MS32-05 **250 Structures later – Friendly Relationships in a Compound Family.** L. Susanne Coles (née Huth), Terry L. Threlfall, Michael B. Hursthouse, *Chemistry, University of Southampton, Southampton, UK.*
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The assembly of functionalised organic molecules in the solid has attracted much recent interest, due to its relevance to both the production of pharmaceuticals and other industrially important compounds on one hand, and the search for novel materials with utilisable properties on the other. Hence small molecule X-ray crystallography has become an important technique for the detailed investigation of the solid state ultimately aiming to understand the (supra)molecular assemblies in crystal structures. With the advent of high-throughput-crystallography large amounts of data are now routinely generated providing the opportunity to analyse this data in a meaningful way. The systematic study of crystal packing patterns together with the application of theoretical calculations can improve the insight into the solid-state assembly, providing feedback for design and prediction procedures.

Here we present the results from our recent case study, which is concerned with the crystallisation and packing preferences of a large set of mono-substituted acylanilides – including the important pharmaceutical paracetamol. An extensive array of closely related molecules has been synthesised: In the course of one year, over 400 closely related acylanilides have been prepared yielding approximately 300 crystalline samples, and more than 250 data sets have been collected, corresponding to *ca.* 200 actual novel crystal structure determinations of acylanilides. Harvesting the Cambridge Structural Database (CSD) increased the number of crystal structures in the library to approximately 250.

Crystal structures of this extensive family of mono-substituted acylanilides have been systematically cross-examined and structural relationships have been identified with the program XPac[1]. Intermolecular interaction energies have been calculated using the OPiX suite of programs[2] allowing the ranking of the identified common features. Furthermore, tendencies and trends in the crystallisation process have been observed dependent on the molecular changes.

The results of this systematic study will be presented and discussed.

[1] T. Gelbrich, M. B. Hursthouse, *Cryst. Eng. Comm.*, 2005, **7**(53), 324-336.
[2] A. Gavezzotti, "*OPiX*, *A computer program package for the calculation of intermolecular interactions and crystal energies"*, University of Milano (2007).

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MS33-01 **Protein Neutron Crystallography with "tiny" crystals of fully deuterated proteins.** Alberto Podjarny[a], Matthew P. Blakeley[b], Michael Haertlein[b,c], Isabelle Petit-Haertlein[b,c], Isabelle Hazemann[a], Andre Mitschler[a], Alexandra Cousido-Siah[a], Stuart J. Fisher[b,d], Andrés G. Salvay[e,f], Christophe Muller-Dieckmann[g], Alexandre Popov[g], Pavel Afonine[h], Oscar Ventura[i], Raul Cachau[j], Steve Ginell[k], Andrzej Joachimiak[k], Flora Meilleur[b], Tatiana Petrova[l], Dean Myles[b] and Eduardo I. Howard[a,e]. [a]*IGBMC, CNRS, INSERM, UdS, France,* [b]*ILL, France,* [c]*PSB, France,* [d]*U. Salzburg, Austria,* [e]*IFLYSIB, Argentina,* [f]*U. Quilmes, Argentina,* [g]*ESRF, France,* [h]*LBNL, USA,* [i]*U.Republica, Uruguay,* [j]*NCI,USA,* [k]*SBC,ANL, USA,* [l] *IMPB, Russia.*
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Large crystal volume (> 1mm^3) has been a difficult requirement for Neutron Protein Crystallography. The use of full deuteration has allowed to diminish this requirement by one order of magnitude, as shown by the neutron diffraction studies of human Aldose Reductase (*h*-AR(D), 36 kDa) [1] and Antifreeze protein (AFP(D), 7 kDa)[2]. Neutron Laue diffraction data from *h*-AR(D) complexed with the inhibitor IDD594 and NADP$^+$ were collected to a resolution of 2.2 Å at room temperature at the ILL on LADI-I from a "radically small (V=0.15 mm^3)" crystal. To complement the neutron data in a joint X+N refinement, X-Ray room temperature data were collected to 1.8 Å at the SLS Synchrotron. The structure was also determined at 100K with X-Ray data collected up to 0.8Å resolution at the APS Synchrotron. The analysis of both the high resolution X-ray maps and the neutron maps suggested the mobility of catalytic protons in the system Asp43-Lys77-Tyr48. These complementary observations allowed the validation a MD-QM model of the proton donation mechanism, which showed that the residue donating the proton is Tyr 48, and that this donation is activated by the movement of neutral Lys 77. Antifreeze proteins (AFPs) bind to ice through an ice-binding surface (IBS), thus inhibiting ice growth *in-vivo* at sub-zero temperatures. We have determined the structure at 293K of a fully perdeuterated type-III AFP(D) by joint X-ray and neutron diffraction, providing a very detailed description of the structure of the protein and its surrounding solvent. X-ray data at 1.05 Å were collected at the ESRF Synchrotron and neutron Laue data at 1.85 Å were collected at ILL on LADI-III, from a "radically small (V=0.13 mm^3) " crystal. The identification of a tetrahedral water cluster both in neutron and X-Ray maps has allowed the reconstruction of the ice crystal primary prismatic face bound to the IBS. The analysis of the corresponding interactions reveals the role of the hydrophobic residues. They bind inside the holes of the ice surface, thus explaining the specificity of AFPs binding to ice versus water. Both examples show how neutron diffraction, combined with X-Ray high resolution diffraction, is able to reveal the structural details necessary for the understanding of complex biological mechanisms.

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