MS36-P3 Inter- and intramolecular interactions of a series of oligoamide foldamers

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Foldamers are synthetic biomimetic molecules composed of simple repeating units. They have been widely studied because of their vast potential as efficient and even stereoselective organocatalysts and as bioreceptor mimics.[1]

We have prepared and crystallized three aromatic oligoamide foldamers of varying sizes, and analyzed their conformational and crystal packing properties.[2] As expected, hydrogen bonding is the most important non-covalent interaction affecting the molecular conformation and the crystal packing preferences. In addition, aromatic interactions play a stabilizing role.

The oligoamide foldamers adopt two distinct conformations, a helical @-conformation (Fig. 1) stabilized by intramolecular hydrogen bonds, and in the case of the longer molecules also by aromatic interactions, and a more open S-conformation. The choice between these two conformations seems to depend on the crystallization solvent; polar solvents facilitate the folding to an @-conformation whereas the S-conformation is obtained in non-polar solvents. As the molecules have several hydrogen bond donor and acceptor moieties they also display a wide array of crystal packing motifs, including molecular pairs, chains and solvent molecule assisted networks.

References

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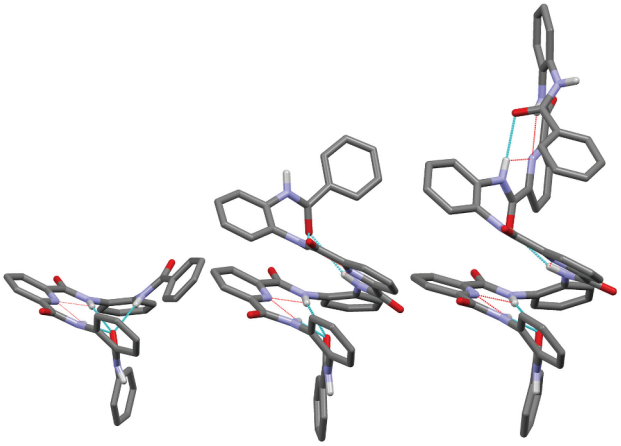

Figure 1. A series of three oligoamide foldamers with one, two and three pyridine core units.

Keywords: Foldamers, hydrogen bonding

MS36-P4 Different compounds from the same reactants: serendipity, misfortune or different reaction conditions?

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The synthesis of chemical entities (pharmaceuticals, ligands, complexes, assemblies, etc.) is classically performed in solution (solvothermal). For example, in the case of Schiff base systems, Lin *et. al* [1] reported that in the solvothermal method of the synthesis of a carboxamide (***o*pda2pica**) derived from *o*-phenylenediamine (***o*pda**) and 2-picolinic acid (**2pica**), 70 mL of different solvents (pyridine, methanol, triphenylphosphate) was used. The reactants were dissolved, mixed and heated for more than 24 hours. The carboxamide was subsequently also coordinated to gallium(III) by means of the same solvothermal method using 40 mL of solvents. The total time required for this procedure was 24 hours yielding only 29% of the **[Ga(*o*pda(2pica)$_2$)]** coordination compound.

In order to investigate these systems for biological and possible radiopharmaceutical evaluation but to use as little solvents as possible, we have applied a simple solution based method. Only 7 mL of methanol was used and the solutions were mixed and incubated at room temperature. After few hours serendipity played its role in chemistry and only a 1:2 co-crystal of ***o*pda** and **2pica** was obtained. As (almost) solvent-free methods of synthesis (neat, liquid-, seeding-, ion-assisted grinding) have been recognised as potentially faster, environmentally friendly and economically acceptable ways to prepare new but also already known compounds, we re-evaluated the synthesis of the carboxamide and/or co-crystals of ***o*pda** and **2pica** in few stoichiometric ratios.[2]

The success of the methods used was evaluated by means of FT-IR, PXRD, DSC and TG thermal analysis and NMR. Molecular and crystal structures were studied using SCXRD. This presentation will discuss the data obtained from this study to elucidate the reasons that lead to formation of co-crystals and/or carboxamide derived from ***o*pda** and **2pica**.

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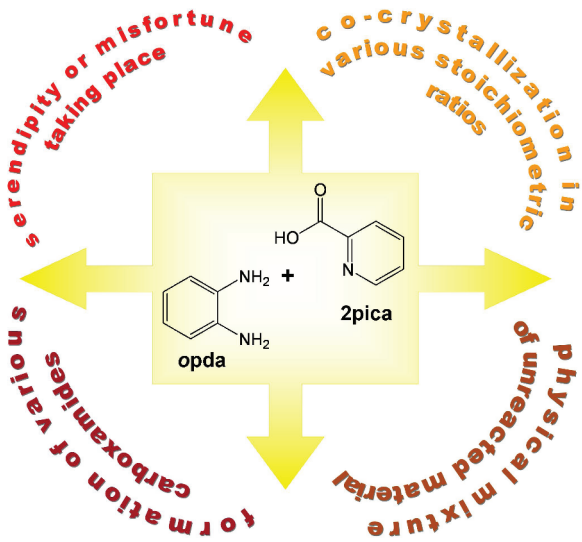

Figure 1. Schematic view of several possibilities of reaction of o-phenylenediamine (*o*pda) and 2-picolinic acid (2pica).

Keywords: Carboxamide, Co-crystal, Solvothermal method, Solution based method, Grinding

MS36-P5 Intermolecular interactions of benzimidazole derivatives

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Imidazole is a constituent of the essential amino acid histidine what is present in many proteins and enzymes and plays a vital part in the structure and binding functions of hemoglobin. Imidazole is present in many pharmaceuticals, in antifungal, antiprotozoal and antihypertensive medications. It is a constituent of mercaptopurine, an immunosuppressive drug. There is benzimidazole moiety in vitamin B_{12}. A number of substituted imidazoles are selective inhibitors of nitric oxide synthase, which makes drug targets in inflammation, neurodegenerative diseases and tumors of the nervous system. The thermostable polybenzimidazole contains imidazole fused to a benzene ring, and acts as a fire retardant. Imidazole has been used extensively as a corrosion inhibitor on certain transition metals, such as copper.

The way to the aim to produce new substances with required properties is based on the knowledge of the structural properties of widely characterised solids. There is a long time effort to influence or favourably fine tune structural properties of solid materials by substituents and / or guest molecules. Their different sizes, shapes and chemical composition consequently alter the physico-chemical properties. In a crystal both steric requirements and electrostatic forces play a role in the architecture. A given packing arrangement may tolerate small changes caused either by the gradual change in site and/or size of substitution or in guest molecules incorporated into a host lattice. When the tolerance is terminated a different packing arrangement and/or a different molecular conformation appears. Occasionally the packing motifs may still remain but the motifs are moved relative to each other. The non-covalent interactions have an influence on the packing arrangement and the molecular recognition processes.

We present on the example of a series of benzimidazole derivatives how the balanced spatial requirements and electrostatic forces play a role in the arrangement of packing motifs in the crystals. Influencing the intermolecular interactions shows how the supramolecular synthon can be engineered.

Keywords: intermolecular interactions, isomorphy, packing arrangement