Breakthrough in development of new drugs

May 25 2010

A breakthrough made at STFC's ISIS neutron source could lead to faster and more cost-effective methods of developing new drugs.

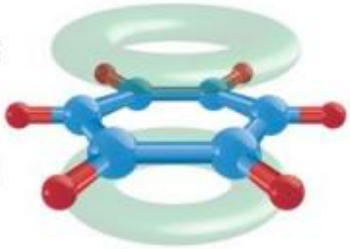
Scientists, led by University College London, have demonstrated how aromatic molecules arrange themselves in liquids, which turns out to be more complex than assumed when simulating these effects. Interactions between aromatic molecules - the most famous of which is benzene - are a factor in the way many important biological molecules including DNA and proteins are made up.

In the early stages of drug design, simulations are frequently used to determine the likely interaction of the drug with the target molecule. Current calculations are based on the interaction of just two aromatic molecules but new data from neutron experiments gives a more accurate picture of the way in which many molecules are orientated in the liquid and shows that this is an important factor in predicting their chemical reactions.

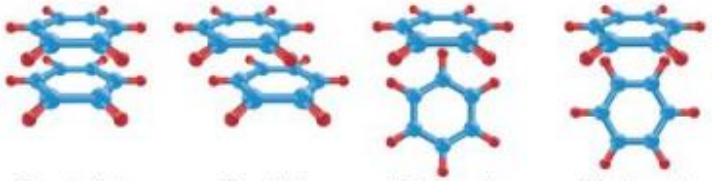
Figure 1

a) Benzene structure

Benzene molecules have a simple ring structure, with a ring of delocalised electrons either side of the molecule. These electron rings affect how benzene molecules are arranged in relation to each other. *(hydrogen – red; carbon – blue; electron cloud – green).*



b) Scientists typically visualise benzene interactions via four 'motifs'



Sandwich geometry (S)

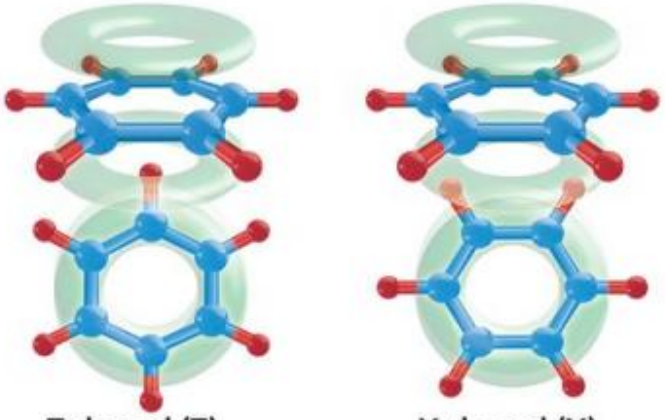
Parallel displaced geometry (PD)

T-shaped geometry (T)

Y-shaped geometry (Y)

c) Difference between T and Y

A slight shift in molecule orientation effects how the benzene molecules interact chemically with other molecules such as proteins. This is because topography is critical.



T-shaped (T)
has a single hydrogen atom pointing into the centre of the pair benzene molecule.

Y-shaped (Y)
is slightly rotated so that two hydrogen atoms are pointing to the other molecule's delocalised electron ring. This makes sense chemically as hydrogen atoms have a slight positive charge.

This discovery will have an impact ranging from basic chemistry through to our understanding of the self-assembly of biological molecules. It will in turn make drug discovery more efficient and accurate, reducing the time and cost of developing new drugs.

Provided by University College London