

MS15 O1

Constructing, deconstructing, and reconstructing molecular cocrystals Christer B. Aakeröy *Department of Chemistry, Kansas State University, Manhattan, KS, 66506, U.S.A.* E-mail: aakeroy@ksu.edu

Keywords: hydrogen bonds; co-crystals; molecular recognition

The design, properties and even definitions of cocrystals continue to receive considerable attention. Our understanding of the way in which molecules communicate and assemble is still incomplete, which means that supramolecular synthesis of discrete or extended molecular assemblies held together by non-covalent forces, remains a major fundamental scientific challenge. In this presentation, we outline a hypothesis-driven three-step protocol for the construction of ternary cocrystals and supermolecules where stoichiometry and primary intermolecular interactions can be readily rationalized [1-5].

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MS15 O2

New Avenues in Co-crystal Studies: Boronic Acids in Supramolecular Chemistry V. R. Pedireddi, *Division of Organic Chemistry, Solid State & Supramolecular Structural Chemistry Unit, National Chemical Laboratory, Pune 411 008, India.* E-mail: vr.pedireddi@ncl.res.in

Keywords: boronic acids, co-crystals, supramolecular Synthesis

Supramolecular synthesis employing noncovalent bonds such as hydrogen bonds is the major focus of contemporary research in the solid state studies, for the creation of assemblies of exotic architectures with tailor-made properties. For this purpose, co-crystallization of molecular entities possessing various acceptor-donor functional groups like -COOH, -CONH₂, etc. were thoroughly explored because of their ability to yield robust hydrogen bonds. However, boronic acids, with a general formula of R-B(OH)₂, which have been found to be highly versatile organic moieties in various conventional synthetic and application arenas have not been explored in the supramolecular synthesis despite their ability to form hydrogen bonds, until recently. In this connection, our first report employing boronic acids for the creation of ladder type of architectures followed by the elegant examples evolved from others lead to the systematic exploration of this novel functional group for the creation of exotic assemblies by co-crystallizing with numerous organic components as well as metal ions. Salient features of design and synthetic strategies would be discussed in detail in the presentation.

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MS15 O3

Absorption and adsorption of ETBE and mesitylene in and on ice Martin U. Schmidt^a, Sonja M. Hammer^a and Elke Fries^b ^a*Institute of Inorganic and Analytical Chemistry, University of Frankfurt, Max-von-Laue-Str. 7, D-60438 Frankfurt am Main, Germany.* ^b*Institute of Environmental Systems Research, University of Osnabrueck, Barbarastraße 12, D-49069 Osnabrueck, Germany*
E-mail: m.schmidt@chemie.uni-frankfurt.de

Keywords: molecular modelling; force fields; ice

The absorption and adsorption of ETBE (ethyl-*tert*-butylether) and mesitylene (1,3,5-trimethylbenzene) in and on ice I_h were simulated by force field calculations and measured in laboratory experiments.

Clouds in the upper troposphere consist mainly of ice. Ice I_h is the only stable ice polymorph at atmospheric conditions^[1]. When ice crystals begin to form in the troposphere, volatile organic compounds (VOCs) can adsorb at the surface or be incorporated into the ice crystals. Thereby VOCs may be removed from the atmosphere and pollute snow and water on the earth's surface.

Two representative VOCs are ETBE and mesitylene. ETBE is produced industrially in large amounts since a few years. It is used as antiknock compound in fuel. Because of production, storage and use, it is contaminating the atmosphere^[2]. Mesitylene is produced industrially as well. It has been found in snow samples^[3]. Recent laboratory investigations show that mesitylene is taken up by growing ice crystals^[4]. The same is assumed for ETBE. From the experiments it is not yet clear, if the organic compounds only adsorb on the ice surfaces, or if they are included in the ice bulk.

For the simulation of the adsorption and absorption of ETBE and mesitylene on and in ice crystals, three cases were investigated: the adsorption on the (0001) surface of ice I_h, the absorption into bulk ice (by substituting one or more water molecules, as a point defect), and the absorption on a small-angle grain boundary (as an example for a lattice defect).

For the force field calculations a modified Dreiding force field^[5] was used. All calculations were made with periodic boundary conditions with up to 768 water molecules and a single organic molecule.

At the surface, as well as in the bulk ice or at a small-angle grain boundary, the ETBE molecules form hydrogen bonds with water molecules. When ETBE enters the bulk ice it replaces one water molecule and distorts the surrounding ice lattice. When ETBE adsorbs at a small-angle grain boundary it replaces two water molecules. The adsorption at the surface is energetically more favourable than an absorption in the bulk ice. Absorption at a grain boundary is in between.

For the adsorption of mesitylene on ice surfaces we found the energetically best structure with the mesitylene molecule being almost parallel to the ice surface.

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MS15 O4

Acid-base systems, understanding the formation of co-crystals versus salts. G. Ramon, L.R. Nassimbeni, *Supramolecular Crystallographic Group, P.D. Hahn Building, Chemistry Department, University of Cape Town, Rondebosch 7701, South Africa.*

E-mail: gaelle.ramon@uct.ac.za

Keywords: synthon, co-crystal, salt

We have employed the concept of supramolecular synthons¹ to prepare acid-base molecular aggregates and have studied their structures. The synthon chosen was the carboxylic-acid: 2-aminopyridine pair, which display mutually compatible hydrogen bonding interactions of the type N-H...O and O-H...N (Figure 1a). We observed that the hydrogen of the acid carboxylic group could be transferred to the nitrogen of the pyridyl group according to the difference in the pKa of the two compounds (Figure 1b).

From the results obtained, we correlated the O...N distances with the difference in pKa of the two compounds. The O...N distance decreases with larger values of ΔpK_a .

In the meantime, we decided to study the relative stability of the structures obtained by calculating their lattice energy. Because of the proton transfer, the fragments of the structures are charged. From these calculations, we predict the results of competition experiments. These experiments consist in studying from which acid one base crystallises when placed in a mixture of two acids. The competition experiments are then repeated at different pH conditions so that the selectivity could be enhanced or inverted.

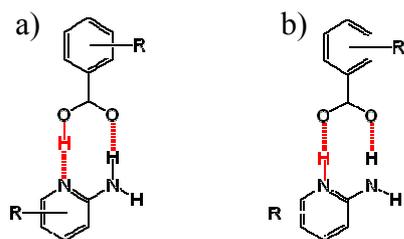


Figure 1: the carboxylic-acid: 2-aminopyridine synthon

- formation of the co-crystal
- formation of the salt with transfer of the proton (in red)

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MS15 O5

Complementarity of cocrystal formers in the CSD László Fábian, Pfizer Institute for Pharmaceutical Materials Science, Cambridge Crystallographic Data Centre, Cambridge, UK. E-mail: fabian@ccdc.cam.ac.uk

Keywords: cocrystals; databases; statistical analysis

A database of 62109 reliable and complete organic crystal structures was extracted from the Cambridge Structural Database [1]. Sum formulae and InChI identifiers [2] were calculated for each residue. Using this data and a list of common solvents [3], 1914 structures were identified as cocrystals. Molecular descriptors, usually applied in QSAR studies, were calculated for all molecules in the cocrystal dataset. The resulting database describes pairs of molecules that form cocrystals with each other in terms of the calculated molecular properties.

The cocrystal properties database may serve a dual purpose. It can be a source of empirical rules and it can form the basis of a computer application to screen a database for likely cocrystal formers. Both potential applications require statistical methods to extract important and significant information from the large amount of data available (2 x 130 descriptors for each molecule pair).

The simplest approach to distinguish between likely and unlikely cocrystal formers is a classification of molecules, followed by an assessment of which classes of molecules crystallize together frequently. Since the applied descriptors are strongly correlated, principal component analysis was used to transform the 130 descriptors into a set of 20 independent variables. Ward's hierarchical agglomerative clustering method identified 15 clusters. The majority of the clusters can be described in chemical terms (e.g., electron donors; zwitterionic amino acids). Preferences for cocrystal formation were investigated by computing relative frequencies (treated as probability estimates) of each possible group pairing (15x15). Strong preferences, i.e., frequent combinations of groups were apparent from the data. They usually coincide with rules one would expect using chemical knowledge. For example, polyaromatic hydrocarbons frequently occur in cocrystals with charge-transfer acceptor molecules, perfluoro compounds or with each other. The successful identification of such preferences in a purely mathematical approach suggests that a molecular descriptor based classification can be a useful component in an automatic screening application.

A more detailed understanding of the compatibility of cocrystal formers can be obtained from the analysis of individual molecular properties. Is there a relationship between the size, shape, polarity or donor-acceptor imbalance of molecules in a cocrystal? Spearman's correlation coefficients (ρ) were calculated for all possible descriptor pairs (130x130) to check for the existence of such relationships. (The strongly biased distribution of descriptor values limits the usability of more conventional statistical descriptors.) Two-dimensional density plots were created for all variable pairs showing a correlation with $|\rho| > 0.25$. The statistical significance of such correlations was further elucidated using box plots. Representative examples of both strongly correlated variables (e.g. those related to shape) and expected but not observed correlations (e.g. difference between the number of donors and acceptors) will be presented and discussed.

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