oxidation or reduction.

So, you can have the shuttling between these two states. So, these are two different electronic states: one in which the copper can exist in a tetrahedral arrangement. If you oxidize copper, it will now shuttle and change into the [6+6] arrangement, and again when you reduce it and return to Cu+1, it will bring it back to the [4 + 4 + 4] helicate structure.

So, this kind of control can happen when you have the metals in specific oxidation states. Essentially, this can function as a nice electrochemical system where you can control the electronic motion and the nuclear motion as well, depending on the oxidation state of the metal ion.

So, with this in mind, this is what we have to discuss regarding the metal complexes. Now, towards the end of this particular lecture, I would like to take up a couple of case studies of self-assembly processes in DNA, which is also called the molecule of life. So, here DNA is responsible for encoding the genetic information that makes life possible.

This is the function of DNA. What is characteristic about DNA is that it is only the double helical structure that is the active form of DNA. So, DNA is a very unique example where, if you have two single strands of DNA and simply bring them close to each other, allowing them to interact via the formation of hydrogen bonds between the ATGC pairs, it is not known to be the active form of DNA.

So, if you were to simply have two simple strands of DNA, bring them close to each other, and they are going to form these hydrogen bonds that are not going to be the active form. And what has been realized is that it is actually the helical twist of the DNA that further reinforces a pi-pi stacking interaction between the base pairs. So, now we have the four base pairs: A, T, G, and C.

And it is a simple single-strand DNA interacting with another single-stranded linear DNA. It does not give rise to the active form. It is actually the double helical structure. And here we can see again that this particular information is contained within the system. And here we would like to see how these ATGC hydrogen bonds exist.

This is a very specific kind of hydrogen bonding. And we can draw the ATGC pairs here. So, we have the adenine, we have the thymine, and you can see that there are specific hydrogen bonding interactions here: N-H...N and N-H...O hydrogen bonds.

So, there are two hydrogen bonds here, which again make it very specific between A and T. And when you go to the G-C pairs now, this is my backbone. So, we can now have the specific hydrogen bonds: N-H...O here, N-H...N here, and N-H...O here. So, we have this bond, we have N-H...N, and we have another N-H...O.

So, this is between the guanine and the cytosine. There are two N-H...O and one N-H...N hydrogen bond. Here, there is a set of N-H...N and N-H...O hydrogen bonds. So, you see this is a very specific hydrogen bonding pattern, and now once you have these hydrogen bonds between the AT and the GC pairs. Let us look at these distances; the distances are slightly long.

This is around 2.9, this is 2.8, this is 2.84, this is 2.91, and this is 2.84. Although these hydrogen bonds are quite long, they are highly directional. So, the directionality is what is very important when it comes to these particular hydrogen bonds here.

So, this kind of specific hydrogen bonding formation is there, and now once you have these hydrogen bonds, you have these ATGC pairs. As you see, they have a large surface area, and they are aromatic in nature. There is electron density. So, now they can further have the helical twist where these actually stack co-facially with each other via pi-pi stacking interactions. So first you have the single strands coming close, forming hydrogen bonds.

Then this forms the pi-pi stacking, giving the helical twist to the structures. In this process, it is actually trying to make the DNA very, very compact and go into a very, very compact and dense conformation or configuration.

Such that the hydrophobic parts interact with each other, the hydrophilic parts also interact with each other, and this gives rise to a major groove area as well as a minor groove area in the double helical DNA structure.

So, the formation of the DNA helical structure is extremely important, but how is it that this DNA double helical structure formed? Again, the formation of the DNA helical structure proceeds via a nucleation and growth mechanism.

And you see, this is the interesting thing about nature: you have nucleation and growth processes, but then you also have self-assembly, which operates over time scales as well as length scales, because you can now assemble small units and make larger units.

So, you can increase the size of the molecule, and these processes can take place over a finite period of time. For example, let us consider one strand to start with. Let us consider A, G, T, A, A, C, G, and T. Then we have another strand, which is called T, G, A, T, T, G, C, and A.

So, the strand here. A we know is complementary with T, G is complementary with C, T is complementary with A, A with T, C with G, G with C, and T with A. And so, we now have the first hydrogen bonding recognition, where we have the T hydrogen bonding with the A, and then we will have the G hydrogen bonding with the C, and then we will have the C hydrogen bonding with the G. So, in this case, this is first of all the nucleation step.

Now, in the nucleation step, as we have also studied in our initial lectures, it is a very important step, and it is a step in which there is a decrease in the number of molecules. So, now you are creating the necessary order, because the two single strands, which were actually quite conformationally flexible, now need to come into a particular orientation,

and that decreases the entropy of the system.

So, initially, there is a loss in the entropy of the system; there is an entropy loss associated with the process. But as the process of growth now takes place, and as more and more hydrogen bonds are formed, enthalpy considerations take over.

An entropic penalty reduces, and that is the reason why this double-stranded DNA is now easily formed by this hydrogen bond association. So, this is also referred to as a zip mechanism, where you actually have two single strands, and it starts forming hydrogen bonds from the bases, and then finally it forms the helical double strand as well. So, this nucleation and growth process actually facilitates the formation of the DNA, and here we will have the propagation step.

This is the propagation step. This was the nucleation step, where they come close to each other, start forming hydrogen bonds, and then propagate over the entire length of the DNA strand to form double-stranded DNA. So, this brings us to an end of our discussion on self-assembly processes, and in the next lecture, we will take up the next set of discussions on other applications of supramolecular systems.

Thank you.