MS31 The role of supramolecular interactions in polymorphs and co-crystals

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Fingerprinting the solid state assembly of cyclic peptoids: solvatomorphic behavior & sorption properties

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Biological processes rely on control of the dynamic behaviour of biomolecules, the intrinsic flexibility of proteins enables accurate guest recognition and specific substrate conversion. Cyclic peptoids for their biostability and potential diversity seem to be the ideal candidates to evoke biological activities and novel chemical properties both in solution and in the solid state.

Peptoids differ from peptides in the backbone position of the side chains, which are attached to the nitrogen atom. Due to the lack of the amide proton, CH···OC hydrogen bonds, CO···CO and CH-pi interactions play a key role in the solid-state assembly of cyclic *a*-peptoids: face to face or side by side arrangement of the macrocycles mimick *b* -sheet secondary structure in proteins. We also demonstrated that side chains may act as pillars, extending vertically with respect to the macrocycle plane, inducing the columnar arrangement of the peptoid macrocycles (Tedesco et al., 2014).

Recently, we reported that a cyclic hexapeptoid strategically decorated by propargyl and methoxyethyl side chains undergoes a reversible single-crystal to single-crystal transformation upon guest release/uptake involving a drastic conformational change. The extensive and reversible alteration in the solid state is connected to the conspicuous movement (more than 110°) of two propargyl side chains that generate new stabilizing CH-pi interactions with the formation of an unprecedented reversible "CH-pi zipper", which reversibly opens and closes, thus allowing for guest sensing (Meli et al., 2016).

These findings prompted us to perform a polymorph screening of the peptoid compound with a view to understanding the role of the crystallization solvent in the solid state assembly (Macedi et al., 2017).

Here we will explain how the observed extensive solvatomorphism is related to the peculiar conformational flexibility of the peptoid macrocycles and to the role of the solvent molecules in the early stages of nuclei formation. We will visualize the supramolecular architecture of the obtained crystal forms by using Hirshfeld surface analysis and PIXEL energy calculations to compute the intermolecular interaction energies.

We will also show how the solid state assembly of the macrocycles determines the peculiar sorption properties as highlighted by *in-situ* single crystal X-ray diffraction and high resolution X-ray powder diffraction studies.

References:

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