

W0325

**Hydrothermal Crystallization of Organic Molecular Solids: Applications to Pharmaceuticals, Co-crystal Engineering and Neutron Diffraction Studies.** Ian D. Williams, Fanny L-Y. Shek, Samuel M-F. Lo, Herman H-Y. Sung, Dept. of Chemistry, Hong Kong Univ. of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, China.

The application of hydrothermal and related methodologies to the growth of organic crystals will be discussed. The advantages can include enhanced crystal size and quality, as well as high isolated yield. Hydrothermal crystallization can be applied to both natural product characterization and pharmaceutical formulation. We present several examples from this area; the anti-malaria drug artemesinin and its derivatives have been studied for polymorphism and hydrolytic breakdown products. The dopamine receptor antagonist dl-tetrahydropalmatine has been crystallized as a variety of salts and neutral co-crystals and its chiral resolution achieved. In the field of crystal engineering, hydrothermal methods can be used to form organic co-crystals between aromatic acids and bases with high phase purity and stoichiometric control. In certain systems the different molecular stoichiometries can have intriguing chemico-structural consequences, for example various bipyridines and phthalic acid form both a 1:1 neutral molecular adduct with N--HO hydrogen bonds, as well as a 1:2 organic salt with NH--O. In other crystals such as  $2[4,4\text{-bipyH}_{0.5}][\text{C}_6\text{H}_2\text{-}1,2,4,5\text{-(COO)}_4\text{-H}_3]$  and dinicotinic acid short single well N-H-O hydrogen bonds are found. Crystals of 0.5cm dimension suitable for neutron diffraction, including deuterated forms, have been readily prepared by hydrothermal methods and the resulting studies allow new insight into this important class of hydrogen bond. Finally we have found facile formation of large crystals of cyclodextrin-adducts by this approach, which has implications for X-ray structural characterization of drug inclusion complexes.

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