MS27 O1

Crystallization of high-pressure polymorphs. Examples of kinetic control. Elena Boldyreva[a,b]. [a]*Novosibirsk State University, Russia;* [b]*Institute of Solid State Chemistry SB RAS, Novosibirsk, Russia.* E-mail: *boldyrev@nsu.ru*

Keywords: polymorphism, high pressures, kinetic control

The study of the high-pressure polymorphism is still in its infancy. More often than not, the transformations give metastable forms, and not the thermodynamically preferable one. The following facts can indicate at the kinetically, and not thermodynamically controlled transformations:
1. Different forms are obtained at the same conditions from different starting polymorphs.
2. Different forms are obtained on compression and on decompression, transformations are not reversible.
3. Effect of pressure is different for single crystals and for powder samples.
4. The transformation is characterized by a pronounced induction period, a hysteresis, is incomplete, or is extended in a wide pressure range.
5. Different forms are observed, depending on how rapid compression / decompression were; on how long the sample was held at a selected pressure.
6. The transformation is sensitive to the choice of the pressure-transmitting liquid (in which the sample is emerged in hydrostatic loading experiments) / to the presence of even traces of a liquid in a slurry.
This will be illustrated using a few examples. Crystallization of liquids, crystallization from solutions, and solid-state polymorphic transformations will be considered.

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MS27 O2

Crystallization techniques for small molecules compounds: A review. Juan Manuel García-Ruiz. *Laboratorio de Estudios Cristalográficos. IACT. CSIC-Universidad de Granada. Granada-Spain and Factoria de Cristalización.* E-mail: *jmgruiz@ugr.es*

Keywords: crystallization, small molecules, polymorphism

There is an increasing need of crystals of small molecules compounds for different applications, ranging from their use for X-ray diffraction structural studies to the control of their polymorphic precipitation or crystal habits. Research groups working on structural studies of organometallic, coordination compounds, dendrimers, macrocycle chemistry, etc. require nowadays crystals of specific compounds to advance in the understanding of designing structures with specific chemical properties. In addition, the pharmaceutical industry as well as the manufacturing industries of pigments, cosmetics, foods, etc., requires a precise knowledge of the kinetics aspects of the crystallization of small molecules in order to control and tailor the structural and morphological properties of the crystals. The crystallization of specific compounds are in many cases the bottleneck for advances in crystal engineering and inorganic solid state chemistry research programs. The world of biomineralization and biomimetic compounds not only requires a deep knowledge of the crystallization behavious of mineral phases but also of their interaction with biological molecules or the mimicking synthetic counterparts.

This communication will analyze the current landscape in the research of small molecules crystallization and will offer a review of the crystallization techniques currently used.

MS27 O3

Halogen···halogen interactions in pressure-frozen liquids Andrzej Katrusiak, Roman Gajda, Anna Olejniczak, Marcin Podsiadło *Faculty of Chemstry, Adam Mickiewicz University, Poznań, Poland.* E-mail: katran@amu.edu.pl

Keywords: halogen-halogen interactions, high pressure structure, disordered molecular crystals

The research on the crystal structures of halogenated compounds is constantly gaining interest. The short halogen···halogen contacts are considered to evidence attractive forces, considerably stronger than van der Waals interactions, and therefore vital for the molecular arrangement in crystals [1, 2]. According to other theories, the close inter-halogen distances result from molecular packing [3].
Methanes and ethanes are simple carbon compounds with the molecules interact by van der Waals forces, and at the same time small molecules do not impose severe restrictions on their close packing in the crystal structures. In these respects the methanes and ethanes can be considered as models for the aggregation of molecular fragments in many organic substances. Thus structures of halogenated methanes and ethanes can be used for studying the basic aggregation patterns involving halogen···halogen contacts.
A series of crystal structures of dihalomethanes (CH_2XY, where X, Y = Br, Cl, I) have been determined by single-crystal X-ray diffraction. They show clearly systematic isostructural relations resulting from the specific intermolecular interactions in theirs pressure frozen phases: CH_2Cl_2 and CH_2ClBr crystallize in space group *Pbcn* [4], for CH_2Br_2 and CH_2BrI space group *C*2/*c* was observed. CH_2ClI exhibits polymorphism, and forms *Pnma*-symmetric phase α, and also a polar phase β in space group *Fmm*2, isostructural with the pressure frozen-

phase of CH_2I_2 [5]. In the polar *Fmm2*-symmetric phase the dipole moments of all molecules are parallel.
A group of isostructural crystals has been identified for a series of 1,2-dihalotetrafluoroethanes $X(CF_2)_2Y$ (X = Br, I; Y = Br, I). Despite their isostructurality the molecules behave differently. The $BrCF_2CF_2Br$ structure is completely ordered, in ICF_2CF_2I the $-CF_2-CF_2-$ moiety rotate about I···I molecular axis, but it orders at pressure higher than 1 GPa, and in the $BrCF_2CF_2I$ structure the Br and I atoms are disordered. The formation of isostructural crystals by these compounds and different types of molecular disorder can be rationalized by the similar patterns of intermolecular interactions.
In the crystal of dichloroacetic acid ($P2_1/n$), molecules are connected by chlorine···chlorine interactions into infinite zigzag chains
While the structures of the series of halogenated methanes and ethanes are clearly governed by halogen···halogen interactions, we encountered also structures where this type of interactions was absent. For example, in the crystal structure of chlorotrimethylsilane $Si(CH_3)_3Cl$ ($Pmn2_1$), no such intermolecular contacts shorter than 5Å have been observed [6].

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MS27 O4

The influence of environment on structure: Polymorphs of γ-aminobutyric acid (GABA) and gabapentin. D. C. Levendis and H. Reece, *Molecular Sciences Institute, School of Chemistry, University of the Witwatersrand, PO WITS 2050, Johannesburg, South Africa.* Email: demi@chem.wits.ac.za

Keywords: GABA, gabapentin, polymorph, solvate

The neurotransmitter amino acid γ-aminobutyric acid (GABA) has previously been found to exist as two polymorphs: a monoclinic and a tetragonal form. The molecular conformation of GABA in each of these forms is significantly different, influenced by both strong intermolecular N-H···O=C and weak C-H···N or C-H···O hydrogen bonds. Changes in the environment (solvent, amino acids in the solutions, temperature) are known to influence the crystallization of simple amino acids [1] and recently strategies to form co-crystals of GABA have been described [2]. In this work we report on the crystallization of a novel hexagonal form of GABA, which occurs as an ethanol solvate. The long, needle shaped crystals ($P6_2$: a = 15.9164(4), b = 15.9164(4), c = 7.8769(4)Å) retain their structure until 1-2°C before melting (~190°C). There are two crystallographically independent GABA molecules in the unit cell with disordered ethanol molecules tightly bound in the hexagonal channels. The ethanol is released from the hexagonal channels (Fig. 1), close to the melting point, as clearly detected by hot stage microscopy. The structures and hydrogen bonding networks in two previously unreported monoclinic polymorphs of the GABA analogue, 1-aminomethyl-1-cyclohexane-acetic acid (gabapentin) will also be reported in this paper.

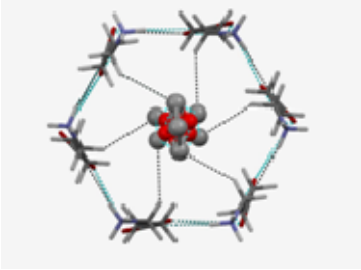

Figure 1. A projection down the c axis of the new hexagonal form of GABA showing disordered ethanol molecules in the 6_2 hexagonal channels.

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MS27 O5

In-situ **cocrystallisation combined with Raman spectroscopy** Michael T. Kirchner, Roland Boese *Department of Chemistry, University of Duisburg-Essen, Germany.* E-mail:michael.kirchner@uni-due.de

Keywords: crystal growth, hydrogen bonds in organic crystals, Raman spectroscopy

Fast characterization of the products from cocrystallisation experiments is highly important since there are no general rules for appropriate growth conditions. Therefore a large number of experiments have to be performed to find the right conditions which favor the growth of a cocrystal over the growth of the individual components. For *in-situ* crystallization on a single crystal diffractometer this is especially important as characterization by diffraction is time consuming. We therefore incorporated a Raman probe into our *in-situ* laser zone melting apparatus. First results from systems containing acetylene, dioxane, formamide, formic acid and formaldehyde are highly promising. Already in the Raman spectra of the liquid mixtures we found hints to the formation of molecular aggregates which might be precursors of the cocrystals. After solidification and zone melting growth we used Raman spectroscopy to identify the formation of a cocrystal. Basic research in cocrystal formation is of increasing interest to pharmaceutical science as cocrystals of active pharmaceutical ingredients can have advantageous properties.