Conference Visit Report

Crystal Growth of Organic Materials (CGOM-09)

Nanyang Technical University, Singapore, 4th – 8th August 2010.

Firstly let me express my gratitude to the BACG for their kind and generous support to attend this, without which my attendance would have been financial challenging. Thank you!

The Conference was held in the Executive Centre of the Nanyang Technical University which, like much of modern Singapore, is a fine and splendid facility, dedicated as the Conference and extended Education Centre of an equally modern and well equipped campus. The choice of venue was very good, as was the timing of the Conference, given that two days later the island was both celebrating its 45th "birthday" (the territory gained independence in 1965) and hosting the first ever "Youth Olympic Games". No doubt the crowds were flying in just as we departed!

Thus the domestic arrangements for the Conference were very good; the accommodation was modern, smart and comfortable; and it was augmented with a good social programme.

The Conference was attended by over 70 delegates from a wide range of nations and included 41 academics and 35 students. The organisers had received 70 submitted contributions that had been reduced to 51 final presentations. The structure was one of two parallel sessions with each main session being preceded by a combined plenary session. The presented posters were divided into two sessions.

The Conference got off to a very good start. This was pleasantly surprising given that the first plenary was to be given in absentia by Prof. Michael Doherty (University of California, Santa Barbara) who had been unable to travel for medical reasons. The presentation was a pre-recorded DVD format, and this worked amazingly well. It is a testament to modern technology that the quality was so good that the speaker appeared to be present in the lecture theatre. Prof. Doherty gave a very clear lecture which challenged the conventionally accepted Cabrera – Vermilyea model of crystal growth step pinning mechanism for systems that contained only a dilute concentration of "impostor" molecules. He termed any molecular entity that was different from the substrate host as an impostor molecule, and this could include solvent molecules, impurities, deliberate additives. From his work, Prof. Doherty proposed that the only point at which the dynamics of the system could change was at the point of the first turn of the spiral. Although there were local temporal changes in step growth rate, on average the step growth rate does not change. Prof. Doherty and his co-worker Jacob Sizeman had used D-alanine as an impostor in the growth of α-glycine and intended to extend this work to other systems. It was a limitation of this mode of presentation that questions could not be answered immediately by the presenter, which was a shame because an important difference in understanding arose about the model. This could have been answered straightway by Prof.Doherty if present. He did however offer an e-mail address from which he would promptly reply to posted questions.

Another good plenary lecture was given by Prof. Ashwini Nangia (School of Chemistry, University of Hyderabad, India) on the topic of co-crystals and polymorphs to modify the physical characteristics and pharmacokinetic profile of pharmaceuticals. In the view of the

presenter, co-crystals (and polymorphs) offered a chance to technically "resurrect" active compounds that had failed in development. He gave good reasons why this might be the case and was worthy of investigation. However the presentation seemed to miss the point that most pharmaceutical compounds fail in development for reasons of poor safety (toxicity) and inadequate clinical efficacy, rather than reasons of pharmaceutical development per se. Thus the area might have "rich pickings" but the approach probably does not address the main reasons for developmental failure, and could lead to the same disappointments. Addition of a second molecule (as a co-crystal) presumably also carries more scope for having to control molecular (polymorphic) complexity. It would not seem to be a panacea.

Prof. Juan Garcia-Ruiz (University of Granada, Spain) gave a very comprehensive lecure on crystallisation of materials in gels. He spoke both of the rationale for doing so (removal of the effects of mass transport; removal of convective heat effects; reduction or evaporation and avoidance of segregation) and gave examples of how such gels could be used in practice with good effect. He gave a very clear "crossing roads" analogy to crystal growth, being the probability of encountering new molecules as function of concentration and velocity). Usable gels included a hydrophilic set (agarose, silica gels and Sephadex) and various molecular weight versions of polyethylene oxide which could be used with most solvents.

Generally the quality of the shorter technical presentations kept up the high standard set by the plenaries. Twenty minutes were allowed per presentation, but it was clear that some presentations would have benefitted from longer (perhaps it is dependent on the amount of technical detail or explanation that has to be imparted). For others, the stated aim of "workshop" format was more appropriate and a longer question time was suitable.

There were 46 such presentations and clearly not possible to comment on all here. Some highlights could be identified, from this delegate's perspective.

A visually powerful presentation was given by Drs. Kieran Hodnett and Denise Croker from the University of Limerick, Ireland. This gave some extremely good video footage of solution mediated polymorphic transformations in carbamazepine, sulphathiazole and piracetam systems. The value of this type of experimental data is very clear, watch the system over and over and you can see some highly specific and informative phenomena occurring. Particularly revealing was the appearance (it was there all the time) of a sandwich layer of Form 4 between two layers of Form 2. Different speeds of dissolution could be observed.

Dr. Jerry Heng from Imperial College, London gave two very clear talks. One concentrated on the PhD work of a co-worker Ji Khoo who had done an extensive study of the drying of different physical forms of carbamazepine and how some of these forms were inter-related. The studies were done as a function of the drying environment, T, P, RH, P/Po. Relevance to larger scale still probably needed to be established. His second presentation involved the enhancement of crystal growth of protein, and involved a patented system of forced flow through capillaries. He demonstrated how the surface characteristics of the capillary were quite influential and gave examples of how different silanating agents could modify this surface. This had been done with co-workers, Michael Roberts and Prof. Daryl Williams.

The Manchester University group were well represented at this Conference. A particularly interesting talk was given by Vicky Fawcett (J.McCabe, S.Schroeder, Prof.R.Davey) on trying to ascertain influential factors for the likelihood of generating polymorphs. No assumption was made in advance regarding propensity to form polymorphs, nor was any

actual polymorphic data used. It was therefore a genuine attempt to predict. Each experiment had generated 180 “data points”, and in answer to questions Ms.Fawcett confirmed that the dataset was complete (ie. all 180 points were present for all experiments). An attempt was being made to construct a neural network that would recognise the influential parameters for polymorphic potential. An interesting addition to this was the application of Principal Component Analysis (PCA) to cluster these various factors together. This work is in progress and it is worth watching to see if it is successful. It deserves to be.

In terms of logistical organisation the Conference displayed some shortcomings. Whilst the technical content was divided into parallel sessions, the division seemed somewhat arbitrary. As a result, it was likely that one might wish to attend a presentation in either parallel stream at conflicting times. One can accept that one will miss certain presentations, but control over the timing of the presentations was poor, and therefore the timings of the parallel sessions were not in synchronicity. This could have been addressed by taking a different approach to timing in a number of ways, eg. dispensing with parallel sessions altogether; running continually through the available times (dispensing with formal break times); or not having a formal poster session. The general impression was that the organising committee had not tailored the running of the event to the received submissions or attendance numbers, but had just stuck with a formulaic structure. This was a shame. Additionally there were hardly any announcements about “domestic arrangements” which led to a number of confusions.

An “advertisement” was made for the next Conference in this series CGOM-10 scheduled for 2011 at the University of Limerick in Ireland. This will be part supported by the Solid State Pharmaceutical Cluster, which brings together five Irish Universities and a host of industrial sponsors. The call was made by Dr.Denise Croker (University of Limerick), who made the point that the Irish economy is very dependent on the success of the pharmaceutical industry in that location, and that on the other side there is a very significant technical contribution made by Ireland to the manufacture of these products. All the elements of a good Conference are in place and, with some attention to logistical arrangements, it should be a good success.

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