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New developments using the "in situ" crystallization with a CO_2-laser

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The "in situ" crystallization method applying a CO2-laser (OHCD-Laser System) has allowed the crystallization and structure determination of several compounds which are difficult to achieve in crystalline form under standard conditions [1]. Main point of such experiments is that the samples under investigation generally need to have a melting point allowing its crystallization when using the "in situ" methodology. The standard procedure to obtain single crystals is to apply a repetitive melting zone which allows to obtain a high quality cylindrical single crystal filling a part of a quartz capillary after a purification of the sample.
The latest state-of-the-art diffractometers allow obtaining high resolution data of excellent quality based on the cylindrical crystal generated in capillaries. Hence, data obtained are suitable for charge density studies. As examples the charge density studies of toluene and trifluorotoluene are presented.
In order to avoid the known limitations requiring a single-component sample with a sharp melting point, a series of new methodologies have been developed allowing the crystallization of new types of samples. A useful approach to crystallize samples with no sharp melting point or samples which exhibit solid-solid phase transitions, is adding a solvent to the sample in the capillary where the crystallization procedure is performed. This solvent can be added in different amounts ranging from diluted to concentrated solutions. As an example the structure of the ordered low temperature phase of cyclopentane was obtained by "in situ" crystallization at -181 ºC adding 1-pentene (30 %) as a solvent [2].
The previous procedure can be combined with the addition of crystal seeds, polymers or other compounds. For example, the crystallization procedure may be influenced by adding crystal seeds even with a micro syringe with the aim to obtain a specific crystalline phase. Also, minute amounts of polymers can be added to the sample to facilitate the formation of new crystalline phases. Finally, the capillary can be filled with mixtures of compounds with the intention to form co-crystals or crystals originating from chemical reactions [3]. The described methodologies are of special interest in the crystallization of polymorphs, salts and co-crystals of pharmaceutical compounds.
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Figure 1: Image of a capillary showing the results of the "in situ" crystallization with a CO_2-laser applied on a solution of the sample. The single crystal in the center could be further increased by heating the surrounding solids.

Keywords: in situ crystallization, charge density studies, multi-component samples