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**The importance of being weak: how weak interactions trigger solid state dynamics**

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Peptoids are N-substituted polyglycines with useful biological activities and interesting chemical properties both in solution and in the solid state [1]. In this contribution we will show how the lack of the amide proton prevents the formation of NH···CO hydrogen bonds and makes peptoids the ideal platform for evidencing the influence of weak intramolecular and intermolecular interactions, as CH···OC and CO···OC interactions, in stabilizing molecular conformations, triggering conformation polymorphism and phase transitions, and ultimately determine the dynamic behaviour in the solid state.

Our group reported on how inter-annular CH···OC hydrogen bonds can provide face-to-face or side-by-side arrangement of the macrocycles mimicking secondary structure in proteins [1]. Then, by combining in-situ powder and single crystal X-ray diffraction, thermal analyses, hot-stage optical microscopy we evidenced how environmental changes (such as temperature, humidity, gas pressure, etc.) may trigger the dynamic behaviour of cyclic peptoids in the solid state [2].

Thus, we established the solvatomorphic behaviour of a cyclic hexapeptoid decorated with four propargyl and two methoxyethyl side chains, which led to the discovery of two pure crystalline forms and four solvates [2,3]. Interestingly, the methanol solvate and the hydrate form result in a stable porous molecular framework, which adsorbs gases as propyne or carbon dioxide, but not methane [4], while the acetonitrile solvate undergoes a reversible single crystal to single crystal transformation at 40 °C, where two propargyl side chains move by 113° and form an unprecedented “CH-π zipper”, which may be unzipped by exposure to guest vapours [2]. By conformational energy and lattice energy calculations we demonstrated the role of intermolecular CH···OC backbone-to-backbone interactions in tightening the peptoid porous framework and the role of CH···OC and CH-π host-guest interactions in the re-opening [5].

More recently, we highlighted the role of intramolecular backbone-to-backbone CO···CO interactions and CH···OC hydrogen bonds in the stabilization of enantiomorph right- and left-handed polyproline type I helices in cyclic dodecapeptoids (Fig. 1) [6].

Finally, peptoids as peptidomimetics allowed us to appreciate that CH···OC interactions in peptoids replace NH···OC interactions in peptides and similarly produce secondary, tertiary and quaternary structures.

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**Figure 1.** Right- and left-handed polyproline type I helices in a cyclic dodecapeptoid decorated with propargyl side chains.


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