Fundamentals and Applications of Supramolecular Chemistry
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Week 02
Lecture 06

W2L6_Aromatic Interactions

So, hello everybody. So, now this is the second week of the course and today we are going to start discussing about the next module, where we are going to talk about a different class of non-covalent interactions. For example, we are first going to discuss on aromatic interactions, stacking interactions. Then we are going to go to sigma hole driven interactions, pi hole driven interactions which are primarily present in halogens, chalcogens and carbon containing compounds.

And towards the end of the second module, we will be discussing, about the principles of close packing that govern recognition events in solid state as well as between molecules in liquid and as well as the gas phase. So, to start with today we will focus on aromatic interactions which we also call as pi...pi stacking interactions. Now we have realized that interaction between atoms is important.

Any pair of atoms interact with each other. For example, our focus has been on ion-ion interactions, ion-dipole interactions, dipole-dipole interactions. But it is also important to realize that we can have interactions in principle between any two atoms, say for example, X...X, where X is equal to, say carbon, oxygen, nitrogen, fluorine, bromine, iodine, sulphur, selenium.

In principle, we can take any two atoms in the periodic table, and they can always interact with each other, such that the separation between the two atoms is in the vicinity of the sum of the van der Waals radii of the two interacting atoms. This is the underlying principle of recognition, and this is something we have already discussed. We can also have interactions between two different atoms.

For example, carbon...oxygen, oxygen...nitrogen, nitrogen...sulfur, chlorine...nitrogen so on and so forth. So, this is a very general concept that in general we can have interactions between a pair of atoms, and this is true for any state of matter, whether it is gas, a cluster of molecules in the gaseous phase, a collection of molecules in the liquid state or a large number of molecules which form the crystalline state or the solid state.

Now to understand and appreciate pi...pi stacking we would like to look at the different models proposed to rationalize pi...pi non-covalent interactions.

So, the model 1 considers displaced pi...pi stacking. We also call this the face-to-face interaction. And this is very important because this is what is responsible for the slippery nature of graphite and also the lubricating properties of graphite.

So, in graphite we know that we have got the fused aromatic hydrocarbons and the separation between this between the parallel layers because every layer is actually having a having the fused benzene rings that is the graphitic sheet and once the graphitic sheet is held with the neighboring graphitic sheet by these pi-pi stacking interactions where the separation between the sheets is approximately 3.5 angstrom. And the origin of this value is it is approximately equal to twice the van der Waals radii of carbon.

So, the van der Waals radii of carbon is 1.75 angstrom into 2 assuming carbon-carbon contact. this comes out to be around 3.5 angstrom. You can also have cases where the separation can increase to 4 angstrom and you can also have cases where the separation can decrease to 3.1 angstrom depending upon the kind of substituents which are present on the aromatic cream.

Depending on the kind of substituents which are present on the benzene nucleus, the separation can change from 3 angstrom to 4 angstrom and even beyond that. The next model is referred to as the edge-to-face model where we have got the hydrogen atom with the benzene ring in this particular arrangement or this particular orientation.

So, unlike the pi...pi stacking or the face-to-face interaction, where the center of one benzene nucleus interacts with the corner atom. In this case, it is the hydrogen atom which interacts with the center of the benzene nucleus.

This is also reminiscent of C-H...pi interaction, where the edge atom that is the hydrogen being slightly more electropositive interacts with the relatively more electron rich ring and this is the basis of the edge-to-face model. Scientists have tried to rationalize the origin of the pi...pi stacking model in terms of the role of electrostatics.

So, what is the role of electrostatics in these stacking models. So, as you can see here that when you have got pi...pi stacking each benzene nucleus is associated with a pi electron cloud and when the two benzene nucleus come close to each other at a distance which is going to be shorter than the sum of the van der Waals radii then there is going to be electrostatic repulsion between the electron clouds and the benzene rings are going to move away from each other.

So, when they come close there is a certain amount of attraction between the nuclei of the carbon atoms and the pi electron density, but when they are pushed close there is electrostatic repulsion and therefore, the equilibrium separation is approximately equal to 3.5 angstrom.

In order to minimize this electrostatic repulsion, the pi rings are now displaced as you can see in the displaced pi...pi stacking where you actually minimize the electrostatic repulsion between the pi clouds and that is the reason why the displaced pi...pi stacking is a very favorable arrangement.

And in this regard, Hunter and Sanders have proposed a model on the basis of electrostatics to account for the observed geometries for pi...pi interactions for pi...pi non-covalent interactions.

And to start with the benzene nucleus the benzene framework is considered as having the sigma framework, which is positively charged, and the electron density which corresponds to the pi electron cloud, above and below the plane of the benzene nucleus constitutes the pi framework.

This constitutes the pi framework. And on account of this distribution, benzene is associated with a quadrupole moment. And let us see the arrangements of the quadruples.

So, quadrupole moment essentially corresponds to the present of four discrete charges, such that the ends of the sigma framework are positively charged and the electron density or the pi cloud above and below corresponds to the minus charges. So, this arrangement essentially constitutes a quadrupole, this constitutes a quadrupole.

The net dipole moment is equal to 0, because essentially it constitutes two dipoles which are opposing each other. But this arrangement results in a quadrupole distribution of charges, and it is actually the interaction between these quadrupoles that gives rise to the expected geometries for pi...pi non-covalent interactions.

So, let us now try to see how these quadrupoles interact. So, the first case, we have got the sigma framework, then we have got the minus pi cloud and now we would like to have the other benzene ring here and this is plus, this is minus and this is minus. So, we would expect favorable interactions between the minus and the plus region here and we will also expect favorable interactions between this plus and this minus region.

So, there are going to be attractive interactions between the pi region and the sigma framework and the pi framework of this with the sigma framework of the adjacent aryl ring and that is what drives this particular association in the case of model 1. In the case of model 2, this is the hydrogen, and we have minus cloud here.The sigma framework is now going to interact with the pi framework via the C-H...pi interaction.

So, you see that the favorable alignment of the quadrupole moments of benzene are able to explain the two different models, one based on the face-to-face stacking and the other on the basis of the edge-to-face stacking for C...C interactions. And these two models, the magnitude of the stabilization of such weak pi...pi contacts which approximately is in the range, of, as low as close to 1 kilo joule per mole to around 20 kilo joule per mole.

This is the range of pi...pi stacking that we have. This magnitude depends upon the relative orientation as determined by the combination of nucleus-electron attractions and minimization of the electron-electron repulsions. So, this is the same hypothesis that any system when it interacts it tries to maximize the nucleus-electron attraction and minimizes the electron-electron repulsion which gives rise to these favorable geometries.

If you were to look at why face-to-face stacking is rare, then definitely there is going to be severe repulsion. There is going to be severe repulsion between the electronic clouds and to minimize this repulsion, the distance is going to increase and become more than 4 angstrom.

Or to start with, this will definitely be greater than 3.5 angstrom, which is the sum of the van der Waals radius.

So, pi...pi stacking which is exactly co-facial stacking where the two pi...pi rings come exactly one on top of each other is also present. But in that case because of the repulsion between the electron clouds you would like to minimize this repulsion and in that case the pi rings move away from each other such the equilibrium separation, increases and this distance can be greater than 3.6 and it can lie between 3.6 to say 4.2 to 4.3 angstrom, such that you have minimized the repulsions which are present.

Now these were the initial structural models. However later on it was observed and it was due to the presence of advanced computational calculations, it was proposed that it is not only electrostatics which govern pi...pi stacking.

But Craig Wilcox at University of Pittsburgh, USA suggested that London dispersion forces, which we have already studied, that are dispersive interactions might play a prominent role in comparison to electrostatic interactions. This is a very important hypothesis which was suggested by Craig Wilcox that London dispersion process are going to play a more important role keeping in mind that these are non-polar molecules that they do not have any net dipole moment, they have a quadrupole moment.

But the fluctuating electron density which is present in benzene can lead to dispersive forces being present where you have a fluctuating dipole. It is an instantaneous dipole which can induce a dipole in the neighboring benzene molecule and then there occurs attraction. And we have also seen that these kind of pi-pi stacking interactions depends upon the area of contact between the two pi surfaces.

More is the area of contact between the pi surfaces, more is going to be the stacking interactions. And this can extend to other polycyclic aromatic hydrocarbons, other polycyclic aromatic hydrocarbons. For example, this can extend to anthracene, naphthalene and others as well, phenanthrene, and extended polycyclic aromatic hydrocarbons.

The fact that they are solids, it has been observed that pi...pi stacking or pi...pi non-covalent interactions drive the molecular assembly. So, the interesting thing is that when you have these kind of aromatic hydrocarbons or carbon, hydrogen containing compounds, it is essentially the CH...C or the C...C contacts which play a crucial role in molecular recognition.

And depending upon the extent of association between the molecules, this can lead to the existence of these in different states of matter. For example, gas, liquid or in solids. So, anthracene and naphthalene we know are solids, but we know that benzene is a liquid and acetylene is a gas.

So, you can also consider for example, acetylene where the hydrogen atom of acetylene interacts with the pi electron density of another acetylene molecule and we all know from traditional knowledge of chemistry that these hydrogens are very acidic.

Why? This is because the C-H bond has got a high dipole moment. Why? Because carbon is sp hybridized. So, because of the sp hybridization of carbon atom this is delta minus this is delta plus and this is delta minus.

So, there is a favorable electrostatic contribution in this CH…pi contacts, but we also need to keep in mind that there is going to be contribution of dispersive interactions as well dispersive forces towards the stabilization of acetylene molecules.

In fact, people have been able to crystallize acetylene molecules as well and form solids wherein such CH...pi contacts have been observed. Now, we can also consider, as for example, ethane, ethane, propane, butane. And methane we know is a spherical molecule and methane is a gas.

So, definitely when one methane molecule interacts with another methane molecule the origin of the interactions is purely dispersive, such that at any moment, because of the fluctuating electron density distribution you will have an instantaneous dipole which will then induce a dipole in the neighboring methane molecule and they will be expected to interact with each other.

As you increase the molecular weight of the hydrocarbon, we have studied that the energetic stabilization is proportional to the polarizability of the molecule. That means more is the number of electrons, so, the molecular weight is more and more is going to be the polarization of the electron density.

And this can lead to greater aggregation between the molecules resulting in the formation of liquids as is observed in case of higher weight hydrocarbons and also in case of solids. For example, as we have observed in case of wax and other long chain fatty acids where the number of such C...C contacts increases dramatically resulting in the formation of either the liquid state or the solid state.

So, as we go on increasing the number of carbons then there will be a critical number when the hydrocarbons will become liquids and finally, they will also become solids. We also know, for example wax, and by and large these are solids or liquids because the extent of dispersive interactions increases.

More is the contact area between the molecules, more is the extent of aggregation, the dispersive interactions extend further and give rise to the liquid state and further aggregation can give rise to the solid state depending upon the number of carbons and hydrogens.

So, although dispersive interactions primarily are very weak, but when the number of these increases that can result in substantial change in the state of aggregation of the substance. These substances lack any strong hydrogen bond donor or acceptor like oxygen, nitrogen, sulfur or halogen and are primarily carbon and hydrogen containing compounds.

And, we know that large part of the organic chemistry contains carbon and hydrogen. So, the presence of these interactions is extremely important and crucial to understanding how they interact with each other to form different arrangements of molecules, particularly in case of solids.

And, we can also look at for example, we can also look at the interaction between ethylene molecules as well and in this case, you can expect a 2 plus 2 cycloaddition reaction if you shine light to give you cyclobutane.

Now the fact that the final product is cyclobutane involves involves rearrangement of the electron density distribution right such that the two pi bonds now become two sigma bonds and the molecules actually need to come close to each other to perform the chemical reaction and this approach of the molecules towards each other is actually guided by the dispersal interactions. So, when you have this ethene molecules you can get the corresponding cyclobutane product.

So, this overall we see that this pi...pi stacking interactions are really interesting. Now, the next question is how we enhance the pi...pi interaction strength, how do we increase the pi...pi interaction strength.

So, one way to do it is to modify the electron density distribution on the benzene nucleus by introducing electron donating groups or electron withdrawing groups. For example, to start with, we can add electron withdrawing groups for example, fluorine and convert benzene to hexafluorobenzene.

Now, this is a highly electron deficient species because fluorine is a highly electronegative atom. It withdraws electron density and therefore, the benzene ring is now deficient, electron deficient system.

And now, it can favorably interact with a relatively electron rich system forming pi...pi stacks. And interestingly in this case the complete co-facial pi-to-pi stack geometry is favorable because it is a maximization of the electron rich region that is the pi electron cloud of one benzene nucleus with the most electron deficient region on the hexafluorobenzene.

They were maximizing the amount of charge transfer. So, this process, this interaction which is driven primarily by electrostatics here because you have modified the electron density distribution such that this is a relatively electron rich system.

This is a relatively electron deficient system you have now modified the electronic environment such that the two benzene rings now come much closer to each other and the equilibrium separation is also in this case less than the sum of the van der Waals radii such that you maximize the attraction between the electron rich region and the relatively electron deficient covalent backbone. So, the nucleus here is more electron deficient compared to the benzene. So, it strongly attracts the pi electron cloud of the benzene ring.

And these kinds of systems lead to the formation of co-crystals. The resulting compound, 1 is to 1 combination of benzene and hexafluorobenzene gives rise to a new chemical entity which we called co-crystals and this is a new phase altogether.

This is a new solid-state phase where the properties of the 1 is to 1 adduct of benzene with hexafluorobenzene are very different from the properties of benzene and hexafluorobenzene separately.

We can now modify this further. For example, by adding electron donating substituents on the benzene nucleus. For example, we can now introduce a methyl group or we can take hexamethyl benzene and try to see whether we can form a much stronger adduct between hexamethyl benzene and hexafluorobenzene.

Now when this process of formation of co-crystal takes place, we see that there is a charge transfer CT, there is a charge transfer from the electron rich species to the electron deficient species. Because the amount of charge transfer is a fraction and this obviously is greater than 0 but less than 1.

So, the donor molecule loses some amount of charge, and the acceptor molecule now receives some amount of charge. So, these are also referred to as donor-acceptor complexes and these are purely of organic origin is a purely of organic origin.

So, organic donor acceptor complexes and now we can actually make a large number of these complexes by modifying the electron density distribution on the benzene nucleus as well as the hexafluorobenzene.

We can put chloro, we can put bromo, we can put cyano, and we can put nitro. So, nitro is strongly electron withdrawing, cyano is strongly electron withdrawing and we can have large number of combinations of this electron rich donors and electron deficient acceptors, which can give rise to this very interesting class of compounds which we call co-crystals which are new chemical entities, which are new solid state phases, where in the properties of the 1 is to 1 adduct is different from the individual molecules.

And this is one arrangement where they actually stack, such that we have the donor, acceptor, donor, acceptor, donor, acceptor and then in the next layer we have the acceptor, donor, acceptor, donor, acceptor, donor. So, this is arrangement 1 and then we can have arrangement 2, where we have donor molecules and interacting with the acceptor molecules.

So, we have the donor stacks, we have the acceptor stacks, then we again have the donor stacks, then we again have the acceptor stacks. So, we can have two definite arrangements where we have alternative donor-acceptor.

Or they can interact again, across, or we can have donor stacks interacting as a whole with the acceptor stacks. So, this we call as mixed stacking and this we call as segregated stacking. So, with this we come to an end of the discussion on van der Waals interactions and I hope you have been able to appreciate the concepts and now in the next lecture we will go to the other class of non-covalent interactions.

Thank you.