Crystallization of α-glycine by anti-solvent assisted by ultrasound

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Introduction

In this work, we studied the crystallization of α−glycine by addition of an anti-solvent (ethanol) assisted by ultrasound. The glycine is an amino acid presenting three polymorphs: α−glycine, γ−glycine and β-glycine. At room temperature, the γ−glycine is the most stable [1, 2]. It is soluble in the water and insoluble in ethanol.

Previous works on cooling crystallization of glycine with ultrasound in aqueous phase showed that a purer crystalline phase with moderate power is formed with more regular faces [3] and a decrease of the induction time when the ultrasonic power increases [4].

Materials and Methods

Pure α−glycine is used for experiments (VWR CHEMICALS, 99,9 % purity). The experiments of crystallization are conducted in a solution of 150 ml shaken by a magnetic rod. A solution of concentration 0.26 kg α−glycine / kg water is prepared at 35 °C (5 °C above the temperature of saturation). This solution is then cooled at 30 °C (temperature close to the temperature of saturation of the initial solution). The ultrasound is then applied to various powers thanks to a plunging transmitter (generator Bioblock, 20 kHz). Once the temperature is stabilized at 30 °C, ethanol is added at a constant flow rate by means of a syringe pump. The addition rate varies between 0.04 in 0.36 g of ethanol/min. The measurement of refractive index of solution permits to follow the concentration of glycine $C_{glycine}$ during the experiment. The supersaturation ratio (S) is calculated by the ratio of C and $C_{\alpha-glycine,eq}$. $C_{\alpha-glycine,eq}$ is the equilibrium concentration of α−glycine measured for this study. At the end of the experiments, the suspension is filtered, the solid washed with ethanol and dried at 60 °C. The final crystals are characterized by their final size distributions measured by laser granulometry, their morphologies observed by scanning electronic microscope (SEM) and their crystalline structures by differential scanning calorimetry (DSC). The influence of ultrasonic power (continuous or pulsed modes) measured by calorimetry method is studied for different addition rates. The maximal supersaturation ratio S_{max} and the induction time (time between S = 1 and S_{max}, Fig.1) are observed.

Results and Conclusion

Analysis by DSC with a heating rate of 5 °C/min between 20 and 200 °C show no endotherm of transformation of α−glycine towards γ−glycine [1]. This means that pure metastable α-form is obtained whatever the operating conditions. A decrease of induction time and of S_{max} is observed in the presence of ultrasound (Fig. 1).

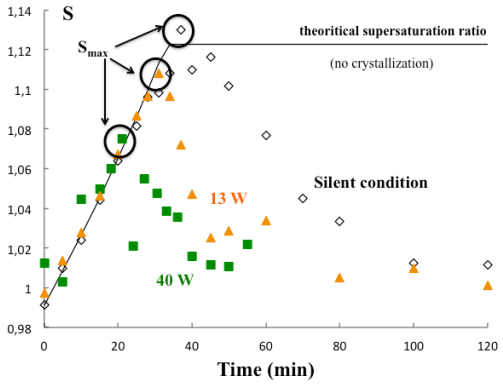

Figure 1. Supersaturation ratio as function of time for experiment conducted with an addition rate of 0.19 g ethanol/min in silent condition or with ultrasound (13, and 40 W)

In presence of ultrasound, smaller crystals with a monomodal size distribution are obtained at the end of the crystallization (final supersaturation ratio equal to 1). The rate of de-supersaturation is higher in presence of ultrasound inducing a higher nucleation rate or a higher growth rate or both. From experimental results, modeling of crystallization will permit to conclude on crystallization rates.

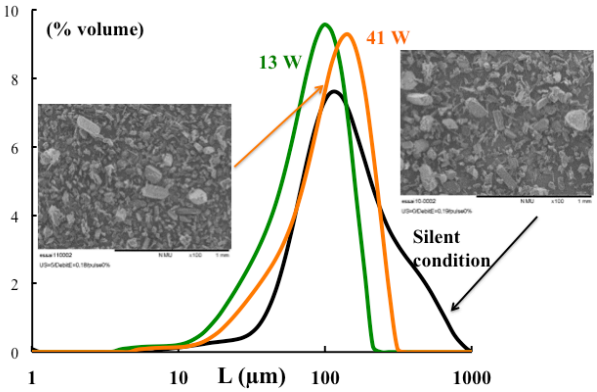

Figure 2. Size distributions of final crystals for experiment conducted with an addition rate of 0.19 g ethanol/min in silent condition or with ultrasound (13 and 40 W)

The use of pulsed ultrasound (50 one/50 off) seems to be interesting because similar results are obtained: same size distributions and same concentration profiles.

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