Study real time crystallization process in organic crystals using Liquid Cell Transmission Electron Microscopy and electron crystallography techniques on PDIs

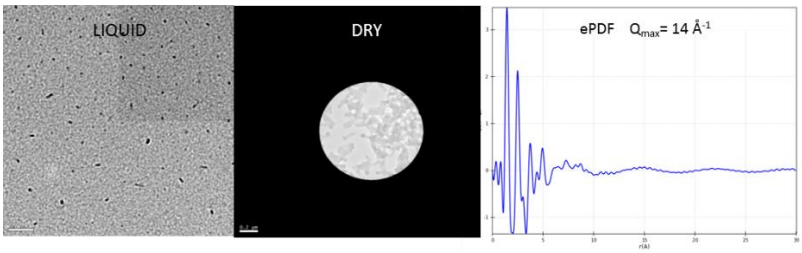
[1]Alejandro Gómez Pérez, [2]Yael Tsarfati, [2]Boris Rybtchinski, [1]Partha Pratim Das, [1]Stavros Nicolopoulos

[1]NanoMegas SPRL, Boulevard Edmond Machtens 79, B1080 Brussels, Belgium
[2] Department of Organic Chemistry, Weizmann Institute of Science, Rehovot 76100, Israel
alex@nanomegas.com

The industrial and scientific importance of organic crystals is revealed in a wide number of applications in various fields (pharmaceutical, biology, material science, etc.). Comprehension of the precipitation and crystallization process in those materials is of great importance; however, the mechanisms behind those processes are still not well understood [1]. It has been reported that "non classical" crystallization via amorphous intermediate precursors in solution is quite common [2]. The study of organic precursors evolution into final crystalline and defined morphologies poses real challenges to understand the process behind this [1]. Since the major part of such process occurs in solution, direct observation of the different reaction steps is usually followed either by spectroscopy methods and/or by drying the solution at different reaction time intervals and using TEM (Cryo) electron microscopy [3]. However, for a better consistency between "in-vivo" experiments carried out in solution and TEM cryo-electron microscopy observations, samples should have been prepared under exactly same conditions (i.e. avoid the drying process at different reaction time intervals)

In the last decade, new type of sealed liquid cells has been emerged for sample observation in a liquid environment in a TEM microscope. In those cells, thin (20 nm) amorphous Si_3N_4 films have been used as membranes containing a liquid layer (200 nm to several microns) and supported on Si microchips, usually placed on specially designed TEM holders; such design has allowed a number of exciting new experiments in materials and life science applications (crystal growth and catalysis, "in-situ" electrochemical processes, etc.)

On the other hand, using Electron Pair Distribution Function (e-PDF) allows to study local order of different substances (liquids to high/medium/low-range ordered solids) where is actually possible to perform such experiments in a TEM microscope at local nm scale. e-PDF technique (or alternatively X-Ray PDF) allows to monitor precisely crystallization and ordering effects in various systems [4]. Using ePDF within the LC has allowed to monitor also precisely the onset of crystallization from amorphous aggregate during the chemical reaction process.



Following the work done by [3] about the crystallization process in organic crystals and combining the power of novel TEM related techniques ("in situ" LC-TEM imaging + ePDF). We found exciting new evidences from the morphological to crystallographic point of view and crystallization process in case of organic compounds.

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