A Journey into the Extraordinary World of Fampridine Hydrochloride

Speaker

Riccardo Montis

Università degli Studi di Urbino Carlo Bo

+ <u>10 July 2025</u> 11:00 Room MA2 CMIC I Mancinelli

Politecnico di Milano

Via Luigi Mancinelli, 7 20131 Milano

Crystals are formed through a periodic and symmetrical array of atoms, ions or molecules, which are assembled together via a variety of intermolecular interactions and weak forces. Depending on the intrinsic features of the interacting entities (such as their shape and the type and the strength of the intermolecular interactions involved), molecules, atoms and ions can self-assemble generating different crystalline forms. Excluding rare cases, small organic molecules tend to form simple supramolecular arrangements, producing crystal structures with relatively small unit cells. Although molecular self-assembly in the solid-state has been extensively investigated, sometime, a simple serendipitous discovery can remind us that we are still far to understand the rules governing crystallization processes.

In this contribution one of these serendipitous cases is described. A simple hydrochloride salt of a small and rigid molecule, fampridine, crystallized as four different crystalline phases, two of which adopted an incredibly complex self-assembly. ¹ The two structures represent the first observation of Frank-Kasper (FK) phases in small organic systems, a special class of crystalline phases previously observed only in metal alloys and different classes of supramolecular soft matter. The two FK structures crystallized from a precursor dense liquid obtained after a liquid-liquid phase separation. Investigation of the liquid phase by cryogenic electron microscopy reveals the presence of spherical aggregates, suggesting that a complex pre-organization is in place prior the nucleation. NMR investigations and theoretical calculations provide an explanation for this unusual self-assembly.² These structures, together with the experimental procedure used for their preparation, open different perspectives for the design of novel organic crystalline materials.



R. Montis, L. Fusaro, A. Falqui, G. Coquerel et al. Nature, 2021, 590, 275–278. https://doi.org/10.1038.
L. Fusaro, N. Tumanov, G. Saielli and R. Montis. Pure and Applied Chemistry 2023. https://doi.org/10.1515/pac-2022-1208

POLITECNICO MILANO 1863

DIPARTIMENTO DI CHIMICA MATERIALI E INGEGNERIA CHIMICA GIULIO NATTA Riccardo Montis graduated in Chemistry at the University of Cagliari in 2006, under the supervision of Prof. Vito Lippolis. In 2011, he received his PhD in Chemistry under the supervision of Prof. Mike Hursthouse. After several postdoctoral positions in different Universities, such as the University of Southampton, Université libre de Bruxelles, University of Cagliari, Imperial College London and the University of Manchester, in 2021, he joined the University of Urbino "Carlo Bo" as Assistant Professor. His research interests cover different aspects of Supramolecular Chemistry, including crystal engineering and the design of receptors for anion binding and sensina