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.
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Keywords: design, supramolecular, complexes

P09.04.07

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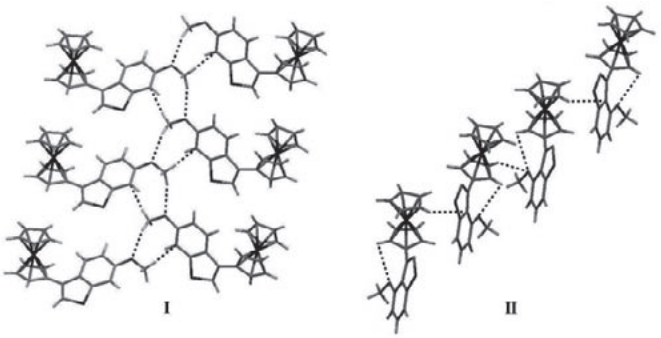
Supramolecular interactions in 3-ferrocenyl-methoxy-benzothiophenes, non steroidal drug precursors

Joao L.A. Ferreira da Silva[1], Andre P Ferreira[1], Matilde Marques[1], Fatima Minas da Piedade[2]
[1]Instituto Superior Tecnico, Centro de Quimica Estrutural, Avenida Rovisco Pais, Lisboa, Lisboa, 1049-001, Portugal, [2]Departamento de Quimica e Bioquimica, FCUL, Campo Grande, 1749-016 Lisboa, Portugal, E-mail：joao.luis@ist.utl.pt

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

Miao Du, Zhi-Hui Zhang, Wei Guo, Xiao-Juan Fu
Tianjin Normal University, Chemistry, College of Chemistry and Life Science, Tianjin Normal University, Tianjin 300387, P. R. China, Tianjin, Tianjin, 300387, China, E-mail：dumiao@public.tpt.tj.cn

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

P09.02.09

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

Srinivasulu Aitipamula[1], Pui Shan Chow[1], Reginald B.H. Tan[1,2]
[1]Institute of Chemical and Engineering Sciences, Crystallization and Particle Sciences, 1, Pesek Road, Jurong Island, Singapore, 627833, Singapore, [2]Department of Chemical & Biomolecular Engineering, National University of Singapore, 4 Engineering Drive 4, Singapore 117576, E-mail：srinivasulu_aitipamula@ices.a-star.edu.sg

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

and co-crystal former.
[1] (a) S. Aitipamula and A. Nangia, Chem. Commun., 2005, 3159; (b) J. Bernstein, Polymorphism in Molecular Crystals, Clarendon, Oxford, 2002. [2] O. Almarsson and M.J. Zaworotko, Chem. Commun., 2004, 1889.

Keywords: pharmaceutical co-crystal, polymorph, phase transformations

P09.01.10

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New crystal forms of gabapentin

Maria Teresa Duarte[1], Vania Andre[1], Maria de Fatima Minas da Piedade[2]
[1]Instituto Superior Tecnico, Centro de Quimica Estrutural, Avenida Rovisco Pais, Lisboa, Lisboa, 1049-001, Portugal, [2]Departamento de Quimica e Bioquimica da FCUL, Campo Grande, 1749-016 Lisboa, Portugal, E-mail：teresa.duarte@ist.utl.pt

Gabapentin (GBP) is an API used against epilepsy, neuropathic pain and in the treatment of limb tremor[1]. Several polymorphs of GBP have been reported and characterized, but only SCX of Form II was known until very recently. Our group managed to obtain two new SCX structures of different polymorphs[2,3]. These new forms are not as stable as Form II, proved by several experiments. Form IV can even be considered a disappearing polymorph [3] because it readily transforms into another form. New crystal forms of GBP were obtained on acidifying the solution. We obtained GBP chloride hemihydrate, an ethyl ester of GBP and a co-crystal of GBP-lactam and benzoic acid [Fig.1] in different crystallization conditions. All these structures were determined by SCXRD, presenting different physicochemical properties and supramolecular arrangements [5]. Intramolecular interactions are only observed in Form IV and GBP Cl hemi-hydrate.

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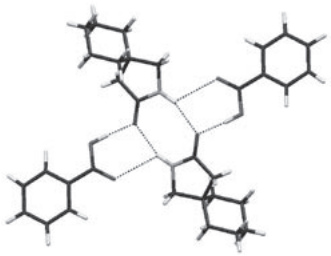
[3] M. T. Duarte et al, NJC, submitted
[4]J. D. Dunitz et al,Acc.Chem. Res. 28 (1995) 193.
[5]V. Andre et al CrystEngComm, in submission.



Keywords: crystal engineering, cocrystal, polymorphism

P09.02.11

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Molecular cocrystals of peganole with peganine

Akmal Tojiboev, Rasul Okmanov, Kambarali Turgunov, Bakhodir Tashkhodjaev, Nuriddin Mukarramov, Khusniddin Shakhidoyatov
Institute of the Chemistry of Plant Substances of Academy Sciences of Uzbekistan, X-ray Crystallography department of Laboratory Physical Methods of Investigations, Kh.Abdullaev street, bd 77, Tashkent, Mirzo Ulugbek district, 100170, Uzbekistan, E-mail：a_tojiboev@yahoo.com

Earlier we studied solid solutions of biologically active derivatives of tricyclic quinazolines, the peganole (**1**) with the 6-bromopeganole (**2**) in different stoichiometry [1] using by single crystal X-ray diffraction methods. In all solid solutions, centrosymmetrical hydrogen-bonding interactions are found between the molecules of **1** and **2**, which forms dimers, by O-H...N hydrogen bonding associations. Recently have been prepared of cocrystal of peganole (**1**) and peganine (**3**) in the ratio of 1:1 which similar dimers connected with hydrogen bonds O-H...N. Individual **1** crystallizes as racemate. As against it **3** crystallizes in enantiomorfic forms, that confirm X-ray analysis of single crystals of **3** received by us and the literature [2]. In the unit cell of cocrystals both enantiomorphic forms of each substance (**1** and **3**) are located. Thus, individually peganine crystallizes in enantiomorph form, but in cocrystal take part both enantiomorfic forms. Probably, racemat peganole promote to cocrystallization of racemate peganine.

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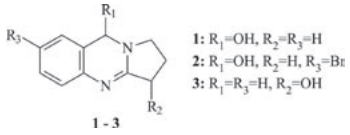
[2] CCDC refcode: TATBEX.



Keywords: cocrystals, solid solutions, hydrogen bonds

P09.02.12

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Subtle relationships between the structures of some aspirin derivatives

Riccardo Montis, Michael B Hursthouse
University of Southampton, School of Chemistry, Highfield, Southampton, Hampshire, SO17 1BJ, UK, E-mail：rm13@soton.ac.uk

Prompted by the identification of a second polymorph of the simple analgesic molecule aspirin, we have made a structural systematics study of some simple derivatives of aspirin. The main aim of this was to see how robust are the packing features in the two phases of the parent molecule, which have 2D similarity, in view of the small changes in the molecular shape and the possibility that the substituent groups may themselves have some involvement in defining intermolecular interactions. Compounds selected were those in which one aromatic ring proton was replaced by a small substituent group. Two relevant structures were already known - 3-methyl aspirin and 6-methyl aspirin. Further examples, namely 4-Me, 5-Me, 5-F, 5-Cl, 5-Br, 5-I, and 5-NO_2 aspirin were synthesised from substituted salicylic acid derivatives. Structure determinations of the new compounds, and detailed comparisons of all structures using the XPac method (Gelbrich and Hursthouse (2005) CrystEngComm 7: 324-336.) revealed that the family contained two isostructural sets − the 5-Cl-, 5-Br- and 5-I- derivatives, and the 5-F-, 5-O_2N- and 5-Me derivatives. A number of lower dimensional similarities were also identified. The poster will describe the relationships found between the structures.

Keywords: aspirin derivatives, systematics of crystal structures, structural motifs

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The influence of hydrogen bonding on generation and stabilization of self-assembled layer structure

Emmanuel Kwadjo Owusu-Marfo[1], Masafumi Yoshio[2], Takashi Kato[3]
[1]Chemistry Department, University of Nizwa, Chemistry, P.O. Box 33,