Fundamentals and Applications of Supramolecular Chemistry
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Lecture 11

W3L11_Concept of Host and Guest in Supramolecular Chemistry

So, hello everybody. So, let us continue our discussion on the next topic in supramolecular chemistry. In the third week, we are now going to focus on the developments, the introduction to the subject of supramolecular chemistry.

How did this subject start? What were the important discoveries which happened as a function of time? What are the key concepts related to supramolecular chemistry?

As we all know that supramolecular chemistry involves interaction of host-guest systems. We would like to understand what is a host, what is a guest, what are the prerequisites in a host, what are the prerequisites in a guest and then the favorable processes which happen which allow for the host and guest to interact with each other and so on and so forth. So, before we go into these details, I would like to give you a brief overview of the history of supramolecular chemistry.

So, there have been many important discoveries, but the first discovery was way back in 1810 when Sir Humphrey Davy discovered chlorine hydrate. This was the composition where he saw a binary mixture of chlorine and water and this was the first discovered chlorine hydrate which was postulated to be the starting point of supramolecular chemistry.

After a few years, in 1823, Michael Faraday gave the formula of chlorine hydrate. This is interesting because once the compound was discovered the actual composition of chlorine hydrate was proposed by Michael Faraday.

Following this there were many other inclusion complexes, which were discovered where you have got at least two different chemical components and it was observed that these two individual chemical components, they interact with each other via the supramolecular interactions.

And form different kind of complexes which have got different properties compared to the starting materials from which they are composed. And normally it was observed that one compound is included in the structure of the other compound and hence the name inclusion complexes was given.

For example, in 1849, F. Wohler discovered beta-quinol plus hydrogen sulfide inclusion complex. Then in 1891, Williers and Hebb, they discovered cyclodextrin inclusion complexes.

And then came a very important landmark a very important discovery, in the field of coordination chemistry when Alfred Werner discovered coordination compounds, followed by another very important discovery by Emil Fischer who proposed the concept of lock and key mechanism, which is of extreme relevance and significance in the field of supramolecular chemistry, particularly in the field of macromolecular sciences, particularly in the field of biological sciences, molecular biology, how a particular ligand interacts with a protein site.

This lock and key principle has found very important applications and we will be discussing the lock and key principle during the subsequent part of the course. So, this turned out to be, I would say a very, very important discovery.

I will highlight, Alfred Werner discovery of coordination compounds and Emil Fischer discovery of the lock and key mechanism, and then came the introduction of the concept of a receptor by Paul Ehrlich.

Paul Ehrlich introduced the concept of a receptor, that means that particular molecule or species which is involved in a sensing mechanism, which is for example, any molecule which is able to sense, for example, cations or anions in solution is referred to as a receptor.

So, the concept of a receptor was proposed by Paul Ehrlich. And then came the famous scientist, Professor Linus Pauling, who in 1939 proposed the concept of hydrogen bond, which was the basis of the understanding of supramolecular chemistry and that time he wrote a very path breaking book which is today known as the nature of the chemical bond.

And this particular book has very significant details about how to look at non-covalent interactions, hydrogen bonds and their characterization, the structure of compounds containing hydrogen bonds and the properties.

And at this time, X-ray crystallography was picking up and so people were able to determine a large number of structures and that is where the contribution of X-ray crystallography has been extremely important in the development of the field of supramolecular chemistry.

Without the understanding of the structure, without an understanding of the shape of the molecule and how the molecules interact with itself. For example, in the solid state, it has

been extremely difficult to get inputs on what is happening when host-guest interactions takes place.

So, this actually paved the way for further very important discoveries. For example, in 1953, Watson and Crick proposed the structure of DNA. And this we know is a very, very important milestone in structural biology and chemistry, now, because we know that DNA is the molecule of life.

And then in 1956 Dorothy Hodgkin, her full name is Dorothy Crawford Hodgkin, gave the crystal structure of vitamin B12. These are the cyano cobalamines where a cobalt interacts with the organic molecule. The molecule is called vitamin B12.

And please keep in mind we are talking about 1950 and 1960 when technology had not really developed and X-ray diffractometry which is an instrument which is used to determine structures by performing diffraction experiments.

The technology was very very old and it used to take a lot of time to collect diffraction data and the structure determination used to take years.

Today it takes only a few hours to determine the structure of a small molecule assuming you have got high quality crystals. So, with lot of struggles and lot of challenges both Watson and Crick and Dorothy Crawford Hodgkin were very very instrumental in developing the field of supramolecular chemistry by determining the structures of DNA and vitamin B12.

And then followed a series of discoveries by organic chemists, of different kind of receptors, and different kind of organic molecules which are very important for different binding processes. For example, it was in 1967, Charles Pedersen discovered crown ethers. And this class of compounds turned out to be very, very interesting, and we will look at some of the most important applications of crown ethers as well.

Followed by the discovery of cryptands, which are another class of receptor molecules by Professor Jean-Marie Lehn, for which he was given the Nobel Prize in 1937. Subsequently he made very important contributions to the field of supramolecular chemistry for which he was given the Nobel Prize.

This continued and there have been many other contributions and today also we see a very famous scientist who recently just passed, a few days away, Professor J. Fraser Stoddart.

He also has developed a field of supramolecular chemistry and Professor J. Fraser Stoddart, he has also made many pioneering contributions in supramolecular chemistry and who just recently passed away and he also got the Nobel Prize in chemistry for his contributions to supramolecular host-guest chemistry.

So the idea of giving you a background to this particular topic is that we are actually going to learn a lot of interesting chemistry, interesting supramolecular chemistry and all the discoveries as I have highlighted to you have been extremely important in shaping the field, particularly the ones which I have highlighted in red.

Linus Pauling's development, Watson and Crick, Dorothy Crawford, followed by the last 40 years that have seen pioneering developments in the field of supramolecular chemistry. Starting from the discovery of crown ethers to cryptands and followed by many other interesting discoveries and inventions in the field of supramolecular chemistry.

And these have been found to have applications now in nano materials, and nano medicine and all these interesting discoveries are now enriching the field of materials science and engineering.

So, with this background, let us now go a step further into the field of supramolecular chemistry. Now, how is supramolecular chemistry different from molecular chemistry? In molecular chemistry, it is a process where we have a set of molecules, a set of reactants that react with each other to give a product.

For example, we have A plus B plus C giving you a product D and this is the traditional chemistry which involves making and breaking of covalent bonds. So, we have some bonds which are being broken in A, B and C and they are all reacting together to give a new product D and the properties of D are fundamentally different from the properties of A, B and C. On the other hand, in the case of supramolecular chemistry, so this is your traditional chemistry which we also called as covalent chemistry.

In the case of supramolecular chemistry, we have a molecule, say we name it as H, which we refer to as the host, and we have another molecule which is called a guest, and it is the association of the host and the guest to give a new complex which we call the super molecule, which is essentially held by non-covalent interactions.

So, there is no bond making or bond breaking involved, but what happens is a supramolecular association between the host and the guest to form a new species which is of a supramolecular origin.

And this distinguishes covalent chemistry from supramolecular chemistry, we also call this as non-covalent chemistry. Chemistry of the non-covalent bond is what constitutes non-covalent chemistry. Now when we have found a new molecule, what are we interested to know about the new molecule? We are interested to know about the physical and chemical properties of this new molecule.

For example, we are interested in knowing what is the chemical nature, what is the shape of the molecule, what is the size of the molecule, what is the redox behavior of this, the redox property which is very important, what is the homo-lumo gap, what is the polarity of my molecule, whether my molecule is polar or non-polar, whether it is magnetic, whether it exhibits the phenomenon of magnetism or not, chirality etcetera.

So, these are some of the important properties we are interested to know when we make a new molecule D. On the other hand, when we are making a new supramolecular complex, we are interested in the specific characteristics, function and properties of this new complex here and why we are interested.

Because we are interested to know the events of molecular recognition, and this is supposed to have applications in catalysis and transport to start with. So, catalysis is a important function and transport is also very important property.

So, different kind of molecular recognition characteristics can decide the function and the properties of these supramolecular complexes. And when you have this supramolecular complex, we are interested to know what is the degree of ordering, and what are the nature of interactions between the individual units, and we are also interested to know the symmetry of the complex, and the symmetry of the packing, if the complex is a solid.

So, all these things become relevant when we are trying to understand the host-guest behavior. It is not enough to just simply speak that okay I have a host and I have a guest and they interact with each other and that's it.

No, these interactions decide the fate of the molecule and it is also important to keep in mind, we will discuss more and more as we go into the course that apart from these particular features, it is also important to keep in mind the shape, size of both host and guest molecules and then what is the overall shape of the complex.

And in this regard, it is the molecular conformation that plays a very important role. So, what is the molecular conformation of the host when it is not interacting with the guest and what is the molecular conformation of the host when it interacts with the guest.

So, these things are extremely important because that decides the overall shape and the subsequent property will follow from there. For example, we can consider a guest, having this particular shape and we have a host. So now we can have the guest.

So, this is now my guest which is relatively smaller in size, and this is my host which is relatively larger in size and now I would like to see how my guest interacts with the host. To start with there is a void which is present in the structure of the host, and if the guest is able to include itself into this space which is created by the host molecule, then it will form a supramolecular complex where my host will include the guest.

So now you can see I have been able to successfully include the guest molecule into the host molecule, and this is a very important phenomena because this governs molecular recognition that the guest molecule is able to effectively include itself into the void or the space which is created by the host molecule.

And this also is a very important feature of sensing, sensing behavior between molecules. And this is an ideal picture because we are assuming that the host has got the right kind of void in terms of the size and the volume.

And the guest also has got the right shape to include itself into the cavity which is created by the host. But we can also have other modes of molecular recognition as well. And for example, let us look at the different modes of binding of a guest molecule with a host molecule. So, we have now learnt that the host molecule is significantly larger than the guest molecule because there are differences in molecular size and shape.

So, the one which has got the larger molecular size and shape is referred to as the host, and the smaller one is referred to as the guest, and it is the interactions between the host and the guest via the non-covalent interactions that form these kinds of supramolecular complexes, and these are formed by self-association processes.

And the self-association processes did not always happen in the way I just showed. That means there is a strong binding, there is a nice steric fit of the guest into the structure of the host.

For example, we can have, so this is my host molecule, which is the larger one in size, and I have a guest, the guest can be simply included here. This is referred to as a capsular arrangement. Similarly, I can have my host again and I can have the guest sitting on the host, such that it touches one of the faces of the host.

This is referred to as the nesting geometry or the nesting conformation. In the third one, we have got the host and now we can have the guest which essentially sits by interacting with only the edge. It only interacts with the edge of the host molecule. This is referred to

as the perching geometry. Then we can have the guest which is actually included between two host molecules.

The guest is kind of sandwiched between the two host molecules. This is referred to as the sandwich geometry or the sandwich conformation. And then we can have a host which to start with, say, is having this kind of open geometry or open conformation.

This is the host and now when you add the guest, it wraps itself around the guest, the host wraps itself around the guest molecule. This is the guest, this is my host molecule, and therefore this is referred to as the wrapping conformation.

So, as we already mentioned, the initial conformation of the molecule plays a very important role, and there are molecules which can have a fixed conformation, that is there is not much conformation change before and after the guest binding.

That depends upon the rigidity of the host. If the host is very rigid, then when the sensing takes place and when the guest comes in the proximity of the host, there is not much change in the conformation of the host. Whereas, there are cases, for example, the one which I showed now, the last one, where you have a open conformation. This is called the open conformation of the molecule.

The molecule has a very open conformation, and it has got different degrees of freedom which we call as the rotational degrees of freedom. Therefore, it has got rotatable bonds and therefore, this is an open conformation. But now when a guest comes, say you have got a metal ion, which is now put into the solution containing the host.

We will also consider now after sometime the role of the solvent in which these particular experiments have been done. But the moment you put in the guest, it will wrap itself around the guest to accommodate the guest via non-covalent interactions.

In case of metal-ligand complexes, assuming that the host is my ligand and the guest is my metal these forms coordinate covalent bonds. So, formation of coordinate covalent bonds is also a kind of you know non-covalent association to start with, but eventually these go into coordinate covalent bonds, in terms of the strength.

So, we call them essentially covalent bond formation. But they essentially originate from a sensing mechanism where the ligand changes its conformation and wraps itself around the guest to effectively encapsulate and capture the guest molecule. So, these kinds of association processes, are extremely important and this is what constitutes host-guest chemistry.

Now, when you have this host-guest chemistry, which is operational, it is also important to talk about what is a binding site. There are binding sites. There are different kinds of binding sites which are present in the host molecule and the guest molecule would like to come and coordinate and interact with these binding sites.

So, what is a binding site by definition? It is a region of a molecule, that has the necessary size, geometry and functionality to accept and bind a second molecule via non-covalent interactions. So, this is the definition of a binding site, that it is a region where you have the right size, geometry and functionality to bind with a second molecule by non-covalent interactions.

And in this regard the host component is defined as an organic molecule or an ion with converging binding sites whereas the guest component has divergent binding sites in the molecule. So, when you have a host, because the host is effectively going to capture the guest and this approach of the guest towards the host is such that the donor atoms which are involved in capturing the guest molecule needs to have converging binding sites.

For example, I can take this particular conformation, there is a donor atom, it has a nitrogen, there is a donor atom, it has an oxygen, and it is going to capture a metal ion, it must have convergent binding sites.

There is a metal ion on the other hand, metal ion M n-plus is actually swimming around in solution, it is being effectively solvated, and it is looking for a suitable host which will capture it. So, this metal ion has got the entire surface exposed and in all possible directions it can approach towards the host for effective encapsulation.

Therefore, it has got divergent binding sites, the host component has got converging binding sites. So, these are the two additional properties which are important in case of host-guest complexes. That means along with the necessary size, geometry and the relevant functionality we also need to have converging binding sites in host, as well as divergent binding sites in case of guest molecules.

Now in the next lecture, we will extend further our definitions, which are fundamental to a supramolecular host guest design. So, as of now we have discussed about what is supramolecular chemistry, what are the important starting fundamental concepts.

We have looked at binding site, we have got a brief introduction to what is host and what is guest and now we will take up more characteristics which are of relevance in supramolecular host case design.

Thank you.