

## MS24.P24

*Acta Cryst.* (2011) A67, C365**Synthon competition in new pharmaceutical forms: how crystal structure affects properties**

M. Teresa Duarte,<sup>a</sup> Vânia André,<sup>a</sup> Fabrizia Grepioni,<sup>b</sup> Nair Rodriguez-Hornedo,<sup>c</sup> Chinmay Maheshwari,<sup>c</sup> <sup>a</sup>*Centro de Química Estrutural, DEQB, Instituto Superior Técnico, Lisbon, Portugal;* <sup>b</sup>*Dipartimento di Chimica "G. Ciamician", Università di Bologna, Via Selmi 2, 40126 Bologna, (Italy);* <sup>c</sup>*College of Pharmacy, Dept. of Pharmaceutical Sciences, University of Michigan, Ann Arbor, MI 48109, (USA).* E-mail: teresa.duarte@ist.utl.pt

Crystal design and engineering has received much attention in recent years as its implications extend to material science, solid state reactions and synthesis, and drug development.

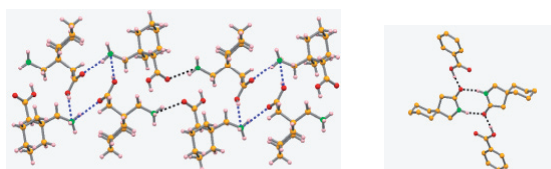
One of the most important issues in this field is the rational design and arrangement of molecular packing, which affects and controls the macroscopic properties of materials. A comprehensive understanding of supramolecular systems is primarily dependent on the knowledge of intermolecular interactions controlling the molecular aggregation, with major emphasis on hydrogen and halogen bonding as well as aromatic stacking.

Synthon formation and breaking is a main key and the driving force in structure-properties relationships.

More significant than knowing the structure of new API forms is to correlate that information with the properties of the novel compounds. Stability and solubility are major factors known to strongly affect API's performance and therefore their correlation with structural and thermal data is of utmost importance.

As an example several cocrystals and molecular salts of gabapentin-lactam (GBPL), a prodrug with proven neuroleptic effects, were unveiled and fully characterized; the pH-dependent solubility of these novel forms were studied and a correlation between solubility data, structural information and thermal stability has been pursued.

Studies with gabapentin (GBP), a neuroleptic drug, yielded several multicomponent crystal forms whose thermal and pH stability have also been determined. With the antibiotic 4-aminosalicylic acid (4ASA) eleven new crystal forms were disclosed, including polymorphs, solvates, cocrystals, molecular salts and salts. A novel hydrated form of the antihypertensive perindopril erbumine was found, the first molecular structures of this API were determined, and the relative stability compared to the commercial forms were studied.



GBP-terephthalic acid

GBPL-benzoic acid

[1] V. André, A. Fernandes, P.P. Santos, M.T. Duarte, *Crystal Growth & Design*, **2011**, accepted. [2] V. André, D. Braga, F. Grepioni, M.T. Duarte *Crystal Growth & Design* **2009**, *9*, 5108-5116.

**Keywords:** synthon competition, pharmaceuticals, properties

## MS24.P25

*Acta Cryst.* (2011) A67, C365**Recognition of weak interactions in porous supramolecular architectures**

Silvia Bracco, Angiolina Comotti, Mario Beretta, Gaetano Distefano, Piero Sozzani. *Department of Materials Science, University of Milano*

*Bicocca, Milan (Italy).* E-mail: silvia.bracco@mater.unimib.it

Nanoporous molecular crystals are attracting large attention in the recent literature for their applications in the field of gas storage, selective recognition and molecular confinement.

We could obtain empty-pore hexagonal crystalline structures held together by weakly directional interactions and fabricate supramolecular architectures that cooperatively stabilize gases or polymers confined in one-dimensional spaces [1].

Multinuclear NMR of the solid and the gas phase is a method of choice for characterizing nanostructured materials, the size and the shape of the cavities, and their interfaces. The recognition of CH $\cdots$  $\pi$  specific interactions that contribute to the overall stabilization is demonstrated by the diamagnetic susceptibility effect of the host aromatic ring currents exerted on the guest molecules and by 2D advanced NMR techniques, which provide highly resolved spectra in hydrogen, carbon and phosphorous dimensions [1]. This multinuclear approach allows a detailed description of the role of weak interactions cooperating to fabricate nanostructured materials that exhibit exceptional thermal stability. The large upfield shift provided a tool for understanding the topology of gases or polymer chains interacting with the inner surface of the porous host [2]. For example, we have demonstrated that flexible polymer chains and suitable aromatic host self-assemble in varied ratios to fabricate crystalline and semi-crystalline materials with robust architectures. The high melting macromolecular adducts were successfully prepared by solvent-free mechanochemical or thermal treatment of the crystalline host and few polymers [3]. This unconventional strategy has been applied for the selective confinement of copolymer sequences in the aromatic host, creating novel architectures composed by alternated crystalline lamellae and amorphous layers. In this case the driving force for the fabrication of the nanostructured materials was based on the establishment of a network of cooperative noncovalent intermolecular interactions between the host and some sequences of the copolymer, while steric effects prevent the formation of the inclusion-crystal with the remaining blocks [4].

[1] a) P. Sozzani, S. Bracco, A. Comotti, L. Ferretti, R. Simonutti, *Angew. Chem. Int. Ed.* **2005**, *44*, 1816-1820; b) A. Comotti, S. Bracco, G. Distefano, P. Sozzani, *Chem. Commun.* **2009**, 284-286. [2] A. Comotti, S. Bracco, P. Sozzani, S.M. Hawxwell, C. Hu, M.D. Ward, *Crys. Growth Des.* **2009**, *9*, 2999-3002. [3] S. Bracco, A. Comotti, P. Valsesia, M. Beretta, P. Sozzani, *Cryst. Eng. Commun.* **2010**, *12*, 2318-2321. [4] S. Bracco, A. Comotti, L. Ferretti, P. Sozzani, *J. Am. Chem. Soc.* **2011**, in press.

**Keywords:** NMR, self-assembly, inclusion

## MS24.P26

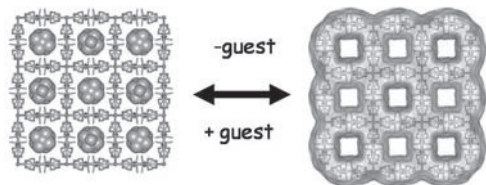
*Acta Cryst.* (2011) A67, C365-C366**Guest Tunable Structure and Magnetism in a Porous Coordination Polymer Followed by parallel In Situ single crystal and powder diffraction**

Suzanne Neville,<sup>a</sup> Keith Murray,<sup>a</sup> Cameron Kepert,<sup>b</sup> Gregory Halder,<sup>c</sup> Karena Chapman,<sup>c</sup> <sup>a</sup>*School of Chemistry, Monash University, Australia.* <sup>b</sup>*School of Chemistry, University of Sydney, (Australia).* <sup>c</sup>*Advanced Photon Source, IL, (USA).* E-mail: suzanne.neville@monash.edu

Developing functional materials with physical properties that can be controlled on the molecular level is an important goal for the realization of nanoscale devices. Spin crossover (SCO) materials, which show dramatic switching response to external perturbations, e.g. temperature, pressure, light and guest/chemical environment, are excellent candidates. Indeed, we have shown that in the nanoporous two-dimensional network material [Fe(bpbd)<sub>2</sub>(NCS)<sub>2</sub>](guest) (bpbd = 2,3-bis(4'-pyridyl)-2,3-butanediol, guest = acetonitrile, acetone,

methanol, ethanol, propanol) the guest molecules dramatically effects the SCO properties [1].

In further studies using parallel *in situ* variable temperature single crystal and powder X-ray diffraction, the desorption and resorption of these guest was followed over the SCO temperature range and revealed distinct correlations, including steric and electronic effects, between the solvates [2]. Thus we have made a large step towards rationally tuning guest-dependent SCO behaviour in such systems.



[1] Neville et al. *Angew. Chem.* **2007**, *46*, 2059-2062. [2] Neville et al. *J. Am. Chem. Soc.* **2009**, *131*, 12106-12108.

**Keywords:** coordination polymers, magnetism, guest sensor

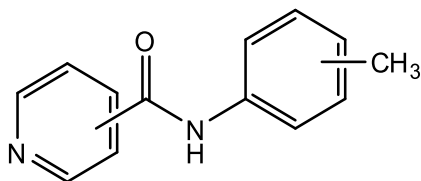
## MS24.P27

*Acta Cryst.* (2011) A67, C366

### Structural systematics and conformational analyses of a 3×3 isomer grid and three chlorinated relatives

John F. Gallagher, Pavle Mocijac, *School of Chemical Sciences, Dublin City University, Dublin 9, (Ireland)* E-mail: john.gallagher@dcu.ie

A 3×3 isomer grid of nine *N*-(tolyl)pyridinecarboxamides (C<sub>13</sub>H<sub>12</sub>N<sub>2</sub>O) as **NxxM** (*x* = *para*-/*meta*-/*ortho*-) was examined to evaluate structural relationships from both *ab initio* calculations (*gas-phase*, PCM-SMD solvation models) and the solid-state. The effect of the pyridine N atom (**Nx**) and methyl group (**xM**) substitution patterns on molecular conformations from calculations and in terms of molecular organization is evaluated for comparison with related **Mxx** and **NxxF** isomer series [1-2]. The **NxxM** isomers aggregate via N-H...N or N-H...O=C hydrogen bonds, while the intramolecular N-H...N interaction influences co-planarity in the aromatic rings of **NoxM**. In addition three 5-Cl-**NoxM** derivatives have been characterised as minor components in the **NoxM** syntheses.



**NmpM** forms catemeric chains via N-H...N interactions in space group P2<sub>1</sub>/c in contrast to **NmpF** which forms tetramers in P1̄ (No.2). The mixed 50:50% **NmpFM** crystalline solid solution forms catemeric chains in Pna2<sub>1</sub> that differ from **NmpM** at the secondary hydrogen bonding level.

Calculations demonstrate that most crystallographic dihedral angles correlate with their computational counterparts by having similar conformations with an average offset of torsion angles of ±20-40° though with some exceptions. Analysis of melting point data reveals a general trend of melting point decrease from the symmetrical **NppM** (162°C) to the unsymmetrical **NomM** (50°C), a trend which follows Carnelly's rule where *high molecular symmetry is associated with higher melting points* [3].

[1] P. Mocijac, M. Tallon, A.J. Lough, J.F. Gallagher, *CrystEngComm* **2010**, *12*,

3080-3090. [2] P. Mocijac, A.J. Lough, J.F. Gallagher, *CrystEngComm*, **2011**, *13*, 1899-1909. [3] T. Carnelley, *Philos Mag*, 5th series, **1882**, *13*, 112-130 & 180-193.

**Keywords:** systematics, isomers, computation

## MS24.P28

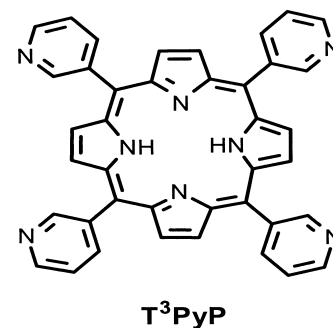
*Acta Cryst.* (2011) A67, C366

### Reactivity of tetra(3-pyridyl)porphyrin in crystal engineering

Sophia Lipstman, Israel Goldberg. *School of Chemistry, Sackler Faculty of Exact Sciences, Tel-Aviv University, 69978 Ramat-Aviv, Tel-Aviv, (Israel)*. E-mail: lipstman@post.tau.ac.il

Formulations of porphyrin-based hybrid coordination networks with metal ion connectors are of particular interest due to the relative robustness of metal-organic-frameworks and their potential utility in practical applications. The chemical and structural diversity of porphyrins allows us to reasonably control their self-assembly process and to alter systematically the composition, topology and porosity of the supramolecular arrays that form. This approach represents an attractive "bottom-up" strategy to tailoring ordered lattice materials from suitably functionalised tetraarylporphyrin building blocks.

In this work we have explored the versatile molecular recognition features of the tetra(3-pyridyl)porphyrin (T<sup>3</sup>PyP) scaffold, and its utility in the construction of porphyrin based supramolecular assemblies via coordination as well as hydrogen bonding interaction synthons. The diversified supramolecular reactivity of T<sup>3</sup>PyP can be attributed to the conformational flexibility of this porphyrin framework, namely the possibility of the four *meso*-substituted 3-pyridyl arms to align in different orientations with respect to the rigid porphyrin plane. Only a small number of T<sup>3</sup>PyP-based supramolecular ensembles have been reported thus far. In order to demonstrate the important role that this building block can play in crystal engineering of framework solids, we report in this study on the preparation and structural characterization of a series of new T<sup>3</sup>PyP network materials.



T<sup>3</sup>PyP

[1] S. Lipstman, I. Goldberg, *Cryst. Growth Des.*, **2010**, *10*(10), 4596-4606.

[2] S. Lipstman, I. Goldberg, *Cryst. Growth Des.*, **2010**, *10*(11), 5001-5006.

**Keywords:** supramolecular, crystal engineering, porphyrin

## MS24.P29

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### Synthesis and characterization of pharmaceutical cocrystals from polymorphic constituents

Heba Abourahma, Devon Cocuzza. *Department of Chemistry, The College of New Jersey, PO Box 7718, Ewing, NJ 08628 (USA)*. E-mail: abourahm@tcnj.edu

The objective of this project is to investigate the polymorphic tendencies of cocrystals synthesized from polymorphic active pharmaceutical ingredients (APIs). Furthermore, the objective extends to evaluate the potential use of these cocrystals as a means