

Potential Energy

Accessing Unexplored Supramolecular Trajectories through Mechanochemistry

Luca Catalano^{1,*}

Luca Catalano received his Bachelor's in Chemistry from the University of Milan (2011) and his MS in Photochemistry and Molecular Materials from the University of Bologna, working with Professor Dario Braga (2013). He then earned his PhD in supramolecular chemistry from the Polytechnic University of Milan under the supervision of Professor Pierangelo Metrangolo (2017). After a first postdoctoral appointment at New York University Abu Dhabi, working with Professor Pance Naumov on molecular crystalline materials, he joined the lab of Professor Andy Cooper at the University of Liverpool, where he is currently Postdoctoral Research Associate working on porous liquids and crystals.

My passion for crystal engineering and solvent-free processes started as an undergraduate student under the guidance of Professor Dario Braga at the University of Bologna. After that enriching experience, I started my PhD at the Polytechnic University of Milan in Pierangelo Metrangolo's lab. As a graduate student, I was fascinated by multi-component molecular crystals and by the central role of non-covalent interactions, with emphasis on halogen bond (XB), to drive their self-assembly. In addition, as many chemists, I was fascinated by molecular systems possessing complex topologies because of their pleasant aesthetics and challenging preparation. So, when Pierangelo proposed that I work on a previously reported class of topologically complex ionic co-crystals based on XB,^{1,2} I was excited to get started!

We have reported the main findings of that project in this issue of *Chem*.³ What is interesting about this research is that it covers many and diverse aspects of solid-state chemistry, such as solvent-free synthesis, mechanochemistry, polymorph selection, co-crystals, and topologically complex molecular crystals. This work has been possible thanks to a huge collective effort of a

talented international team. I have to thank all of them for their help to successfully tackle this challenging scientific endeavor. I wish to thank Pierangelo and Professor Giancarlo Terraneo for giving me the chance to work on such an interesting project and Professor Tomislav Friščić and Dr. Luzia S. Germann, who have given a fundamental contribution to finalize it. Finally, I wish to thank Paolo Nazzari for his help with the graphics.

When I first discussed it with Pierangelo, the initial idea was pretty simple. It is known that crystallization by slow evaporation of an ethanol solution of potassium iodide (KI), 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane (crypt-222), and 1,8-diiodohexadecafluorooctane (DIPFO) in a respective 1:1:1.5 molar ratio leads to a multi-component crystal possessing Borromean-rings entanglement. Although changing the inorganic salt or the length of the chain of the α,ω -diiodoperfluoroalkanes gives access to a broad range of structural motifs and topologies different from the Borromean-type network,⁴ the mixture of KI, crypt-222, and DIPFO has been known to only form Borromean-type entanglement. My initial aim was to perform a polymorph screening to



get new crystal phases from these starting building blocks.

I still remember how happy I was when I first obtained shiny needle-like crystals from a methanol solution of the three target compounds, knowing that the co-crystal endowed with Borromean topology forms crystals with hexagonal habit (Figure 1). Single-crystal X-ray diffraction (XRD) confirmed the formation of a non-interpenetrated polymorph. Thermal analysis coupled with calculations gave us precious information on the relative stability of the two polymorphs. The non-interpenetrated phase was a kinetic form able to convert, through a monotropic phase transition, to the Borromean-type polymorph by heating the system at around 120 °C.

Mechanochemistry by ball milling has recently emerged as a viable solvent-free green route to successfully prepare new molecules and materials and to access new polymorphs and topologies. However, this methodology has remained unexplored for preparing multi-component molecular crystals with complex topologies. With these intriguing findings in our hands, we aimed to fill this gap by studying the solid-state reactivity of the three starting components through ball milling.

¹Materials Innovation Factory, University of Liverpool, Liverpool, United Kingdom

*Correspondence: luca.catalano@liverpool.ac.uk
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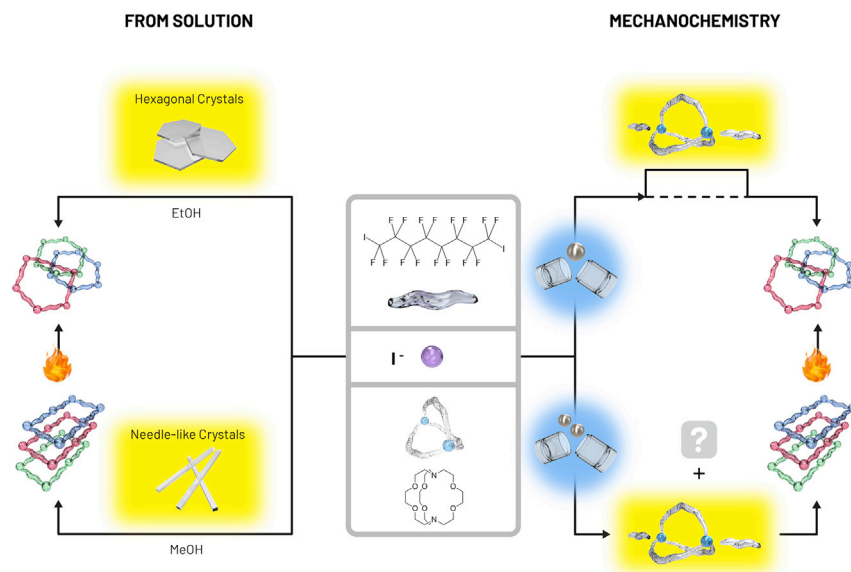


Figure 1. Schematic Overview of the Synthesis of the Two Topologically Distinct Polymorphs K^+ and the complex $K^+ \subset$ crypt-222 cations were omitted for sake of clarity.

What a surprise, when we discovered that by milling KI, crypt-222, and DIPFO in a steel jar with two steel balls (1.38 g each) resulted in the formation of the kinetic non-interpenetrated polymorph, as confirmed by powder XRD, thermal analysis, and infrared (IR) spectroscopy. To gain further insights into the mechanochemical process, we turned our attention to real-time *in situ* monitoring by using synchrotron powder XRD, which unexpectedly revealed a stepwise process involving two different intermediates. One of this intermediate is a previously unknown 1:1 co-crystal involving DIPFO and crypt-222 forming infinite supramolecular chains held together by C–I...N XB. Unfortunately, we did not succeed in isolating the second intermediate for further characterization, but the same system appeared while milling DIPFO and crypt-222, so we postulated it could be a polymorph of the two-component co-crystal. The immediate formation of the binary co-crystal is striking because it shows a preferential supramolecular trajectory over all the possible self-assembly routes of the starting components

that drive the formation of the two three-component polymorphs in solution. This is probably related to the higher reactivity and mobility of DIPFO and crypt-222 in the solid state thanks to their lower lattice energies than KI, an ionic solid held together by strong electrostatic forces.

When the hopes to obtain the Borromean-rings polymorph from ball milling were almost vanished, we decided to introduce a minor change in the milling conditions by switching from two 1.38-g milling balls to a single 2.9-g ball. When I first saw the data of the experiment, I was truly amazed. *In situ* monitoring of the reaction revealed the initial formation of the binary co-crystal of DIPFO and crypt-222 observed with two milling balls followed by the immediate formation of the target co-crystal! A subtle change of the milling media brought to a totally different supramolecular trajectory from a multi-step process that yields a non-interpenetrated polymorph to one that gives access to a molecular crystal endowed with Borromean-type topology (Figure 1).

This work showcases the paramount importance of the experimental parameters, such as the number and size of milling balls, to gain control over mechanochemical processes and solid-state reactivity. It also provides hints of the still untapped potential of ball milling as an efficient and sustainable synthetic route to selectively obtain novel multi-component materials with complex structures.

Working on Borromean rings has been particularly rewarding because it has reminded me my childhood summers in my grandma's house on the Lago Maggiore in Northern Italy, a few kilometers away from Rocca di Angera, a castle belonging to the Borromean family.

After my PhD, I have followed my passion for organic crystals as a postdoctoral researcher working with Professor Panče Naumov at New York University Abu Dhabi and, since March 2020, as a postdoctoral research associate in Professor Andy Cooper's group at the University of Liverpool. In the (hopefully) near future, I would like to start my own research group working on novel molecular functional materials.

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