Fundamentals and Applications of Supramolecular Chemistry
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Week 02
Lecture 09

W2L9_Cation-pai, Role of close packing v/s H-bonding

So, hello everybody. So, now, let us continue our discussion on cation-pi interactions further. So, in the last lecture, we were looking at cation-pi interactions, which actually take place in the presence of cations. So, we looked at the role of lithium, silver, potassium, rubidium, cesium, ammonium ion cation, tetra butyl ammonium cation.

And so, we can have either metal-based ions or we can have organic cations. And essentially what happens is that there is a pi electron density distribution and when you put in a metal ion in a particular oxidation state, it can also be transition metals, it can be lanthanides, actinides.

Then essentially there is a polarization of the electron density by the metal ion. So, there is a role of electrostatics and also there is a role of dispersion. Both electrostatics and dispersion contribute towards the stabilization of cation-pi interactions. And then what was realized is that instead of having a metal ion whether we can use organic cations also to participate in cation-pi interactions.

The interesting thing about cation-pi interactions involving organic cations is that you now have the organic cation which is having highly acidic hydrogens. And these acidic hydrogens can now interact over a large surface area of the benzene nucleus and therefore, there are multiple such N-H...pi contacts.

But essentially the N-H plus is the proton donor and pi is the proton acceptor. So, traditionally these are similar to that of hydrogen bonds, but essentially they come from the category of cation pi interactions. And because the N-H bond is highly polar, it is able to effectively participate in non-covalent interactions with the pi electron density system.

Along the same lines instead of having a proton connected to nitrogen we can also have N-tetramethyl cation as well, we can have isopropyl, we can have propyl, we can have butyl group. So, these kind of a quarternized ammonium salts are there and these can also interact with pi surfaces.

The interesting thing here is that the nitrogen is highly electrophilic. So, it withdraws the electron density from the methyl groups and makes these hydrogens acidic.

And now instead of N-H being a donor it is a C-H which is a donor, and these participate in C-H...pi hydrogen bonds. So you have N plus highly activated CH interacting with a pi system. It is important to keep in mind that here the activation of the C-H bond is being done by a cationic species.

Because now the electron density of the C-H bond is polarized it is drawn towards the nitrogen nucleus thereby it creates an incipient positive charge on this hydrogen. Therefore, this has now got an induced dipole and then it can now polarize the electron density of the benzene nucleus.

So, these are activated C-H...pi contacts but essentially come in the category of cation-pi interactions. And along the same lines, you can now take much bulkier ligands.

For example, we saw, you can take this kind of an adamantyl species, which has got an activated methyl group, which can also participate in C-H...pi interactions.

And then towards the end, we also looked at this kind of an alkyl chain, which has got an activated trimethyl ammonium species, which can also participate in cation...pi interactions. And these cation...pi interactions, the pi again need not necessarily be a benzene nucleus, it can also be a substituted benzene, and more electron rich.

It can also have some electron withdrawing groups and their other combinations are also possible. So, keeping in mind now these facets people have now tried to look at interactions of even larger we can even have larger cationic species.

For example, we can have N plus. So, here we can see we have got this kind of a species, this is a tetra-cationic species, this is a large ligand where all these nitrogen atoms are positively charged, and this can also participate in cation-pi interactions with other electron rich pi systems, and you can also incorporate these features in indole system also. Let us look at one example.

For example, this is a indole based system where we can have N+ and now, we can have the methyl group and now this methyl hydrogens they can actually now interact with the pi system.

So, this particular group comes above the plane of the molecule above the plane of the board and now it can interact with the pi rich system participating in intramolecular C-H...pi hydrogen bonds.

So, we can have intramolecular C-H...pi interactions again activated by the N+ system, where we can have these kinds of cation...pi interactions. Along the same lines, there are other species as well, for example, arginine-based systems are very popular.

We have got a protonated arginine system and here you can see this is stabilized because the lone pair can participate in delocalization and now these hydrogens are acidic enough to participate in N-H...pi contact.

For example, it has been observed that arginine can interact with tryptophan, can interact with tryptophan. So, how does the tryptophan moiety look like? So, this is tryptophan. So, this can now interact with the tryptophan protein. Now, this the orientation of this ring is very important. In this case, we are showing that the tryptophan has got the perpendicular orientation and arginine residue comes on top.

So, this is the perpendicular orientation, but you can also have the parallel orientation. So, both these orientations are allowed when a cationic species comes on top of the surface of the tryptophan system.

So, you can have the perpendicular interaction which is the N-H...pi, like I have shown you here, and you can also have the parallel orientation where the cation interacts with the tryptophan system. You can also have other type of systems, for example, we can consider this system here to interact with the benzene nucleus as well. So, we can have a histidine now this is a histidine moiety. The histidine moiety again has got the N-H protons, so these N-H protons can interact with the benzene nucleus, either in a perpendicular orientation or it can also have a parallel orientation.

In one case it is N-H...pi, in another case it is the cationic surface which interacts with the pi electron rich system. And you can also have other derivatives as well and so there are large number of systems which can participate in cation...pi interactions.

So, now we go further to this particular question. We will now look at the concept of close packing and we will now compare the concepts of close packing with hydrogen bonding interactions. So, we have now looked at all the classifications of different kinds of interactions which are present.

Now, the weakest of all the interactions in this regard are the H...H contacts. Now, these class of contacts are also very interesting because most of the organic molecules have got carbon and hydrogen.

So, for example, if you have got say ethane and you consider a container having ethane molecules and the ethane molecules are continuously you know bombarding and colliding with each other, and now you are applying pressure on ethane gas. So, naturally when you are applying pressure the volume is decreasing and the ethane molecules now come close to each other, and they interact with each other.

So, two ethane molecules interact with each other and again the origin of these interactions is purely van der Waals interactions in nature. Purely van der Waals or dispersive interactions in nature where the attraction is created by the fluctuating electron density which induces a dipole in the adjacent ethane molecules.

And here the nature of contacts is mediated by hydrogens, but it has also been observed interestingly that the carbon. So, if you were to consider the methyl and now there is another carbon here, it has also been observed that hydrogen can interact with the carbon directly. So, you can also have the possibility of hydrogen...carbon contacts.

So, both these hydrogen...hydrogen and carbon...hydrogen contacts coexist when you have got non-polar molecules which actually interact with each other, as there are no other forces which are present here. These essentially involve the weakest of forces. The possibilities are that there is either H...H contacts or there is a possibility of hydrogen interacting with the carbon to have this H...C contacts.

And these approach to within the sum of the van der Waals radius of hydrogen plus carbon.This is the approach and if you were to actually have an equilibrium situation then the separation will be either slightly greater or slightly smaller than the sum of the van der Waal radii in these cases.

And now the idea is to increase the molecular weight of the substances. So, now you can go from propane to butane. You can go to pentane, you can go to hexane, then you can go to heptane, octane, nonane and decane.

And also, it has been observed now as you increase the molecular weight of these hydrocarbons, they tend to go towards liquids and then the higher hydrocarbons exist as solids.

So, naturally more and more of these interactions are responsible for association of the molecules and thereby leading to different states of matter. And the fact that these interactions between the molecules create arrangements such that they facilitate close packing of the molecules.

In other words when you have all these hydrocarbons which contain carbon and hydrogen essentially, they want to maximize the H...H contacts and the C...H contacts preferably. And they pack in such a way, or they interact in such a way that they minimize the voids in the solid.

So, the eventual goal is to look at the solid state where in the solid state you will be able to appreciate the arrangement of the molecules such that they maximize this H...H and H...C contacts and is also another category to this that is you can also have the possibility of C...C contacts.

For example, in case of a benzene, anthracene, naphthalene, we can have these C...C contacts as well and they also some of these hydrocarbons also exist as solid. So, when you look at the solid-state architecture and the arrangement of the molecules in the solid state, then you will see that they pack in a way so as to minimize the void which are present in the solid, such that they increase the density of the solid.

This is because we know the density is equal to rho, the density, that is equal to mass by volume. So, if the volume decreases and the mass remains the same, for a given mass, if the volume decreases, then the rho increases. So, the idea is to have an increase in rho by decreasing the volume.

So, high density or packing density is what characterizes the molecules in the solid state and that time it has been observed that this packing of the molecules depends upon the shape of the molecules, and it also depends upon the size of the molecule.

That is what is the overall shape, what is the geometry of my molecule, and what is the size, that is how many atoms are present in my molecule. And you can have different shapes of molecules.

For example, this is one particular shape I am considering and now when this particular molecule will try to interact with another molecule, it will try to do so in a way that one molecule will fit into the void which is created by the other. So, you see that there is a void created in this region.

So, this void region is where we have this particular shape of the molecule which tries to fit into this particular region such that it maximizes the contacts in this particular region. So, this is the space filling model. In the space filling model, depending upon the shape of the molecule and the size of the molecule, every molecule tries to interact with the other molecule, such that it tries to fit into the voids in the vicinity of a molecule.

So, wherever the voids are present. That particular molecule with its characteristic shape will try to adjust and maximize the interactions so as to reduce the volume, the free volume or the void space available within the molecules such that it can efficiently utilize the space in its vicinity and create a close packed solid.

And the basis of the close packing in case of solids particularly in case of organic solids was proposed by a Russian scientist called A. Kitaigorodsky. He proposed the concept of a space filling model in solids: that solids pack in such a way that they want to minimize the void space and maximize the available space via formation of interactions.

And also, it was proposed on the basis that nature normally abhors vacuum, nature does not like vacuum, nature would always like to pack things in the most efficient way even though it involves the utilization of the weakest of interactions. So, this is the basis of close packing, and this concept can now be even extended to all kinds of organic molecules which have got lot of hydrophobic content.

For example, we can look at long chain compounds. For example, we can consider this long chain fatty acid which has got a hydrocarbon chain and which has got a polar group here. And now when these molecules interact with each other and they coordinate with each other then the idea is to maximize the interactions such that you have a closely packed solid. And during the process of close packing it is also important to minimize the sterics which takes place between the non-polar moieties. And so, the way to look at the close packing is by the determination of the structure of the compounds. It is only after the process of determination of the structure is complete that we can try to appreciate the role of different kinds of non-covalent interactions in the packing in the solid.

And it is where the contribution of crystallography has become very important because it is only through X-ray crystallographic studies where we determine the structure of the compound by growing crystals of the compound. Then performing the diffraction experiments, we are able to get the atomic connectivity which, generates the molecule and then the arrangement of the molecules in the solid state which allow us to appreciate the different interactions which are present between the molecules and that are responsible for the formation of the solid.

And it is only by close inspection of the packing of the compounds in the solid that we will be able to appreciate the concept of close packing. Now, when it comes to close packing, because we know that the dispersive interactions are operational at very very short range that is the attractive at r to the power 6 and the repulsive as 1 by r to the power 12. And when these close packing interactions takes place, directionality is not a very important concept, because you need to maximize the contacts.

So, this directionality is not very important. What is important is how close the molecules can come to each other, interact with each other and form the close packing solid. So, van der Waals interactions or these weak dispersive interactions lack directionality, and they are isotropic in nature, and they are non-directional, ok.

They are non-specific, they are isotropic in nature, and they want to maximize the number of interactions so as to contribute towards the stability of the system. So, keeping in mind that these are weak interactions, they lack directionality because they have to satisfy the concept of close packing.

On the other hand, the hydrogen bonds need directionality. For hydrogen bonds, we need directionality, we need them to be linear as possible, as close to 180 degree, and to create an architecture or arrangement of molecules so as to maximize the hydrogen bonding and to maintain this directionality it creates lot of voids in the structure.

There have been a large number of compounds which assemble via the hydrogen bonding interactions where there are lot of voids in the structure so as to maintain the hydrogen bonding architecture. Further we know that hydrogen bonding is more stabilizing in nature and then that is what the compound prefers in preference to that of close packing.

And when you have both, for example, when you have this kind of an acid, you have both a non-polar part and you have got a polar part, then this nature will try to optimize both these interactions to get the resulting architecture. So, hydrogen bonding interactions on one side is directional, close packing is non-directional, hydrogen bonding are very specific interactions, close packing are non-specific interactions.

So, keeping in mind that these have got very different properties and different characteristics, the final packing of the component in the crystal structure is going to be a subtle interplay of both the close packing interactions as well as the hydrogen bonding interactions. There is going to be a balance and an interplay of both these categories of interactions to give you the final solid. So, let us now try to look at some of the examples now in this category, where we would like to appreciate the role of close packing. So, we can look at different kinds of molecules, different spectrum of molecules, where we will try to appreciate the concept of bonding.

Let us start with first propane. Now, propane is a gas at room temperature, but what researchers have done is that they have been able to crystallize propane and determine the crystal structure of propane.

So, this is the crystal structure of propane as you can see here and you can see very clearly this is the unit cell because when you do a crystal structure determination you have to represent the unit cell which is the basic repeating unit in a crystal structure and here you can very clearly see the arrangement of propane molecule.

So, you have propane molecule here. Then you have another propane molecule here, then you have another propane molecule here, then you have another propane molecule here. And you can very clearly see the conformation of propane, you can see CH3, CH2, CH3 hydrogens, the CH bonds.

And now you can see that one of the hydrogen of methyl group of propane is interacting with the carbon of the methyl group of the adjacent propane. So, this is very, very interesting tells you that hydrogen has got slightly electronegative character which is interacting with the slightly electropositive character of carbon to form these H...C contacts.

So, this is the basis of interactions. So, when you have these propane molecules and the interesting thing about the solid state is now these molecules are crystallographically positioned in the crystal structure. These positions are well defined according to the symmetry of the crystal system. So, the crystallographic symmetry decides the arrangement of molecules.

These arrangement of molecules is not random, but it is well defined according to certain rules of symmetry and hence the positioning of the molecules is very well defined, and the architecture is very very robust and tells you the three-dimensional connectivity of molecules. In this case, I have shown the three-dimensional connectivity of molecules down the a- axis, that is along the bc plane.

So, you can see, this is the bc plane and the a-axis is perpendicular to the bc plane. And it is also very clear that this H...C contacts is responsible for forming a one-dimensional chain which forms here.

Then you have another one-dimensional chain here, as you can see which goes like this, and there is another one-dimensional chain which goes like this. The interesting thing to appreciate is that this particular molecule here tries to fit into the space which is created in the vicinity of the one-dimensional chain.

So, once you have got this one one-dimensional chain, whatever is the space available in its vicinity, the next layer of molecules try to come and fit into that space. So, you can see here that this particular methyl group tries to occupy the space which is present between the non-covalent regime. Similarly, here the central carbon, the methylene group, tries to fit into the space which is created by the one-dimensional chain.

So, whatever space is created in the vicinity of the one-dimensional chain, the next layer, the next chain of molecules come and try to fit into that particular space so as to maximize the density, minimize the volume, based on the principles of close packing that nature always tries to pack things in the most efficient way because it does not like vacuum or empty space.

So, this nice 1D arrangement of molecules via H...C contacts allows for the presence of close packing to prevail in propane. So, then we were interested to also look further at the next molecule which is butane. Now you can see case of butane the formula is C_4H_{10}, this is the molecular formula, and you can see very clearly the molecular structure of butane here is very well represented.

This is not the gas phase model, this is the model or the conformation in the solid state. You can obviously now take out this particular molecule at the crystal geometry and minimize the potential energy of the system and obtain the gas phase conformation. So, from experiments we can now clearly see the molecular structure of butane, you can very accurately determine the C-C bond distances and the angles.

And now you can see that this is one layer of molecules where you have the butane molecules sitting they are periodically translated in the unit cell. And you can also see very clearly that again there is a slight shift in the molecule.

So, you can see that the carbon here faces the methylene group and then the methylene group here again tries to fit into the voids which is created and you have this kind of a translation of the butane molecules. The next layer of molecules is such that the methyl groups try to face each other. So, now you can see one of the methyl group is facing this particular methyl group and again this particular methyl group is facing this particular methyl group.

The next layer of molecules is trying to fit into the voids which is created by the first layer. So that they minimize the sterics. If they come exactly close face-to-face with each other, there will be lot of sterics operating and that is an unfavorable situation.

So, to minimize the sterics the molecules align or orient in a particular way in the crystal structure. So, that they can minimize the steric repulsion and maximize the electronic interactions which will stabilize the molecules via favorable H...H contacts or C...C contacts or you can also say C-H...C contacts.

So, all these are possible here as of now I am trying to tell you to appreciate how these molecules are present so as to maximize these contacts here. So, you can see that you can maximize this context and therefore, enhance close packing. The same thing now operates here. This layer again here is a representation of the first layer.

Again, you can see you can have nice co-facial interactions means interaction between the methyl groups in a certain way such that you can maximize the density and minimize the volume.

So, with this we come to close of this particular lecture and in the next lecture we will take up some more examples where we will illustrate a subtle interplay of close packing and hydrogen bonding interactions.

Thank you.