FA4-MS09-P06

One Instrument to Answer to All Your Challenges? Cu/Mo, Small Crystals and More… Claire Wilson[a], Masataka Maeyama[b], Kimiko Hasegawa[b], Kazuaki Aburaya[b]. [a]*Rigaku Europe, Sevenoaks, Kent UK.* [b]*Rigaku Corporation, Tokyo, Japan.*
E-mail: claire.wilson@rigaku.com

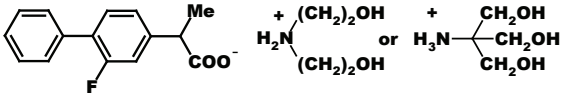
Today's most interesting samples rarely make our jobs easy for us. Unfortunately many of the systems that we want to study crystallise as very tiny crystals. This can be particularly true of pharmaceuticals but is a widespread difficulty in many areas of chemistry and materials where we repeatedly face these challenges. Constant pressure to deliver high quality results and extract as much information as possible are coupled with pressures to do so both cost and time efficiently.
The combination of the Rigaku MicroMax 007HF generator with the RAPID II unique curved, large area image plate detector already provides a hugely flexible tool to address many of these challenges. Advances in optics now mean that this powerful combination of generator and detector can be used with both Mo and Cu radiation (or Cu and Cr) on the same instrument, just by swapping the rapidly interchangeable targets. The image plate is highly sensitive for all these wavelengths providing for high quality data without compromise. The extremely large active area of the detector (-60 to 144°) allows a massive solid angle of data to be collected in a single exposure; ideal for fast high resolution Cu data for absolute configuration determination and equally for very high resolution data with Mo radiation. The exceptional low noise and wide dynamic range also suit the long exposure times often necessary for very tiny crystals – even with a brilliant source - without saturation or excessive noise problems. This single instrument is so versatile that it can replace several others – for single crystal diffraction studies (both small and macromolecular) at both wavelengths as well as powder diffraction. Results of studies using this new dual wavelength capability system will be presented.

Keywords: instrument development; chemical crystallography; absolute configuration

FA4-MS09-P07

Hydrogen Bonding in Flurbiprofen Salts. Carl H. Schwalbe[a], Miren Ramirez[a], Chris J. Bache[a], Simon J. Coles[b], Barbara R. Conway[a], Peter Timmins[c]. [a]*School of Life and Health Sciences, Aston University, Birmingham B4 7ET, UK.* [b]*School of Chemistry, University of Southampton, Southampton SO17 1BJ, UK.* [c]*Bristol-Myers Squibb, Reeds Lane, Moreton CH46 1QW, UK.*
E-mail: C.H.Schwalbe@aston.ac.uk

Flurbiprofen (F) is a valuable anti-inflammatory drug, but its aqueous solubility is only 0.03 mg mL^{-1}. Its salts with cyclohexylammonium or adamantylammonium ions still have limited solubility; in both structures N-H…O hydrogen bonds form ladders [1]. In a series of $H_2NC(CH_3)_{3-n}(CH_2OH)_n$ salts of the carboxylic acid drug gemfibrozil [2] the members with n = 0, 1 and 2 also form ladders; but when n = 3, these change to layers [2]. Hoping that counter ions with OH groups would enhance the solubility of F through hydrophilicity and would improve its mechanical properties by greater hydrogen bonding, we have studied the diethanolamine (DEA) and tris(hydroxymethyl) aminomethane (TRIS) salts.



FDEA forms no ladders, nor any other extended motif. Two anions and two cations use their NH_2^+ and COO^- functionality to form a discrete $R_4^4(12)$ ring. Instead of linking adjacent rings, one ethanolamine OH donates a hydrogen bond to the same carboxylate O atom already accepting from NH, thus appending another $R_2^1(7)$ ring to either side of the main ring. The other ethanolamine OH can link to a carboxylate O atom across the large ring, but its disorder suggests limited importance. Hydroxyl O atoms accept no hydrogen bonds from NH or OH donors. Instability of the crystals due to disorder and the lack of any hydrogen-bonded spine are consistent with the low melting point of 63°C, density of 1.284 g cm^{-3} and the high solubility of >200 mg mL^{-1}.

FTRIS appears to exist as more than one polymorph. The one examined does have hydrogen-bonded motifs extending throughout the crystal. The ammonium ion of TRIS donates a hydrogen bond to each of two carboxylate ions, forming C(6) chains along *x*, and another to OH, while its three OH groups donate to two different COO^- and one OH. Thereby dimeric $R_2^2(10)$ and $R_4^4(18)$ rings link adjacent chains, and conjoined $R_2^2(9)$ and $R_3^2(9)$ rings are appended to each chain. The resulting stability is reflected in the melting point of 148°C, density of 1.345 g cm^{-3} and solubility of 16.34 mg mL^{-1}.

[1] C.H. Schwalbe, S.J. Teat, S.E. David, W.J. Irwin, B.R. Conway, P. Timmins, *Acta Cryst.,* **2005**, A61, C350. [2] E.Y. Cheung, S.E. David, K.D.M. Harris, B.R. Conway, P. Timmins, *J. Solid State Chem.*, **2007**, 180, 1068-1075.

Keywords: pharmaceutical crystallography; hydrogen bonds in organic crystals; solubility

FA4-MS09-P08

Fragment-based Discovery of S100B Inhibitors Combining Computational and Biophysical Approaches. Stefano Mangani[c], Lucia Cesari[b,c], Matteo Andreini[b], Daniela Lalli[d], Rebecca del Conte[d], Paola Turano[d], Alessandro Padova[b], Mariangela Agamennone[a]. [a]*Dipartimento di Scienze del Farmaco, Università "G. d'Annunzio", Chiet.* [b]*Drug Design Technologies Unit, Siena Biotech S.p.A., Siena.* [c]*Dipartimento di Chimica, Università di Siena.* [d]*Magnetic Resonance Center CERM, Università di Firenze - Italy.*
E-mail : mangani@unisi.it