Fundamentals and Applications of Supramolecular Chemistry
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Lecture 08

W2L8_Halogen---pai, anion...pai and cation...pai interactions

So, hello everybody. So, in the last lecture, we were discussing about the presence of sigma hole, the origin of sigma hole. And just to recapitulate, we realized that the origin of the sigma hole is on account of the presence of an electron deficient region along the Cl-Cl bond axis that gives rise to electrostatically positive region. And the lone pair density is perpendicular to this Cl-Cl bond axis which is electrostatically richer.

We also looked at the presence of pi hole which essentially originates from the presence of electron withdrawing groups. For example, fluorine which actually withdraw the electron density from the central pi ring and generates a pi hole which is electrostatically positive.

We can look at this particular system, the di-iodo-tetrafluorobenzene which has got a sigma hole which is represented by the blue region along the C-I bond and then the lone pair density is represented by the yellow region which is perpendicular to the bond axis.

So, this particular molecule has both sigma holes as well as pi holes and the outer portion of the molecule has both regions of electron deficiency or electrostatically deficient regions, for example, the sigma hole as well as the electrostatically negative regions, for example, the fluorine atoms which have the lone pair of electrons. And you can look at this from the side view also, if you were to look at the side view along the C-I bond, the sigma hole is clearly shown to you.

So, with this background, we will now try to rationalize and understand another important class of interactions, which are called anion-pi interactions. Anion-pi interactions, to start with, we will consider, either we will consider a neutral species, for example, halogen and we will then consider an anionic species, for example, chloride, bromide, iodide, fluoride, nitrate, sulfate, silicate, SCN minus and so on and so forth.

So, now, when you have a halogen atom, which is covalently bonded Y-X, the sigma hole, which is electrostatically positive, will interact with the electron rich region on the anion. So, this is the anion, the electron density is spherically symmetrical, electrostatic potential is negative. And so, there is a electrostatic interaction between the sigma hole and the anion lone pair of electrons.

Now, instead of the anion, you can also have the pi electron density, for example, a benzene nucleus, such that the halogen atom, the sigma hole comes in close proximity to the center of the benzene nucleus, which we referred as the centroid and there is an interaction with the electron density of the pi system, between the sigma hole and the pi system.

And the separation between the halogen atom X, and the centroid is represented by small d and the directionality of this halogen bond involving halogen centered X is represented as theta, and phi is the angle between the between the line drawn from the halogen to the centroid to the line drawn from the centroid to the edge of the ring.

So, you have a line which is drawn from the edge to the centroid and a line drawn from the halogen to the centroid. This particular angle is referred to as phi. So, these two are the basic angular descriptors and D is a distance descriptor and these all constitute the geometrical descriptors of the halogen-centered interaction.

We call it halogen-centered because it is with respect to the halogen X. Now, it is not necessary that the halogen atom has to come above the plane of the benzene nucleus that is it is towards the centroid. It can also be in contact with the edge of the benzene nucleus, that is, it is interacting with the bond. We call it the sigma hole, is interacting with the bond.

Again, we will have similar geometrical descriptors, theta, d and phi and we can also have an interaction with an edge that is a particular carbon atom that is it can interact with a single carbon atom as represented by X...C.

So, this is specific to a particular carbon atom, this is specific to a bond, and this is specific to the entire benzene nucleus. So, all these orientations are allowed when you have the sigma whole interacting, with pi rich surface, with pi electrons.

And again, the equilibrium inter nucleus separation is close to the sum of the Van der Waals radii. And if you will now look at the approach, these three are the idealized orientations. But in reality, for example, in solids, you can also have other approaches which are involved.

You can have an angular orientation of the C-X dipole with the centroid of the benzene nucleus. So, in that case, this particular value of phi will be much less than 90 degree and the direction it is defined by theta.

So, you can also have other possibilities where your phi can change from 60 to 90 degree. Obviously, if C-X interacts with the edge or it interacts with a particular carbon atom, then these two are in the plane and phi is equal to 0 degree and this is not allowed to start with, this is not allowed. Why? Because the sigma framework of the benzene nucleus is positive and sigma hole is also positive and that is electrostatically unfavorable situation.

So, the sigma hole can interact with the relatively electron rich regions. Now, this is counter intuitive because normally we have studied that when you have a C-X bond, carbon is delta plus, X is delta minus, on account of the high electronegativity, but in a non-covalent system, the electron requirement is just opposite, because we have a halogen bond donor interacting with a halogen bond acceptor which is the carbon atom.

Now, so in this case, you can see here that the blue color symbolizes the electrostatically positive region, whereas the red region symbolizes the electrostatically negative regions. Now we will go to another class, where we are specifically looking at the anions, instead of the neutral halogen we are now looking at the anions. So, we have the anion which is having the lone pair of electrons and it is interacting with a benzene nucleus which is actually electron deficient.

And therefore, it is electrostatically positive as indicated by the blue region that the pi system is electron deficient. And this is also understood because if you have an electron rich system and it comes close to the benzene ring and benzene has a lot of electron density then there is going to be repulsion.

To minimize this repulsion, the electron density on the benzene ring has to be decreased by the presence of electron withdrawing groups. So, when you put this electron withdrawing groups, there is a decrease in electron density and then an anion can favorably interact with the benzene nucleus such that you maximize the electrostatic interactions. We will look at the nature of this interactions more after some time, but now let us look at the essential geometries.

Again, you will see that similar to your sigma hole...pi interaction as discussed previously, you will now see that the anion can sit above the centroid of the benzene nucleus, where d is a separation between the anion and the centroid and theta is the angle here, which is between the centroid to the edge of the benzene ring. So, we do not here have the directionality because the anion is symmetrical.

So, we have d and theta. Now you can have an anion which is interacting with the edge, and it can also interact with a specific carbon atom. And this is a case where we have already discussed where we talk about electron deficient or electrostatically positive benzene nucleus interacting with electrostatically negative or electron rich system.

For example, in case of C_6H_6, C_6F_6, we have seen that there is a favorable pi-pi stacking between the C_6H_6 and C_6F_6 system to give you a multi component system which we called co-crystals. So, here we can see, now very clearly that the pi region which is also referred to as now pi-h refers to as the electrostatically deficient pi region which we call as the pi hole.

So, the pi hole will now interact favorably with an anion or the lone pairs present. It can also interact for example, with a pi hole can also interact with fluorine, not the sigma hole. This is the electron density, the sigma hole is here, it can interact with electron density of the halogen atom to form, pi-h...lone pair interactions.

So, the lone pair can come also from the halogen that means the electrostatically negative belt of the halogen can interact with the pi hole of the benzene nucleus to have this favorable anion...pi interaction.

And instead of halogens, you can also now consider different kind of anions, for example, nitrate, sulfate, silicate, SCN minus or any anion in principle, which is having electron density will try to optimize this interaction with the pai hole region.

And in this regard electrostatics plays an important role, but it has now been realized as discussed in case of stacking interactions that dispersive forces also play a very important role. That means there is the role of polarization also and the dispersion interactions, because the momentary imbalances in the electron density distribution also are responsible for providing additional stability to this molecular assembly consisting of anion and a benzene nucleus.

So, along with electrostatics, dispersion also plays a very important role in molecular recognition involving anion-pai interactions. So now we can see this thing as well which is the role of directionality.

So, role of directionality is very important where the sigma hole on the halogen tries to interact with a lone pair of electrons so as to maximize the electron-nucleus attraction and minimize the electron-electron repulsion and therefore the directionality ideally should be around 180 degree here.

Whereas if you want to have interaction with the lone pairs then the lone pairs can interact only as I just now mentioned with the electron deficient pi region and the sigma hole will interact with the electron rich pi region. So, this particular geometry if the lone pair is to interact with the deficient region the directionality is then 90 degree, whereas in this case it is 180 degree.

And in a real system, for example, if you were to experimentally look at the crystal structures of halogen involved in interactions with pi regions, you will see that the C-X approaches, the C-X approaches, at around 140 degree approximately. So, an analysis of a large number of crystal structures containing the C-X bond and a phenyl group shows that the approach is around 140 degree and this is effectively the average of 180 plus 90 degree by 2 which is around 135 degree.

So, neither there is a maximization of the interactions involving the sigma hole, nor the lone pairs, but the actual situation is somewhere intermediate, which is more realistic because there is a balance of both the sigma hole interaction as well as the lone pair interaction with different regions of the benzene nucleus.

So, there is another example I would like to show here. For example, you can consider water molecules interacting with benzene and again the same water molecule interacting with C6F6. And you will see interestingly that there is a change in the orientation of the water molecule with the benzene nucleus, because the benzene nucleus is electron rich, and the hydrogens are acidic, there is favorable interaction between the acidic hydrogens with the benzene nucleus.

The oxygen stays further away because there are lone pairs present on oxygen and that provides a stability of around 1.2 kilocal per mole. Whereas, when you have an electron deficient system, for example, C6F6, then we know that there is withdrawal of electron density, then there is a pi hole here.

The pi hole is electrostatically deficient region and then it is now the lone pairs of oxygen which would like to interact with the pi hole and the hydrogens move away because hydrogens are positive and there is going to be unfavorable repulsion between the pi hole and the hydrogens which are positively charged.

So, the hydrogens move away there is a change in the orientation of the water molecule and the lone pairs now interact with the pi hole region and this essentially provides higher stability to the assembly of water with C6F6 in comparison to that of benzene.

So, these kinds of examples, very nicely talk about the nature of anion-pi interactions being very important. So, overall, we can now talk about the applications of sigma hole and pi hole interactions.

And there are many applications, I just wanted to give you a flavor that whatever we are studying in this course, supramolecular chemistry has got very important applications in diverse fields of chemistry.

For example, synthetic chemistry, the role of sigma and pi hole interactions is very relevant, crystal engineering, polymers, anion recognition, catalysis, optoelectronic devices, medicinal chemistry, protein-ligand interactions, all these fields have got relevance of sigma and pi hole driven interactions.

So, I would like to now take up some more complex examples where we can actually play with this anion...pi interactions further. So, we have learnt anion-pi interactions, and

I would like to give you a very important example here further that because electrostatic repulsion has a very significant role here and we need to modify the electron density distribution around the pi region we can do it in different ways.

So, you can have chloride, we can put nitro groups. Nitro groups are electron withdrawing, they withdraw electron density. So, that creates a pi hole and now the chloride can interact with this trinitrobenzene and it has been observed that chlorine has come quite close to the benzene nucleus such that the separation between the chloride and the carbon.

So, in principle you can position here a carbon nucleus or you can put an atom here at the centroid geometrically and look at the carbon...chlorine distance and this is found to be less than the sum of the van der Waals radii of chlorine and carbon or you can also consider the van der Waals radius of chloride. So, that is found to be lower.

That tells you that there is an electrostatic attraction, and there is also the role of dispersion because benzene has got a circulating pi electron density obviously, in this case it is reduced.

So, there is a role of dispersion as well as electrostatics which govern anion...pi recognition. You can also consider cyanobenzene, tri-cyanobenzene and you can have X-position.

You can also have trifluoromethyl groups which are highly electron withdrawing and can interact with X-. You can also have triazines and there is a pi hole here, and that can also interact with the halogens, the halides and any anionic species can interact favorably with these triazines. So, we can also take anions, for example, larger anions SbF_6^-, for example, to interact, and we can actually polarize the pi cloud further.

So, let me give you an example of that. And now you will see that fluoride SbF_6^-, the lone pairs can interact. So, you have the SbF_6 anion sitting on top of this triazine system and this triazine is further polarized by the formation of the N-F bond because now the presence of a positive charge even increases electrostatically the magnitude of the pi hole.

So, the magnitude of the pi hole is increased and fluorine is having the relevant lone pair of electrons and that can interact with this pi deficient species. So, you can have this lone pair interactions with the pi holes. So, this brings us to the end of the discussion on anion...pi.

Now, we would like to focus on the next set of interactions, which are cation...pi in nature. So, in case of cation...pi interactions, a very classical example is benzene complex with C_6H_6, benzene forms this interesting complex, where you have a benzene nucleus.

And you bring a silver ion in its vicinity and the silver ion tends to now polarize the electron density distribution of the benzene nucleus and there is a covalent association where benzene forms complexes with benzene to form this particular species.

So, this is a first classical example of a cation-pi interaction, where you have interaction between the silver ion and the benzene nucleus.

Naturally people were also interested to look at interactions of potassium ion, sodium ion with water molecules which we have studied as cation-dipole interactions.

Here it is an example of a cation-quadruple interaction, but that is purely from the electrostatic perspective, and we also now appreciate the role of polarization and the fact that there is an induced dipole moment in the benzene nucleus.

Now, when the silver ion comes in its proximity and hence these very weak dispersive interactions, because of the induced dipoles are responsible for this association. Then we can also now consider the role of other cations as well. So, you can also take lithium, rubidium, cesium, you can take barium, calcium, magnesium and so on and so forth.

So, the large number of cations which are present in nature and there is always favorable binding with a pi system or even with an anion for example lithium interacts with chloride anion to form an interaction and it forms a stable lattice. But what is also more important is to appreciate the role of organic cations.

So, we can now also have organic cations as well. So, now we can consider ammonium, for example, as an organic cation, we can consider tertiary butyl tetra-ammonium cation, these kinds of cations can also be considered to play an important event in molecular recognition.

For example, we can now look at different kind of species we can have interaction between ammonium ion with the benzene nucleus, and ammonium ion as you see has got a tetrahedral geometry.

The hydrogens are acidic, the N-H bonds are polar, and they can participate in the formation of NH...C interactions, where the carbon is coming from the benzene nucleus. So, the hydrogen here can interact with a carbon atom, it can interact with the edge, and it can interact with the centroid of the benzene nucleus. So, all these three possibilities exist.

So, we have got essentially cation...induced dipole interactions, but essentially, they are hydrogen bonds involving an activated donor. Now, this is called an activated donor because you have NH plus and this interacting with a relatively electron rich carbon, which is the benzene nucleus, and primarily governing the role of cation...pi interactions.

And these cation...pi interactions are very much present in other species. For example, we can consider instead of ammonium, we can consider other species also. For example, we can consider the adamantyl group as well, +NMe3. We can consider this kind of a bulky cation as well. We can consider +NMe3, this kind of an alkyl, we can consider an ester which is having a side chain, consisting of trimethyl ammonium species.

So, we can have all these types of cations which can interact with benzene nucleus. So, with this we are able to appreciate that cations also play a very, very important role in molecular recognition. And now in the next class, we will be taking up more examples of cation-pi interaction and their possible roles in mediating supramolecular recognition in molecules.

Thank you.