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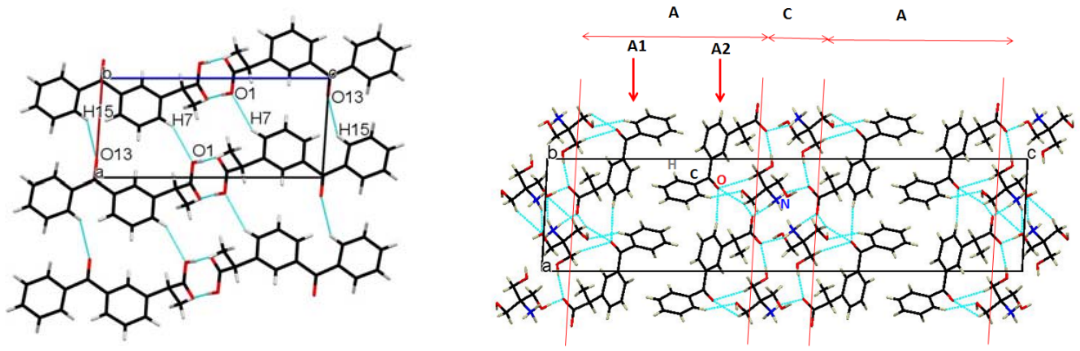
MOLECULAR ORGANIZATION AND THERMODYNAMIC PROPERTIES OF MOLECULAR CRYSTALS

Crystal engineering is becoming nowadays an expanding field of research, aimed at applying the understanding of intermolecular interactions in condensed mater to the many applications of such crystalline phases. The control of molecular organization in the space is therefore one of the most challenging fundamental problems to develop new crystalline molecular materials with potential industrial impact. Three most important aspects involved in the organization of molecular crystals are (i) recognition, (ii) orientation and (iii) intensity of molecular interactions. Accordingly, any modification on the molecular environment modifying the electron distribution of atoms connecting the molecules is a target of study to control the properties of the solid.

The project is based on a deep characterization and analysis of intermolecular interactions which are driving the thermodynamic properties of solids, by using high-resolution X-ray diffraction and quantum chemistry calculations in periodic and gas phases,. This can be done by studying molecular models in crystal phases or molecular systems forming crystalline materials with industrial interest, such as Active Pharmaceutical Ingredients (APIs). Our goal is to the develop the methodology able to extract most important thermodynamic information of crystalline solids (melting point, fusion enthalpy, sublimation energy, solubility,…) from the analysis of the electron distribution in the intermolecular regions of molecular crystals, where those interactions take place.

In this project, particular attention will be paid to crystals of APIs, where the modification of the crystalline thermodynamic properties of the API by means of its association with different co-formers can be of high potential interest (Fig. 1). This part of the project involves additional crystal growth techniques and spectroscopic characterizations (DSC, IR, NMR…).

Wished skills of potential candidates: several among X-ray diffraction crystallography, quantum chemistry calculations, crystal growth, and spectroscopic characterizations.



(a) (b)

Fig. 1 Crystal structures of (a) RS-ketoprofen and (b) RS-ketoprofen/trometamol co-crystal. The solubility of (b) dramatically increases (> 10^5) with respect to (a), solving the problem of the very low bioavailability of the form (a) in pharma industry.