Effects of Process Conditions on Crystals Obtained from Supercritical Mixtures

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Crystalline and amorphous powders with morphologically uniform particles having narrow size distributions are important in a variety of applications, ranging from the manufacturing of pharmaceutical organic products to the use of monodisperse polymer spheres as drug delivery vehicles or as high performance liquid chromatography packings.

The solubility of solids in supercritical fluids is a very sensitive function of temperature and pressure. Because supercritical fluids are highly compressible, small changes in pressure result in large changes in density and solvent power (Kumar and Johnston, 1988); the rapid expansion of a supercritical solution thus gives rise to very large supersaturation ratios. The speed at which pressure perturbations propagate within the fluid allows precipitation from an essentially uniform medium and clearly distinguishes this process from conventional crystallization, where temperature gradients give rise to a wide distribution of nucleation rates within the solvent. The uniform conditions within the nucleating environment should result in the production of particles that are more even in morphology and narrower in size distribution than those produced by conventional crystallization techniques. This has prompted the interest of several researchers, who have performed exploratory studies (Krukonis, 1984; Larson and King, 1986) and investigated the influence of preexpansion conditions on the morphology of organic and inorganic powders obtained from supercritical mixtures (Petersen et al., 1986; Matson et al., 1986 a,b; 1987 a,b).

To date, the influence of post-expansion conditions upon the characteristics of the solid products has not been addressed. In this study, a systematic investigation of the effects of pre- and post-expansion conditions upon the characteristics of naphthalene powders was performed. The powders, obtained by expanding the supercritical mixture into a crystallizer whose bulk temperature, pressure and composition were independently controlled, were found to be crystalline in all cases. Particle size was found to be a sensitive function of pre-and post-expansion temperature and of preexpansion naphthalene concentration, suggesting the possibility of an accurate control of product characteristics through small changes in process variables.

Experimental

The experimental apparatus, Figure 1, has the distinguishing feature of allowing the independent control of all relevant process variables, namely pre- and post-expansion temperature, pressure and composition. The solvent (CO_2, MG "Bone Dry") is delivered by a variable stroke dual-piston pump, A (Milton Roy Minipump), to a preheater, E, which is immersed in a water bath, D, whose temperature is controlled to within ±0.01°C by a heater-circulator, F (Braun Thermomix 1460). The fluid is then introduced into the extraction column, C (2.54 O.D. × 30 cm), which is packed with alternate layers of glass wool and solute. A second piston pump allows the dilution of the saturated exit stream with fresh solvent. The temperature throughout the apparatus is measured by type J thermocouples, and displayed with a precision of ±0.1°C (Omega Digicator, model 412B). The extraction pressure is monitored by a digital gauge (model 901B Heise Gauge, 0-690 bar, ±0.05% accuracy).

The supercritical mixture then enters a laser-drilled, 25 μm ID × 0.25 mm nozzle (made by Advanced Laser Systems, Waltham, MA) designed for rapid expansion, with typical fluid residence times lower than 10^{-5} s. The preexpansion temperature is adjusted through a variable resistance heating cable wrapped around the nozzle. The expanded fluid then enters a high pressure crystallizer, G (Ruska Cell model 2329-800), equipped with a see-through glass window and immersed in a silicone oil bath, D, whose temperature is controlled to within ±0.01°C by another heater-circulator, F, for heating duty, and by an immersion cooler, H (Neslab model IBC-4), together with circulator F, for cooling duty. The crystallizer's pressure, which is controlled by feeding pure solvent through pump B and by venting through micrometering valve I (Autoclave Engineers 30VRRM), is measured by a model 901A Heise Digital Gauge

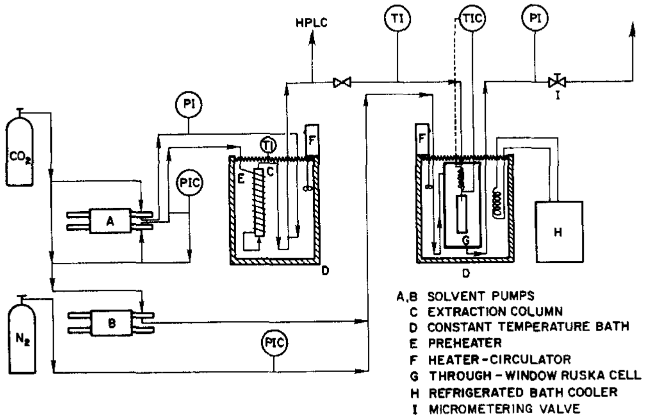


Figure 1. Experimental apparatus.

(0-414 bar, ±0.1% accuracy). An inert, such as nitrogen, can also be fed to lower the solvent's concentration inside the crystallizer. Particles are collected in a glass tube located inside the crystallizer.

The use of low solvent flow rates (between 0.1 and 0.5 std. L/min) guarantees the attainment of saturation conditions at the extraction column's outlet (Kurnik et al., 1981; Chang and Morrell, 1985; Pennisi and Chimowitz, 1986).

Results and Discussion

This work is a part of an ongoing project in which several model systems are being studied in order to understand, and eventually, predict the effects of process variables upon the morphology and size distribution of the solid products obtained by expanding supercritical solutions. In what follows, we describe the trends which we have so far found to be important and reproducible.

Virgin naphthalene particles (Fisher Scientific, N7-500) were charged into the column, C, Figure 1, extracted with CO_2 at 221.4 bar and 45°C, and expanded through the laser-drilled nozzle to 18.7 bar and 45°C, after being heated to 135°C. The

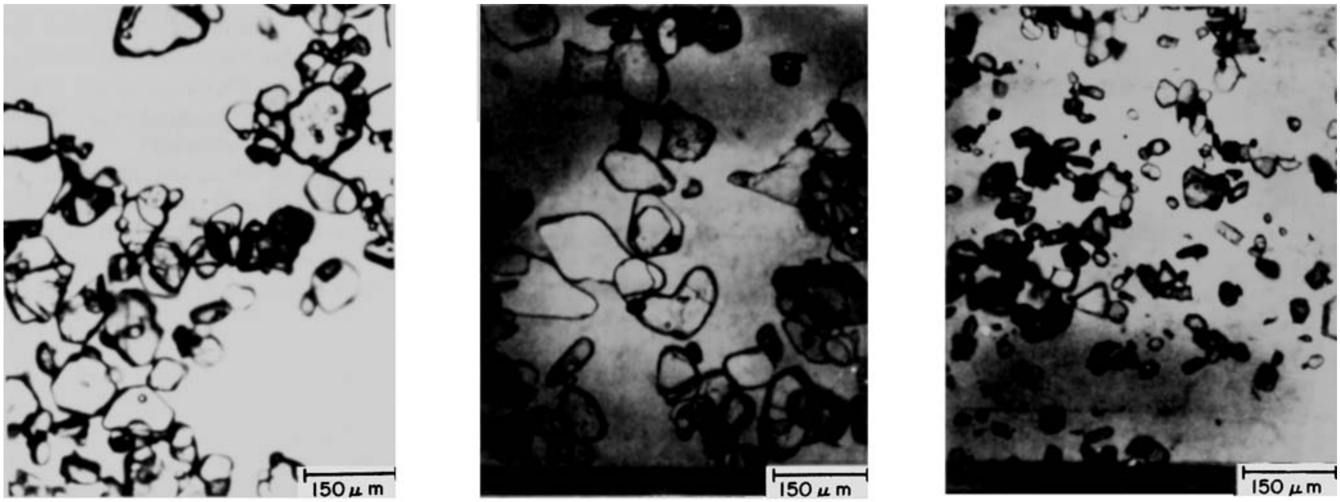
Table 1. Experimental Conditions and Results

	Extraction		Precipitation				
Run No.	Pres. bar	Temp. °C	Pres. bar	Temp. °C	Pre-expansion Temp. °C	$y^* \times 10^4$	Approx. Size† μm
			Preexpansion Temperature (Moderate Concentration)				
2	221.2	45	18.1	45	170	260	38–225
1**	221.4	45	18.2	45	135	260	30–135
3	221.2	45	17.9	45	110	260	8–75
			Preexpansion Temperature (High Concentration)				
6	362.3	55	18.0	45	170	573	4–51
4	362.0	55	17.9	45	135	573	4–38
5	361.9	55	17.7	45	135	573	4–39
7	362.0	55	17.8	45	110	573	2–35
			Post-Expansion Temperature				
1	221.4	45	18.2	45	135	260	30–135
8	221.7	45	18.3	7	135	260	6–29
18	148.4	45	18.0	45	135	192	15–83
9	148.9	45	18.1	8	110	192	2–15
10	148.6	45	18.0	−8	110	192	4–19
4	362.0	55	17.9	45	135	573	4–38
11	361.8	55	18.2	7.5	135	573	2–16
			Naphthalene Concentration				
12	221.5	55	17.9	45	135	444	6–32
1	221.4	45	18.2	45	135	260	30–135
4	362.0	55	17.9	45	135	573	4–38
15	362.2	35	17.9	45	135	188	14–78
			Post-Expansion Pressure				
16	221.2	45	70.0	45	135	260	15–113
17	221.7	45	44.6	45	135	260	15–105
1	221.4	45	18.2	45	135	260	30–135
			Preexpansion Pressure				
15	362.2	35	17.9	45	135	188	14–78
13	221.4	35	18.1	45	135	174	38–188
14	221.3	35	17.9	45	135	174	23–165
18	148.4	45	18.0	45	135	192	15–83
			Reproducibility				
4	362.0	55	17.9	45	135	573	4–38
5	361.9	55	17.7	45	135	573	4–39
13	221.4	35	18.1	45	135	174	38–188
14	221.3	35	17.9	45	135	174	23–165

*Mole fraction of naphthalene as obtained from the data of Tsekhanskaya et al. (1964)

**Base case

†From optical microscopy, using 500× magnification



(a) (b) (c)

Figure 2. Photomicrographs of naphthalene produced with preexpansion solute mole fraction of 260 × 10^{-4} and preexpansion temperatures of: 135°C (a); 170°C (b); and 110°C (c).

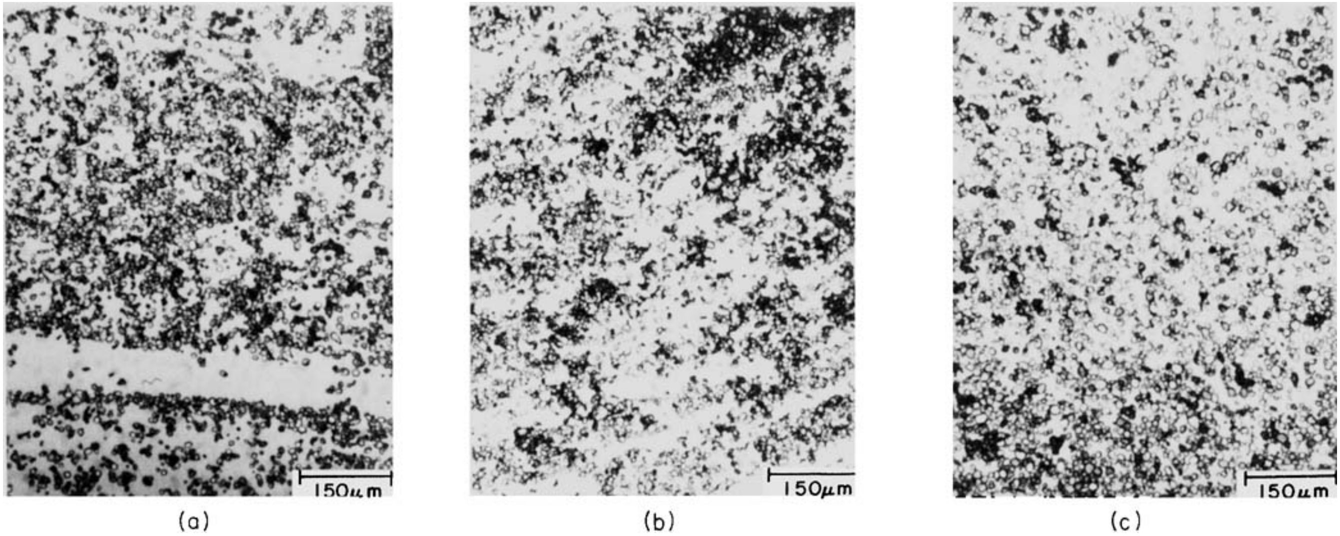


Figure 3. Photomicrographs of naphthalene powders produced by cooling crystallizer to: 8°C (a); 7.5°C (b); and −8°C (c).

precipitated particles ranged in size from 30 to 135 μm, Figure 2a. In subsequent experiments, the pre- and post-expansion temperature, pressure, and composition were systematically perturbed around this base case (Run 1, Table 1), in which the crystallizer pressure corresponded roughly to the solubility minimum of Naphthalene in CO_2 at 45°C (Tsekhanskaya et al., 1964). In all cases, the preexpansion temperature was kept high enough to prevent carbon dioxide condensation upon expansion.

Changes in the preexpansion temperature about the base case value of 135°C resulted in a pronounced effect on particle size. Increasing the temperature to 170°C produced larger particles, while a decrease in temperature to 110°C resulted in smaller particles, Runs 1, 2 and 3; Figure 2. Similar experiments, performed at higher solute concentrations, however, revealed little effect of the preexpansion temperature on particle size (Runs 4, 5, 6 and 7).

The post-expansion temperature (in contrast to the pre expansion temperature) was found to be important both at high and low naphthalene concentrations. Crystallizer bulk temperatures from 8°C to −8°C resulted in the production of naphthalene crystals with similar size distributions that ranged from approximately 2 to 29 μm (Runs 8, 9 at 7 and 8°C, respectively, Figure 3a; Run 11 at 7.5°C, Figure 3b; Run 10 at −8°C, Figure 3c). This large reduction in particle size with respect to the base case is very interesting, since it suggests a decoupling of nucle-

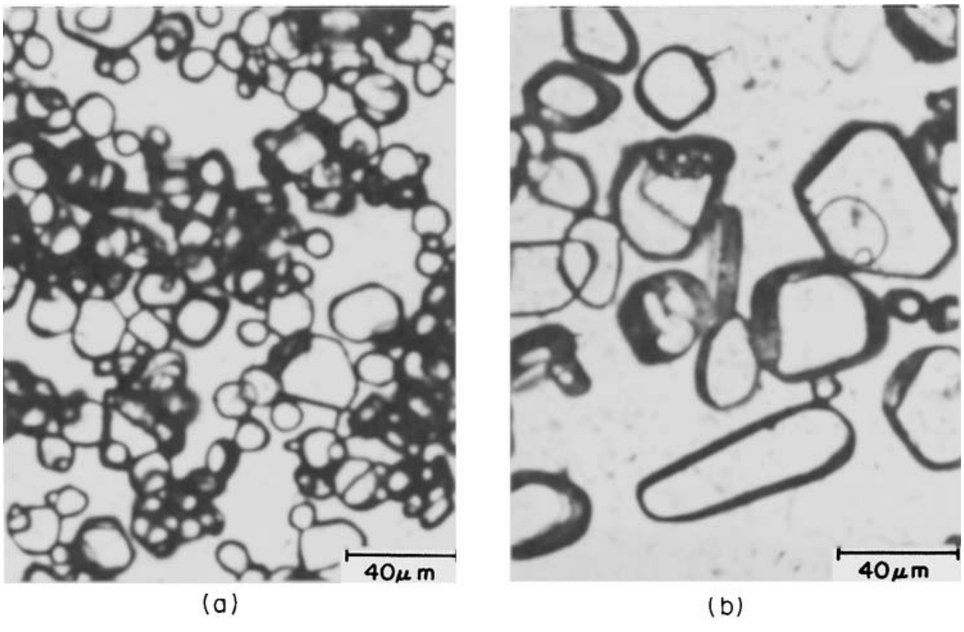


Figure 4. Photomicrographs of powders obtained with pre expansion naphthalene mole fractions of: 573 × 10^{-4} (a); and 188 × 10^{-4} (b).

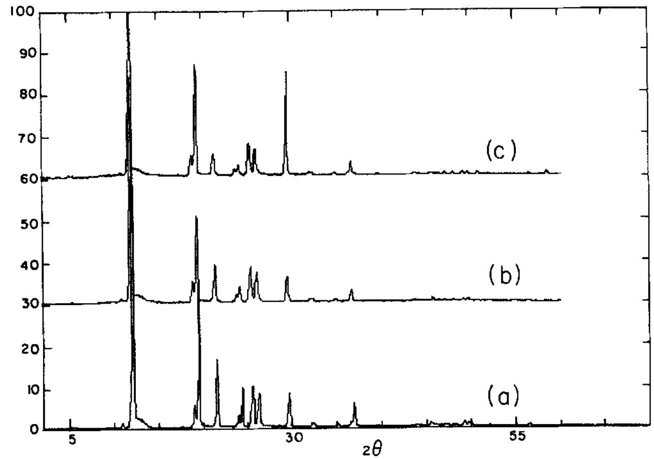


Figure 5. X-ray diffraction patterns: from original naphthalene (a); and from powders produced in runs 1 (b) and 8 (c).

Vertical axis represents intensity in arbitrary units. All other experiments produced similar results.

and growth processes. This separation, which is very difficult to attain in conventional crystallization processes, would allow a very sensitive control of the size of the precipitated product.

The concentration of naphthalene in the supercritical fluid is easily altered by a change in either the extraction temperature or pressure. At a given extraction pressure, increasing the mole fraction of naphthalene before expansion was found to result in a decrease in the size of the precipitated particles (Runs 1, 12, 4, 15, Figure 4). An increase in the naphthalene concentration leads to higher supersaturation ratios in the fluid upon expansion. According to the classical theory of nucleation (McCabe and Smith, 1967; Matson et al., 1987a; Turner et al., 1988), this leads to higher nucleation rates. Since, according to this theory, the particle volume is inversely proportional to the nucleation rate, our results appear to be consistent with simple theoretical predictions.

A moderate decrease in particle size resulted upon post-expansion pressure increase, Runs 1, 16 and 17. Results obtained upon changing the preexpansion pressure proved inconclusive (Runs 18, 13, 14, 15). Sonic conditions existed in all experiments, despite any changes in upstream conditions.

Comparison of the X-ray diffraction patterns of the virgin naphthalene particles and those of powders obtained from supercritical mixtures, Figure 5, indicate identical structure and retention of crystallinity. This was also confirmed upon optical examination of the particles in polarized light.

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