

**MS.90.3***Acta Cryst.* (2011) **A67**, C196**Putting the Squeeze on Hydrogen Bonds**

Craig L Bull, John S Loveday, Richard J Nelmes, Malcolm Guthrie, Kazuki Komatsu, *SUPA, School of Physics and Astronomy, Centre for Science at Extreme Conditions, University of Edinburgh, Mayfield Road, Edinburgh, EH9 3JZ, UK*. E-mail: cbull@ph.ed.ac.uk

The application of pressure provides a unique method of perturbing the hydrogen bond. The application of high pressure allows the hydrogen bond length to be altered cleanly and continuously within the same phase, and changing pressure can produce much larger changes in geometry than can changing temperature.

We present recent developments in high pressure technology and neutron instrumentation which now make it possible to measure the changes of the proton behaviour of the hydrogen bond at hydrostatic pressures up to and beyond 10 GPa. By making use of examples of materials containing hydrogen bonds for example water, squaric acid, KDP and gas hydrates, we will demonstrate the application of these techniques and how they provide insight into the nature of the hydrogen bond at high pressure.

**Keywords:** hydrogen-bond, high-pressure, neutron diffraction

**MS.90.4***Acta Cryst.* (2011) **A67**, C196**Stereochemistry & charge density of hydrogen bonds with oxygen acceptor**

Christian Jelsch, Maqsood Ahmed, Benoît Guillot, Slawomir Domagala, Claude Lecomte, *Cristallographie, Resonance Magnétique & Modelisation (CRM2), CNRS, Nancy Université, Vandoeuvre-Les-Nancy, (France)*. E-mail: cjelsch@crm2.uhp-nancy.fr

Hydrogen bonds play a crucial role in the structure and function of many bioactive molecules. They combine the strength of an electrostatic interaction with the directionality of a dipole interaction to produce specific bimolecular interactions [1]. An understanding of the relative strengths and geometries of the hydrogen bonds is required for the design of new supramolecular materials including the engineering of crystal structures or selection of the functional group replacements in protein ligands to enhance binding affinity [2]. In drug design, the coordinates of the hydrogen bonding atoms in the ligand binding site dictate the position at which it would be advantageous to place the atoms of a novel drug molecule. The directionality of hydrogen bond with respect to the lone pairs of the acceptor atom has been a matter of discussion [3], [4], [5]. The charge density proves to be very useful in the study of hydrogen bonds.

Here we present the result of an extensive survey of the Cambridge Structural Database [6] to analyze the preferential stereochemistry and 3D geometries of the hydrogen bonds in the most common hydrogen bonding groups involving oxygen as acceptor.

The hydrogen bond preferential stereochemistry is correlated to our database [7] describing the electron density of common chemical groups. Fine differences are, for instance, found between hydroxyl groups bound to sp<sup>3</sup> and sp<sup>2</sup> carbon atoms. The geometry of hydrogen bond show also different trends depending on the acceptor-hydrogen atoms distance.

This study can provide new insight into the stereochemistry of hydrogen bonding which can have strong implications in the designing of novel drug molecules, supramolecular crystal engineering and molecular mechanics.

[1] J.E.J. Mills, P.M. Dean, *J. Computer Aided Mol. Design* **1996**, *10*, 607-622.

[2] Nobeli *et al.*, *J. Comput. Chem.* **1997**, *18*, 2060-2074. [3] Taylor *et al.*, *J. Am. Chem. Soc.* **1983**, *10*, 55761-5766 [4] Taylor *et al.*, *Acc. Chem. Res.* **1984**, *17*, 320-326 [5] Lommerse *et al.*, *J. Comput. Chem.* **1997**, *18*, 757-774. [6] Allen *et al.*, *J. Chem. Inf. Comp. Sci.* **1991**, *31*, 187-204. [7] Zarychta *et al.*, *Acta Cryst.* **2007**, *A63*, 108-125.

**Keywords:** electron density, interactions

**MS.90.5***Acta Cryst.* (2011) **A67**, C196**Water structure is important – OH... $\pi$  hydrogen bonds in p-sulfonatocalix[4]arene**

Katharina Fucke, Judith A. K. Howard, Jonathan W. Steed, *Department of Chemistry, Durham University, Durham, (UK)*. E-mail: katharina.fucke@durham.ac.uk

Hydrogen bonding in the solid state is a well recognised and widely studied phenomenon. The simplest model systems to probe hydrogen bonding are hydrated crystal forms, since water can act both as a hydrogen bond donor and acceptor while being a rigid and very small molecule. On the other hand, the incorporation of water into the crystal lattice can cause serious problems in, for example, pharmaceutical compounds due to considerably lower solubility and thus lower bioavailability, making crystalline hydrate research more than an academic interest. Investigating the interactions of water in crystal structures gives vital information about conventional hydrogen bonds as well as the relevance of short and long range interactions which stabilise crystalline hydrates. The compound p-sulfonatocalix[4]arene is reported to crystallise in a triclinic pentasodium salt [1] and an orthorhombic tetrasodium salt [2] both highly hydrated with 14 and 12 water molecules, respectively. The tetrasodium salt hydrate is reported to contain one water molecule in the host's cavity, making this substance the perfect model to study water in hydrophobic environments. During our investigations, we found two novel monoclinic polymorphs of the tetrasodium salt hydrate, also showing the embedded water molecule. Using X-ray and neutron single crystal diffraction, accurate hydrogen positions for two of the tetrasodium salt hydrates and of the pentasodium salt hydrate could be determined, rendering the close investigation of the water clusters possible. The embedded water was found having both hydrogen atoms positioned towards the  $\pi$  electrons of the cavity proving the existence of OH... $\pi$  interactions. In addition, the molecules are 'compressed' with short OH bonds, a direct consequence of the hydrogen bonded water network in the crystal structure. The pentasodium salt hydrate exhibits an intra-cavity water engaging in both OH... $\pi$  and OH...O hydrogen bonding, with the OH covalent bond forming the interaction with the aromatic ring shortened. Using the *ab initio* lattice energy calculation algorithm PACHA [3] based on the neutron coordinates, gives an OH... $\pi$  interaction energy of 6.9–7.5 kJ mol<sup>-1</sup>, and reveals the dominance of the charge assisted interactions to the Na<sup>+</sup> coordinated water molecules. The p-sulfonatocalix[4]arene crystal forms thus represent a model system to investigate water interactions involving comparison of hydrophilic and hydrophobic entities. Such interactions are especially important in protein/water systems but are not trivial to study, either due to the size of the protein or the difficulty in producing crystals suitable for neutron work, mesoscale systems such as p-sulfonatocalix[4]arene represent an accessible simplified model compounds.

[1] J.L. Atwood, A.W. Coleman, H. Zhang, S.G. Bott, *Journal of Inclusion Phenomena* **1989**, *7*, 203-211. [2] J.L. Atwood, F. Hamada, K.D. Robinson, G. W. Orr, R.L. Vincent, *Nature* **1991**, *349*, 683-684. [3] M. Henry, *ChemPhysChem* **2002**, *3*, 561-569.

**Keywords:** hydrogen bonding, hydrate, water structure