frameworks has grown drastically over the past few years. The use of multifunctional ligands, such as organometallic complexes, permits the introduction of other functionalities within the frameworks. We have synthesized and characterized a series of metal-organometallic framework (MOMF) materials, derived from simple [CpFe-(η^6-arenecarboxylate)] bridging ligands. Depending on the reaction conditions, solid state structures ranging from simple 1D polymer chains to three dimensional square grid structures have been obtained. For example, the reaction of $Ni(NO_3)_2$•$6H_2O$ with $[CpFe]^+$-metalated 1,4-benzenedicarboxylic acid (1) results in $[Ni_3(1\text{-}H)_4(H_2O)_2(\mu\text{-}H_2O)_2][NO_3]_2$, a 3D framework material constructed of square grid nickel-carboxylate networks that are interconnected in the third dimension through additional nickel ions. The synthesis, structure and characterization of these materials will be presented.

Keywords: coordination polymers, framework structures, ferrocene derivatives

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Cis-trans isomerizations and rearrangements during hydrothermal synthesis of metal carboxylates

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Hydrothermal conditions provide clean routes for the synthesis of new hybrid organic-inorganic frameworks. However, at elevated temperature and pressure, it is possible to induce reactions in the organic ligand used. For example, carboxylic acids may undergo isomerization, rearrangements, decompositions, hydrogen abstractions, etc. Unsaturated carboxylic acids may, additionally, suffer dimerization, oligomerization, or polymerization. Even though the hydrothermal reaction may not lead to the desired compound, it may produce an interesting derivative not accessible by other means. For instance, reaction at 160 ˚C during 48 h of *cis*-4-cyclohexene-1,2-dicarboxylic acid with $Ca(OH)_2$ afforded *cis*-4-cyclohexene-1,2-dicarboxylato)calcium(II), $[CaC_8H_8O_4]$. However, when using $BaCO_3$, under the same conditions, a product which contains the original ligand in the *trans* conformation, diaquabis(*trans*-cyclohex-4-ene-1-carboxylic-2-carboxylato)barium(II), $[Ba(C_8H_9O_4)_2(OH_2)_2]$, is obtained. Other reactions which involve partial decomposition and rearrangement of the organic moiety, leading to mixed ligand compounds will be discussed. We thank R. Benson (Rigaku-USA) and M. Pink (Indiana University), for support with data collection. This work was funded by FONACIT-Venezuela, through grant LAB-97000821.

Keywords: cis-trans isomerization, hydrothermal synthesis, metal carboxylates

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Real crystal engineering: Solid state reactions in metal-organic compounds

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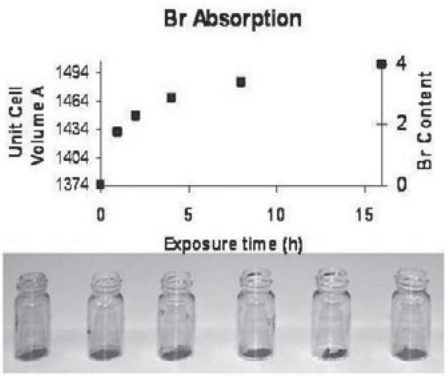
The results of our recent solid state reaction studies applied to the synthesis of hybrid organic-inorganic crystalline solids are presented. Development of methods suitable to prepare solid solutions are reported that allow control of their unit cell dimensions and polymorphism Mechanochemical reactions are shown to be excellent alternatives to traditional solution methods in preparing coordination polymers and metal-organic hydrogen-bonded networks. Similar products can be prepared by gas-solid methods such as hydrochlorination or dehydrochlorination of crystalline precursors. In some cases reactions proceed under topochemical control to give different products. Precise control over unit cell metrics can be achieved by solid-gas halogen-exchange reactions that enable the modification of the unit cell volume, whilst the formation of a two-metal solid solution allows the coordination geometry of one metal to constrain the other and hence the resulting crystal structure and symmetry. Combined, these methods offer promise helping to control composition, polymorphism and unit cell dimension of the crystal species considered: real crystal engineering.



Keywords: crystal engineering, solid state reactions, polymorphysm

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Design of supramolecular complexes: From concept to crystal structures

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In order to understand the hydrogen bond interaction between an active pharmaceutical ingredient (API) and its receptor, we have investigated small complexes with structurally similar bonding patterns. The co-crystallization of specific supramolecular complexes is not a straightforward procedure. The process, from the pre-selection of potential candidates to the successful co-crystallization of small receptor/ligand models, should not be left to chance. Therefore we have developed a concept for designing these structures. After selection of model compounds with complementary functional groups, we calculate the structures and energies of a multitude of alignments (constellations) by means of our force-field program MOMO [1]. These calculations are time-consuming if the molecules possess a number of torsional degrees of freedom and are thus able to adopt different conformations. Various analytical tools are used to identify the intermolecular hydrogen-bond interactions (especially IR spectroscopy and powder diffraction). The most promising combinations are then selected for further co-crystallization experiments. We have studied many different hydrogen-bond arrangements between at least two acceptor or donor groups at each molecule, advancing our examination to three hydrogen bonds with diverse hydrogen-bonding patterns. We are not only interested in forming the desired hydrogen bonds but also how to prevent undesired ones. The prerequisite for this is a thorough consideration

of the distances between the acceptor and donor groups. Finally we have obtained the required supramolecular complexes, if at least three strong hydrogen bonds are formed.
[1] G. Wagner, E. Gemmel, H. Beck, M. Bolte and E. Egert; MOMO Version 2.00; University of Frankfurt (2006).

Keywords: design, supramolecular, complexes

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Supramolecular interactions in 3-ferrocenyl-methoxy-benzothiophenes, non steroidal drug precursors

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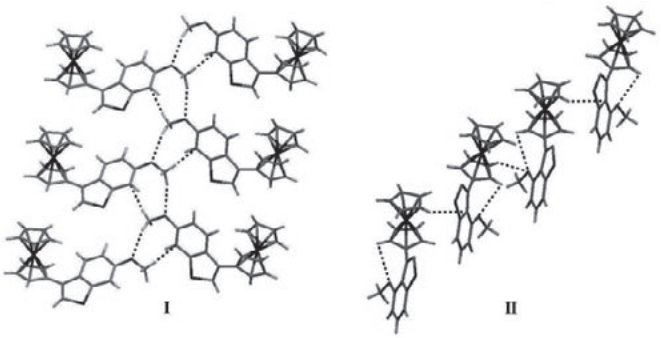
The incorporation of organometallic moieties into known active drugs to improve their therapeutic properties by association of potential cytotoxicity has gained considerable interest in recent years. We prepared a series of benzothiophene derivatives with a raloxifene-type backbone containing a ferrocenyl unit and terminal amino groups (morpholine, piperidine, pyrrolidine, piperazine and dimethylamine). One of the steps involved is the intramolecular cyclisation of 1-ferrocenyl-2-[3-(methoxyphenyl)] that results in two isomers, 3-ferrocenyl-6-methoxy-benzo[*b*]thiophene (**I**) and 3-ferrocenyl-4-methoxy-benzo[*b*]thiophene (**II**). Isomer II presents intramolecular CH-O contacts, that are absent in I. This affects their supramolecular arrays: in I the methoxy oxygen is free to participate in relatively strong intermolecular CH-O contacts that produce a zigzag chain; in II the strongest intermolecular between the molecules is a CH-C, forming a dimer of the two unequivalent molecules; theses dimers organize themselves in chains, this time using a weak CH-O short contact.



Keywords: inter- and intramolecular interactions, supramolecular assemblies, pharmaceutical compounds

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Cocrystallization of a pharmaceutical agent pamoic acid with piperazine or 4,4'-bipyridyl

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Pamoic acid (H_2PA) is a pharmaceutically acceptable organic acid and usually used to obtain long-acting pharmaceutical formulations by decreasing the solubility of basic drugs, which is also of crystallographic interests recently. Pamoic acid has poor solubility in many common solvents and shows inert nature in crystallization. As a consequence, quite limited structural information are available at present, covering coordination complexes and molecular adducts. In this work, cocrystallization of pamoic acid with piperazine (PIPO) or 4,4'-bipyridyl (BIPY) under ambient condition affords two distinct supramolecular assemblies, namely, $[(PA).(H_2PIPO)].3H_2O$ (1) and $[(H_2PA).(BIPY)]$ (2). The former crystalline product shows the unique triple-helix array via charge-assisted N-H...O bonds with the inclusion of helical water chains, in which the pamoate anion has the particular molecular configuration. The triple-helix in 1 is considerably steady, and can be retained after the exclusion of water guests. The later compound displays acid-base tape pattern sustaining by the familiar carboxyl-pyridyl H-bonding synthon. It is known that pamoate salts are generally formed in the modified basic drugs, and this is also found in the molecular adducts of pamoic acid and pyridine/lutidine. As for 1, the ion-paired crystalline product is yielded expectantly due to the strong basicity of piperazine, whereas for 2, remarkably, it represents the first bimolecular co-crystal of pamoic acid. These unusual structural features may provide new insights into understanding the active mechanism of pamoic acid involved drugs.

Keywords: pharmaceutical co-crystal, crystal engineering, hydrogen bonds

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Polymorphism of co-crystals: Co-crystal polymorphs of an analgesic drug, ethenzamide

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Polymorphism1 is a well-studied phenomenon in single-component crystals and active pharmaceutical ingredients (APIs). Polymorphism in multi-component crystals is relatively in its infancy, but gaining interest in the recent times in the context of pharmaceutical co-crystals,2 which are hydrogen bonded complexes between an API and a co-crystal former which is a solid under ambient conditions. These novel solid forms are developed to improve physical and/or chemical properties of the APIs such as density, stability, solubility, bioavailability, etc. We present our recent results on polymorphic co-crystals of an analgesic drug, 2-ethoxybenzamide (ethenzamide) and their synthesis and characterization. Ethenzamide is a poorly water-soluble drug used mainly in combination with other active ingredients. Ethenzamide was cocrystallized with various co-crystal formers and APIs. Two of the co-crystals were found to be polymorphic. Whereas all the co-crystal polymorphs were prepared by solution crystallization, only some of them could be prepared by solid-state grinding experiments. Liquid assisted grinding or solvent-drop grinding produced most stable polymorph of both the polymorphic systems. All the co-crystal polymorphs were characterized by various analytical techniques and their structures were determined by single crystal X-ray diffraction. Polymorphic phase transformations and stability were estimated using thermal analysis. It is interesting to note that the number of polymorphs of a co-crystal is more than the number of polymorphs of its parent API