

**KN-14**

**Solid-State Chemical Reactions.** Menahem Kaftory. *Technion, Schulich Faculty of Chemistry, Haifa-Israel.*

E-mail: [kaftory@tx.technion.ac.il](mailto:kaftory@tx.technion.ac.il)

The history of solid-state reactions goes back to the nineteenth century, however it was considered as “nature curiosity”. The first and most intensive investigated type of solid-state reactions was photochemical reactions. The work done at the Weizmann Institute of Science revealed the well-known “topochemical rules” that are being used also today. Solid-state thermal reactions were neglected and only few cases have been studied. The advantages of solid-state reactions over reactions carried out in solutions are the specificity of the reactions. Much work was devoted to the search for chemical systems that can undergo solid-state reactions, mainly photochemical reactions. In the beginning of the nineties of the last century effort was devoted to use solid-state photochemistry to enhance asymmetric syntheses. Recently the use of templates for solid-state photochemical reactions was successfully demonstrated. In the lecture, historical points in solid-state chemical reactions will be mentioned followed by significant contributions to the subject that will be described. Examples of the work done in our group on thermally activated solid-state reactions, photochemical reactions in neat compounds, and photochemical reactions in solid inclusion compounds will be shown. Important reactions are those that show single-crystal to single-crystal transformations. Those reactions enable monitoring of structural changes during the reaction as well as observing other interesting chemical and physical events. The most interesting systems will be described.

**Keywords:** solid-state photochemistry; solid-state reactions; solid-state reactivity

**KN-15**

**Bridging Protein Crystallography and Chemistry: Structural Insight into the O-GlcNAc Modification and the Structure Inspired Design of Chemical Probes.** Gideon J Davies. *Department of Chemistry, The University of York, York YO10 5YW, UK.*

E-mail: [davies@ysbl.york.ac.uk](mailto:davies@ysbl.york.ac.uk)

The enzymology of enzymes active in the synthesis and breakdown of carbohydrates is one that has benefitted enormously from structural investigation, going all the way back to David Phillips’ pioneering work on the glycosidase lysozyme in the late 1960’s. More recently, protein crystallography has been used to define the reaction coordinate of many glycosidases [1] and also to inspire the synthesis and analysis of transition-state mimics as mechanistic probes and as enzyme inhibitors (for example ref. [2]). One of the major current challenges for structure-inspired inhibitor design is to develop inhibitors with tight binding and high specificity that may be used in vivo to perturb cellular function in what is now called: “chemical

biology”

In this lecture, I will discuss the “O-GlcNAc” modification of eukaryotes which is implicated in type II diabetes and neurodegeneration [3]. I will show how physical organic probing of the reaction mechanism may be interpreted in light of 3-D structure to design tight binding enzyme inhibitors [4]. I will show how these 1<sup>st</sup> generation inhibitors may be further augmented, based upon structural comparisons, to enhance specificity and hence alleviate the potential complex phenotypes obtained with more promiscuous inhibitors. Applications in the areas of type II diabetes [5] and tau-dependent neurodegeneration [6] will be discussed.

[1] Vocadlo, D., and Davies, G. J. *Curr Opin Chem Biol*, **2008** *12*, 539-555. [2] Tailford, L. N., Offen, W. A., Smith, N. L., Dumon, C., Morland, C., Gratien, J., Heck, M.-P., Stick, R. V., Blériot, Y., Vasella, A., Gilbert, H. J., and Davies, G. J. *Nature Chem Biol*, **2008** *4*, 306-312. [3] Hart, G. W., Housley, M. P., and Slawson, C. *Nature*, **2007** *446*, 1017-1022. [4] Dennis, R. J., Taylor, E. J., Maculey, M. S., Stubbs, K. A., Turkenburg, J. P., Hart, S. J., Black, G., Vocadlo, D. J., and Davies, G. J. *Nat Struct Mol Biol*, **2006** *13*, 365-371. [5] Macauley, M. S., Bubb, A. K., Martinez-Fleites, C., Davies, G. J., and Vocadlo, D. J. *J Biol Chem*, **2008** *283*, 34687-34695. [6] Yuzwa, S. A., Macauley, M. S., Heinonen, J. E., Shan, X., Dennis, R. J., He, Y., Whitworth, G. E., Stubbs, K. A., McEachern, E. J., Davies, G. J., and Vocadlo, D. J. *Nature Chem Biol*, **2008** *4*, 483-490.

**Keywords:** enzyme mechanism; carbohydrates; glycosylation

**KN-16**

**Engineering Co-crystals Using Molecular Sense and Supramolecular Sensibility.** Christer Aakeroy. *Department of Chemistry, Kansas State University, Manhattan, KS, 66506, USA.*

E-mail: [aakeroy@ksu.edu](mailto:aakeroy@ksu.edu)

What is the most likely outcome when a homogeneous solution containing two different molecular solutes is allowed to evaporate to dryness? Unless a chemical reaction driven by the formation of covalent bonds takes place between the two solutes, one would, as a rule, expect the appearance of two separate molecular solids – the equivalent of a simple recrystallization. In the supramolecular laboratory, however, the very same process provides an opportunity to move in a completely different direction – a co-crystallization is a deliberate attempt at bringing together different molecular species within one periodic crystalline lattice without making or breaking covalent bonds. Recrystallization and co-crystallization processes are, in essence, only distinguishable by their intents. The goal of the former is a homomeric product, whereas the latter procedure strives for a heteromeric product and, in general, the odds are stacked firmly in favor of a homomeric product, so how do we go about developing reliable, effective, and versatile synthetic methods for the directed assembly of heteromeric co-crystals? This presentation will (a) outline practical strategies for modular and directed assembly of co-crystals and (b) demonstrate how thermal stability and solubility of an active ingredient