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

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

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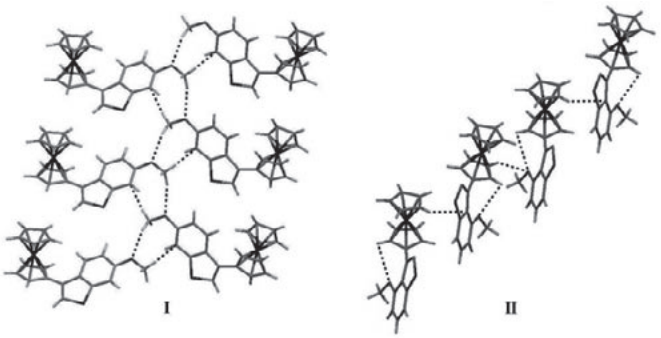
The incorporation of organometallic moieties into known active drugs to improve their therapeutic properties by association of potential cytotoxicity has gained considerable interest in recent years. We prepared a series of benzothiophene derivatives with a raloxifene-type backbone containing a ferrocenyl 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