



UNIVERSITÀ DEGLI STUDI DI SALERNO



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Abstract

Solid state dynamic behaviour of organic molecules

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The main interactions characterizing the crystals of organic molecules are weak interactions such as hydrogen bonds, van der Waals forces, hydrophobic interactions, etc.¹

Considering the weak nature of the forces involved, the crystals subjected to specific treatments such as heat treatments, tend to suffer dramatic consequences such as the loss of crystallinity of the material. In some cases, solid-to-solid crystallization processes, induced by heat treatment, have been recently demonstrated. However, due to the complexity and the instability of organic crystals, the solid-to-solid crystallization process of organic molecules is still poorly understood.

For this reason, understanding what are the effects that external stimuli induce on crystals and powders of organic molecules is fundamental. In this thesis work, they are analysed in detail through experimental techniques, such as X-ray diffraction analysis, differential scanning calorimetry and thermal gravimetric analysis. Computational methods, which are fundamental to understand how organic molecules reorganize themselves in the solid state after the exposure to external stimuli, are also employed.

This thesis work is focused mainly on the discussion of the results of the solid state behaviour of four different cyclic hexapeptoids. Cyclic peptoids are *N*-substituted glycine, which differs from peptides since the side chain is attached to the nitrogen atoms, the peptoid unit is achiral and the tertiary amide bond can undergo a *cis/trans* isomerization.² The side chain attached to the nitrogen atom guarantees the possibility to use a great variety of primary and secondary amines³ and the *cis/trans* isomerization allows the side chains to control the structure of peptoids.⁴ Cyclic peptoids, for their peculiar properties, are useful building blocks for the construction of supramolecular architectures with novel chemical properties.⁵

The present thesis is divided into five main chapters. In the first introductory chapter, the role of non-covalent interactions in crystal engineering and a brief introduction to the solid state dynamic behaviour are given. In this chapter, a description of a class of cyclic peptoids, investigated in this thesis, is also provided.

The second chapter is dedicated to an in-depth investigation about the energy aspect of a single-crystal-to-single-crystal transformation of a hexacyclic peptoid decorated with four propargyl and

¹ G. R. Desiraju, *Crystal Engineering: The design of Organic Solids*, Elsevier Scientific Publisher, Amsterdam and New York, 1989.

² R. N. Zuckermann, *Biopolymers*, 2011, **96**, 545-555.

³ J. Sun and R. N. Zuckermann, *ACS Nano*, 2013, **7**, 4715-4732.

⁴ E. J. Robertson, A. Battigelli, C. Proulx, R. V. Mannige, T. K. Haxton, L. Yun, S. Whitlam and R. N. Zuckermann, *Acc. Chem. Res.*, 2016, **49**, 379-389.

⁵ a) A. Meli, E. Macedi, F. De Riccardis, V. J. Smith, L. J. Barbour, I. Izzo and C. Tedesco, *Angew. Chem. Int. Ed.*, 2016, **55**, 4679-4682; b) E. Macedi, A. Meli, F. De Riccardis, P. Rossi, V. J. Smith, L. J. Barbour, I. Izzo and C. Tedesco, *CrystEngComm*, 2017, **19**, 4704-4708; c) C. Tedesco, E. Macedi, A. Meli, G. Pierri, G. Della Sala, C. Drathen, A. N. Fitch, G. B. M. Vaughan, I. Izzo and F. De Riccardis, *Acta Crystallogr., Sect. B: Struct. Sci., Cryst. Eng. Mater.*, 2017, **73**, 399-412.

two methoxyethyl side chains. On this compound, non-ambient powder diffraction analysis was performed too.

The third chapter is dedicated to an in-depth characterization of the dynamic behaviour of different crystal forms of hexacyclic peptoids decorated with four methoxyethyl and two propargyl side chains by means of variable temperature single crystal X-ray diffraction analysis and variable temperature X-ray powder diffraction analysis.

In the fourth chapter, the solid state transformations of two hexacyclic peptoids decorated with alkyl side chains with five and six carbon atoms, respectively, were investigated by means of variable temperature single crystal X-ray diffraction analysis. Thermal analysis and computational study were also carried out.

Finally, the last chapter is dedicated to a different class of compounds, the isoindolinone. In particular, the crystal packing and the thermal behaviour of a toluene solvate crystal form of a 3,3-disubstituted isoindolinone are deeply investigated. Moreover, thanks to a variable temperature single crystal X-ray diffraction analysis, a phase transformation was highlighted.