Fractional Crystallization by Gas Antisolvent Technique: Theory and Experiments

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The efficacy of CO_2 as an antisolvent was studied experimentally for the precipitation of naphthalene and phenanthrene from their solutions in toluene at 298 and 310 K. Phenanthrene was salted out of solution at every condition investigated, whereas naphthalene was never segregated as a solid phase. These behaviors are explained by a model representing the composition of the phases and supersaturation of the solution as functions of pressure. Based on results from ternary systems, experiments were performed with the quaternary system CO_2-toluene-naphthalene-phenanthrene: starting from an equimolar solution of the two solids in toluene, phenanthrene with a purity higher than 98.5% can be collected in the precipitation cell, while naphthalene with about 13% of phenanthrene is recovered from the liquid phase after expansion. The simulation of the process was able to account for the experimental evidence. Although the solutes used do not have a practical application, a general method is outlined to exploit the possibility of using the supercritical antisolvent technique for separation.

Introduction

When a solid mixture is to be separated into single components, classical separation techniques are not always suitable. In general, distillation is not applicable with heavy compounds. Selective solvent extraction, or selective precipitation with a liquid antisolvent, are surely more useful. However, it can be difficult to purify the separated products from the extraction solvents used. This may require high temperatures, sometimes under vacuum, and it is still not always possible to obtain a completely dry and pure solute. This result is usually acceptable in common industrial practice, but can represent a problem in the pharmaceutical, food and fine chemicals industries, where materials of great value need to be produced at very high purity and completely solvent-free.

In this field, supercritical fluid technology can play a role of primary importance (McHugh and Krukonis, 1993). Although extraction with dense gases is successfully used to obtain essences, flavors, aromas from solid or liquid matrixes, or on the contrary to purify a matrix from noxious impurities, they can be applied more profitably for material processing. Techniques such as the Rapid Expansion of a Supercritical Solution (RESS) and the gas antisolvent recrystallization (GAS) are promising in this respect.

Recently, these techniques, which were initially used only to obtain the comminution and micronization of difficult-to-handle materials, have been evaluated as interesting potentials for the development of novel separation processes. An attempt to use RESS for the fractionation of solid mixtures was performed by Liu and Nagahama (1996) and Nagahama and Liu (1997). Starting from supercritical solutions of naphthalene and phenanthrene in CO_2, they obtained some enrichment in naphthalene of the precipitated particles. Such a result is probably due to the fact that the supercritical solution is more diluted in phenanthrene. Therefore, the supersaturation is higher for naphthalene, while some phenanthrene remains in the gas phase and is carried away by CO_2. The enrichment factor β is defined as follows by the referred authors

$$\beta = \frac{x_{Na}/x_{Ph}}{y_{Na}/y_{Ph}} \tag{1}$$

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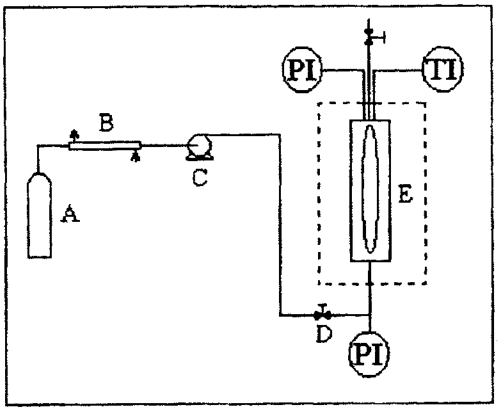

Figure 1a. Experimental apparatus for precipitation pressure measurements.

(A) CO_2 reservoir; (B) cooler; (C) pump; (D) regulation valve; (E) precipitation cell.

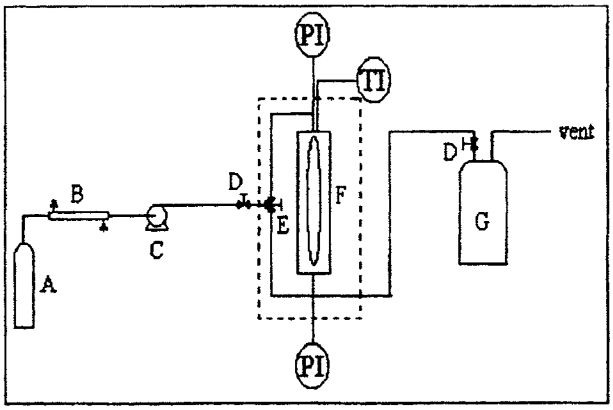

Figure 1b. Experimental apparatus for separation experiments.

(A) CO_2 reservoir; (B) cooler; (C) pump; (D) regulation valve; (E) three-ways valve; (F) precipitation cell; (G) expansion vessel.

where x_{Na} and x_{Ph} are the mole fractions of naphthalene and phenanthrene in the precipitated crystals, while y_{Na} and y_{Ph} are those in the supercritical solution before expansion. A maximum β value of 3.19 was observed by Liu and Nagahama.

According to the GAS technique (Gallagher et al., 1989; Yeo et al., 1993), the precipitation can be performed by adding an antisolvent (usually CO_2) to a solution of the solute of interest with a suitable organic solvent. The dissolution of CO_2 lowers the solubility of the solute and forces it to precipitate; the solid phase is usually obtained at moderate pressure (60 to 100 bar). Even with the same solvent-antisolvent pair and at the same conditions of temperature and initial solute composition, the precipitation pressure is generally different for different solutes. This can be exploited to separate substances. For example, Dixon and Johnston (1991) measured the solid(S1)-solid(S2)-liquid(L)-vapor(V) equilibrium for the system CO_2-toluene-phenanthrene-naphthalene and discussed, from a theoretical point of view, the potential of using a GAS technique to separate naphthalene from phenanthrene. Chang et al. (1994) proposed an approach to evaluate the possibility of fractionating two solutes without using information about the quaternary system solute1-solute2-solvent-antisolvent. Shishikura et al. (1991, 1992, 1994) presented a method to separate citric acid from sugar impurities and oxalic acids by using CO_2 as the antisolvent. Acetone was used as the solvent; in a first step, carried out at 30°C and 25 bar, impurities were removed, and in a second step, at 30°C and 50–57 bar, citric acid was precipitated from the solution, while oxalic acid was not.

Catchpole et al. (1996) applied GAS separation to mixtures of lecithin and soya oil: even if experiments with single solutes showed different precipitation pressures, the difference in their values was much lower when processing the two solutes together. Therefore, the authors concluded that it is impossible to predict the possibility of separating a mixture starting from precipitation pressure measurements on the single solutes.

Finally, Foster et al. (1997) showed how ortho- and para-hydroxybenzoic acids could be fractionated using methanol as a solvent and CO_2 as an antisolvent. The authors obtained a product containing 99% of para-isomer, and observed that the possibility of achieving a separation is connected qualitatively to the different solubilities of solutes in CO_2: the higher the solubility, the higher the precipitation pressure.

The objective of this work is to demonstrate how the GAS process can be used to separate mixtures of phenanthrene and naphthalene. Simulation and experiments of batch GAS processes applied to both ternary and quaternary systems are presented. These solutes, which are not of interest for practical application, have been selected because they are well characterized. Equilibrium data with toluene as the solvent and CO_2 as the antisolvent are available (Dixon and Johnston, 1991), and they can be represented well by a simple thermodynamic model (Kikic et al., 1997b).

Experimental Apparatus

The experimental apparatus for the precipitation pressure measurements is sketched in Figure 1a. The view cell (Klinger, type K model), with an internal volume of about 50 cm^3, is the main component of the apparatus. It is equipped with a glass window on the full length and with a porous metallic filter (frit, Supelco, 5-8255) at the bottom, to prevent liquid from flowing out of the cell during loading, and to filter the precipitated solid. It is thermostated within ±0.1 K in an air-bath thermostat (Memmert, ULE 500). Liquid CO_2 from the reservoir is cooled down and then pumped into the cell by a syringe pump (ISCO). A regulation valve (Whithey, SS-21RS4) allows the control of CO_2 flow rate to the cell. Two pressure transducers (Druck Limited, ±0.1 bar accuracy) are used. The first transducer is located under the frit, and the second is located on top of the cell. They allow measuring the pressure drop through the porous frit. When a consistent pressure drop (that is, higher than 5 bars) is detected, the frit is becoming clogged. In all cases, a maximum pressure drop of 10 bar is allowed so as not to damage the frit. Temperature inside the cell is measured by a RTD platinum probe accurate to ±0.1 K.

At the beginning of the run, a small amount (5 cm^3) of solution of known composition is charged into the cell. CO_2

is fed from the bottom and bubbles through the liquid phase dissolving in it. The pressurization is performed in increments of about 5 bar. Between each increment, the system is allowed to equilibrate for approximately 20 to 30 min. The run is stopped when the precipitation has occurred or when the cell is filled with the liquid phase, as a consequence of the volumetric expansion induced by CO_2 dissolution. A ball valve at the top of the cell allows fast evacuation at the end of each run.

Some modifications of this apparatus were needed for the fractionation experiments, as represented in Figure 1b. A three-way valve (Whithey, SS 41XS2) allows CO_2 to enter the cell either from the bottom or from the top. At the bottom, a discharge pipe is now inserted, which allows CO_2 to flow through the cell continuously. A regulation valve (Whithey, SS-21RS2) is used to maintain a constant pressure and is heated by an electrical resistance to prevent freezing. Finally, the liquid solvent and the solid particles which eventually segregate from the gas phase due to the pressure reduction are collected in an expansion vessel.

To perform the experiment, the solution with the two solutes at known composition is first loaded into the cell. Pressurization is induced from the bottom, step by step, until precipitation is observed. Then, CO_2 is allowed to flow into the cell from the top by switching the three-way valve, in order to wash and dry the precipitated particles from liquid solution and solvent residuals. This operation is performed at constant pressure. The solute, which has not been precipitated, is segregated by expanding the liquid and gas phases and can be collected in the expansion vessel. After about 30 min under CO_2 flow, the cell is depressurized and the precipitated particles can be sampled.

Materials and Analysis

Naphthalene (99%) and phenanthrene (98%) were obtained by Aldrich, and used without further purification; CO_2 with a purity of 99.98% was purchased by SIAD; toluene (HPLC grade, 99.98%) was supplied by Carlo Erba (Italy).

Quantitative analyses of the samples collected in the cell and in the expansion vessel were performed in a HPLC system, equipped with a double-piston pump (Waters, 510 model) and a UV/Visible detector (Waters Absorbance Detector 441, with a zinc lamp at 214 nm). *N*-heptane was used as solvent and mobile phase with a flow rate of 1 mL/min; 5 μl samples were injected and separation was performed by a Chrompack column (4.6 mm ID, 25 cm long) with Petrospher A as the stationary phase. The signal was recorded by an integrator (Shimadzu C-R3A), which calculated the wt. % of each substance detected, providing directly the quantitative determination of naphthalene and phenanthrene. The expected error in the mole fractions is $\pm 0.1\%$.

Experimental Results

Three-component systems

For the system CO_2-toluene-phenanthrene, the precipitation pressure of phenanthrene, that is, the pressure value at which the first appearance of solid is detected, is shown in Table 1 as a function of initial solution concentration and temperature. Note that precipitation also takes place when the initial solution is diluted. At a lower initial concentration of the solute, a higher pressure is needed to obtain precipitation. In fact, a more diluted solution requires a higher CO_2 mole fraction, that is, a higher pressure, to obtain the same level of supersaturation.

Table 1. Experimental and Calculated Precipitation Pressures for the System CO_2-Toluene-Phenanthrene

T (K)	$x_{0\text{phen}}$	P_{precexp} (bar)	P_{precalc} (bar)
298.5	0.15	52.2	51.1
299.2	0.10	58.0	55.5
299.2	0.05	62.0	59.1

For the system CO_2-toluene-naphthalene, experiments have been performed at 299 K, 309.5 K, and 319 K, and with initial naphthalene mole fractions of 0.25, 0.35, and 0.452, respectively.

Precipitation of a solid phase was never observed as a consequence of pressurization with CO_2, even if the initial concentrations were very close to their saturation value at the operating temperature. At $T = 299$ K, a pressure of 66 bar was reached, which caused a volumetric expansion of the liquid phase of over 1,000%. At $T = 309.5$ K, a vapor-liquid critical point was observed at a pressure of approximately 85 bar. Therefore, by further increasing pressure, a unique supercritical phase containing CO_2, toluene, and naphthalene was obtained. At $T = 319$ K and $P = 88$ bar, the liquid phase splits into one CO_2-rich and one naphthalene-rich phase. At first, the liquid became hazy, then the two phases separated, the meniscus became evident, and the two liquids finally cleared up. These two phases merged again at 90 bar. All of these findings are in good agreement with phase equilibrium literature data (Hong and Luks, 1992).

Four-component system

In order to explore the possibility of separating phenanthrene from naphthalene, additional runs were carried out in the same apparatus starting from toluene solutions of both compounds. Experimental conditions and results are summarized in Table 2. Note that mole fractions are as follows: $x_{0\text{phen}}$ and $x_{0\text{napht}}$ refer to phenanthrene and naphthalene in the initial solution, x_{phencell} and $x_{\text{naphtcell}}$ to phenanthrene and naphthalene in the samples from the cell, and x_{naphtexp} to naphthalene in the samples from the expansion vessel. The separation factor S is defined as follows

$$S = \frac{x_{\text{phencell}}/x_{\text{naphtcell}}}{x_{0\text{phen}}/x_{0\text{napht}}} \tag{2}$$

Table 2. Experimental Results for the System CO_2-Toluene-Phenanthrene-Naphthalene

T (K)	$x_{0\text{phen}}$	$x_{0\text{napht}}$	P_{prec} (bar)	x_{phencell}	x_{naphtexp}	S
298.0	0.17	0.17	58	0.987	0.868	75.9
298.0	0.17	0.17	60	0.984	0.871	61.5
308.0	0.252	0.199	78	0.967	—	29.3

In all experiments, before precipitation started we noticed the appearance of a second liquid phase. In the first two runs, precipitation was detected soon after the two liquid-phase split; in the third run, demixing occurred at 70 bar, while precipitation began later (78 bar).

At all conditions explored, high purity phenanthrene was collected from the cell. The purity decreased with increasing temperature. We note that, in the first run at 298 K (Table 2), the purity is slightly higher than in the second run at the same temperature. In the first run, the feed of CO_2 was stopped immediately after precipitation started, while in the second run the feed of CO_2 continued and precipitation was allowed to occur for a longer time. Thus, a larger amount of powder was produced in the cell and probably was coated by the remaining solution; during the following washing process, toluene evaporated from the surface of the crystals leaving a little amount of naphthalene. From Table 2, we also note that the powder obtained in the expansion vessel is naphthalene, with about 13% of phenanthrene. At 308 K, nothing was precipitated in the expansion vessel, since both naphthalene, which has a high sublimation pressure, and toluene have been carried away in the gas phase.

It was concluded that phenanthrene can be successfully separated from naphthalene by the GAS technique, even though a little of its initial amount was lost, since precipitation was not complete at the conditions considered.

All samples collected from the cell and from the expansion vessel are solvent-free: the liquid phase is completely withdrawn from the cell and, after expansion, toluene can be completely removed by simply flowing CO_2 for a suitable time (30 to 45 min).

In our case, the quaternary system behavior can be predicted almost exactly from experiments performed on the ternary systems. As a conclusion, an almost complete separation of the two compounds is possible. This result is also confirmed if, according to Foster et al. (1997), we compare the solubility of the solutes in the supercritical antisolvent. Naphthalene is much more soluble than phenanthrene in supercritical CO_2 and only a little amount of it is expected to be precipitated by the CO_2 antisolvent action.

Modeling the GAS Process

We attempt to understand why phenanthrene always precipitates (even if the initial solution is diluted), while naphthalene does not (even if the initial solution is very close to saturation).

In order to explain these different behaviors, it is useful to develop a model of the batch GAS process. In this way, the composition profiles of the liquid and gas phases in the cell as a function of pressure can be simulated, starting from the given initial composition of the liquid at atmospheric pressure. The pressure at which the solution becomes supersaturated is also calculated.

Three-component systems: thermodynamics

In the GAS process a solute is precipitated from a liquid solution by means of the antisolvent action of a dense gas, whose solubility in the liquid is increased by increasing pressure. From a thermodynamic point of view, a solid-liquid-vapor (S-L-V) equilibrium has to be modeled. Since the effect of pressure is of large importance, an equation-of-state approach is needed. Note that the effect of pressure is simply indirect, because when pressure is increased, the amount of CO_2 in the liquid phase also increases, and when enough CO_2 is solubilized the solute precipitates. The Peng-Robinson equation of state (PR EOS) with classical mixing rules was used for the liquid and vapor phases, while the solid phase (supposed to be pure solute) was represented by means of a subcooled liquid reference state, using the heat of fusion and the melting temperature of the solute itself. The model is extensively described elsewhere (Kikic et al., 1997a,b), and correlates well with the available literature data of S-L-V equilibrium for CO_2-toluene-naphthalene and CO_2-toluene-phenanthrene (Dixon and Johnston, 1991).

Three-component systems: process

Before precipitation starts, only two phases (liquid and vapor) coexist in the cell. It is assumed that they are always at equilibrium: this requires the pressurization rate to be slow, as is the case of our experimental procedure. Three equilibrium equations can be written for the antisolvent (CO_2, index 1), the solvent (toluene, index 2), and the solute (naphthalene or phenanthrene, index 3) in the liquid and vapor phases

$$x_1 \varphi_1^L P = y_1 \varphi_1^G P \tag{3}$$

$$x_2 \varphi_2^L P = y_2 \varphi_2^G P \tag{4}$$

$$x_3 \varphi_3^L P = y_3 \varphi_3^G P \tag{5}$$

where x and y are the mole fractions of each component in the liquid and vapor phases respectively, while φ^L and φ^G are the fugacity coefficients of each component in the two phases which are calculated by means of the PR EOS.

The total amounts of solute (n_{30}) and solvent (n_{20}) in the cell are constant during the experimental run (even if they split differently between the two phases), so the material balance leads to

$$R = \frac{n_{30}}{n_{20}} = \frac{(1-k)x_3 + ky_3}{(1-k)x_2 + ky_2} \tag{6}$$

where k is the vapor fraction (moles of gas/total moles in the cell).

Finally, a last condition is imposed by the volume of the cell

$$V = n\text{tot}[(1-k)\nu_L(T,P,\bar{x}) + k\nu_G(T,P,\bar{y})] \tag{7}$$

where ν_L and ν_G are the molar volumes of the liquid and vapor phases, respectively, V is the volume of the cell and $n$tot is the total number of moles in the cell

$$n\text{tot} = \frac{n_{30}}{x_3(1-k)} \tag{8}$$

Note that Eq. 8 holds if the solute mole fraction in the gas phase is negligible, as is the case. Equations 3 to 8, together with the condition that in each phase the sum of the mole fractions equals one, allow the calculation of the composition profile of each phase as a function of pressure and of the relative molar distribution of the phases k.

A simplified approach can also be performed. Since, at the conditions of interest, the amounts of solvent and solute in the gas phase are negligible, the terms in Eq. 6 containing y_2 and y_3 can be dropped, that is, the gas can be considered pure CO_2. Equations 3 to 6 are solved independently to calculate the equilibrium composition in each phase. Accordingly, Eq. 7 is not used, and it is not necessary to know the volume of the cell. Results obtained with this simplified method are very close to those obtained with the rigorous method. However, the use of this simplified approach has to be carefully evaluated if more volatile solvents (like, for example, acetone) are used together with higher temperatures (50°C and over).

The pure solid solute fugacity as a function of temperature and pressure is calculated by the PR EOS with a subcooled liquid reference state (Kikic et al., 1997a). When the pure solid solute fugacity becomes lower than the corresponding fugacity in the liquid phase, precipitation is likely to start. The system loses one degree of freedom, because an additional condition can be written

$$x_3 \varphi_3^L P = f_3^{0S} \tag{9}$$

and the composition of each phase is calculated once P and T are set according to the S-L-V equilibrium model briefly outlined in the previous paragraph.

If the volume of the cell and the amount of solute initially charged are known, it is possible to calculate the mol % of each phase (k_G, k_L, and k_S for the gas, liquid, and solid phase respectively)

$$R = \frac{n_{30}}{n_{20}} = \frac{k_G y_3 + k_L x_3 + k_S}{k_L x_2 + k_G y_2} \tag{6}$$

$$V = n\text{tot}[k_L v_L(T, P, \bar{x}) + k_G v_G(T, P, \bar{y}) + k_S v_S(T, P)] \tag{7}$$

$$n\text{tot} = \frac{n_{30}}{k_S + k_L x_3 + k_G y_3} \tag{8}$$

$$k_L + k_G + k_S = 1 \tag{10}$$

The amount of precipitated solute (PCP) with respect to its initial amount is given by

$$PCP = \frac{k_S}{k_S + k_L x_3 + k_L y_3} 100 \tag{11}$$

Also, in this case it is possible to neglect in Eqs. 6 and 8 y_2 and y_3 without affecting the calculated results. Since precipitation does not take place exactly at equilibrium conditions, a certain supersaturation of the solution is needed. Here, supersaturation SS is defined according to Liang (1994) as the ratio of the fugacities of the solute in the supersaturated liquid phase and in the solid phase

$$SS = \frac{f_3^L}{f_3^{0S}} \tag{12}$$

SS can be calculated as a function of T, P and the initial liquid composition.

If the amount of solution initially charged is large, it is possible that the cell fills up with liquid before precipitation is induced. At this point, the liquid in the cell is at equilibrium with the last bubble of gas and its composition can be calculated by the proposed model. After that, the precipitator contains only one phase, whose composition can be calculated from the further amount of CO_2 added to the cell. The molar density is written as

$$\rho = \frac{n_{30}}{x_3 V} \tag{13}$$

Pressure can be calculated by means of the PR-EOS. If the cell fills up after the precipitation has started, the situation is similar, since only the equilibrium equation of the solute in the liquid and solid phases is added to calculate the composition of the liquid.

Three-component systems: results

In order to interpret experimental data, several simulations were performed.

In Figure 2 the phenanthrene mole fraction in the liquid phase as a function of pressure for different liquid initial compositions is presented. The addition of CO_2 dilutes the liquid solution, providing a greater mass capacity for the solute so its mole fraction is lowered at increasing pressure. Whatever the initial composition is, the three-phase equilibrium (saturation) line is eventually crossed, which means that phenanthrene is precipitated: the higher the initial solute mole fraction, the lower the pressure required to reach this point, but the differences in pressure are small.

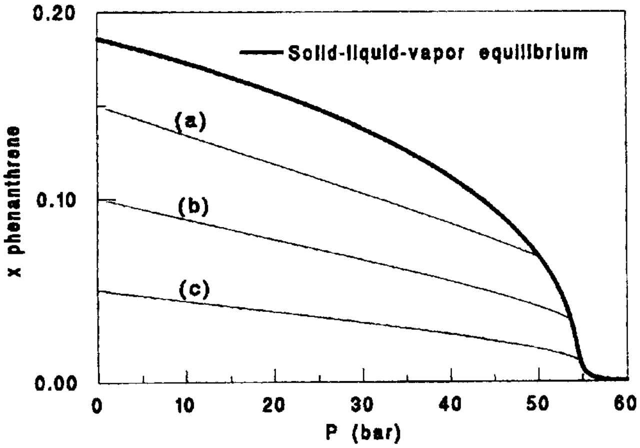

Figure 2. System CO_2-toluene-phenanthrene: S-L-V equilibrium and composition of the liquid phase during the pressurization at $T = 298$ K and different initial solute mole fraction.

(a) = 0.15; (b) = 0.10; (c) = 0.05.

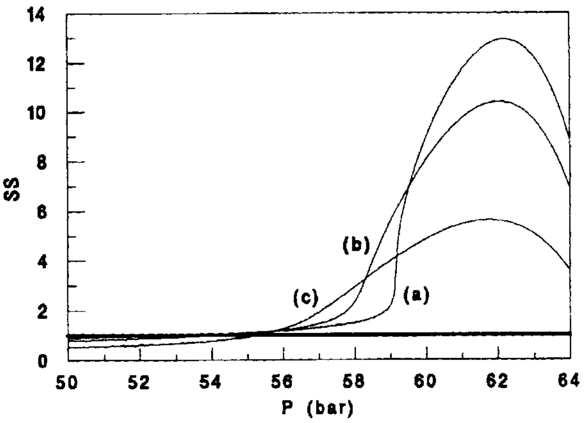

Figure 3. System CO_2-toluene-phenanthrene: solute supersaturation (SS) in the liquid phase at $T = 298.5$ K.

Initial solute mole fraction: (a) = 0.13; (b) = 0.10; (c) = 0.05.

In Figure 3, the supersaturation of the solution (SS) as a function of pressure at $T = 298.5$ K and the initial compositions from Figure 2 are plotted. High values of SS are also reached ($SS > 10$) in the case of a low-concentration starting solution. Even though there is a maximum, the high supersaturation values ensure precipitation of the solute at all initial conditions.

In Table 1 the last two columns report the experimentally measured and the calculated precipitation pressures for different initial solution mole fractions. It can be seen that the observed values are a bit larger than the corresponding predicted ones at equilibrium. The precipitation does not occur exactly at equilibrium conditions, because some driving force is required and it is given by solution supersaturation.

The presence of a maximum in the SS curve (Figure 3) sounds somehow strange. It is due to the behavior of the fugacity in the supersaturated liquid phase, which goes through a maximum. However, the precipitation starts at a pressure well below the maximum (see Table 1) and, hence, it refers to a merely hypothetical condition.

In Figure 4 the amount of precipitated phenanthrene with respect to the global amount initially charged is reported as a function of pressure. The calculation is performed with Eqs. 6, 7, 8, and 10, as if precipitation occurred at equilibrium conditions. A lower precipitation pressure corresponds to a higher initial concentration. In the latter case, precipitation is slower at the beginning (less-steep curve), which might suggest the formation of larger particles. A little amount of phenanthrene always remains in the liquid phase, but around 90% is recovered in the solid phase. Note that precipitation stops when the vessel is filled by liquid. This condition is unfavorable and has to be avoided.

As far as the system CO_2-toluene-naphthalene is concerned, the dissolution of CO_2 leads again to the dilution of the solution at increasing pressure, because of the greater mass capacity of the solution itself; however, in this case the only way to cross the S-L-V equilibrium line and to obtain supersaturation is to start with an almost saturated solution (Figures 5a, 5b, and 6). Moreover, the range of pressure where the solution becomes supersaturated is really narrow (Figure 6), that is, about 5 bars; after that, the S-L-V equilibrium line is crossed again (Figure 5b). These two features (low supersaturation value and small pressure range) make the precipitation of naphthalene impossible from a practical point of view at the temperature considered, even if the initial solution is concentrated. The same behavior is calculated also at higher temperatures (Figure 7). With phenanthrene, the antisolvent effect is always greater than the dilution effect, leading to the precipitation of the solute. With naphthalene, the antisolvent effect is again large (the solubility of naphthalene decreases from a mole fraction of 0.3 at atmospheric pressure to 0.0108 at 60.3 bar) (Dixon and Johnston, 1991), but it is always smaller than the dilution effect. It can be concluded that it is extremely difficult to precipitate naphthalene by the antisolvent action of CO_2.

We note that during the first phase of pressurization, CO_2 can also be regarded as a cosolvent, because the solution departs from saturation. This is not a real thermodynamic property of the system, because the mole fraction of naphthalene at equilibrium decreases monotonically when more CO_2 is dissolved. Rather, the cosolvent effect is a consequence of how the process is carried out, and in particular of the dilution effect caused by the dissolution of the CO_2 in the liquid.

Four-component systems: thermodynamics

This case involves four components: (1) antisolvent; (2) organic solvent; (3) first solute; (4) second solute. Since naphthalene and phenanthrene form a eutectic system, two solid phases are obtained rather than a solid solution, each one made of a pure solid solute.

According to experimental data by Dixon and Johnston (1991), both solutes were present as solids. Therefore, either four phases (S1, S2, L, V) or five phases (S1, S2, L1, L2, V) may coexist. In the first case the system has two degrees of freedom, which are saturated once P and T are set. In the

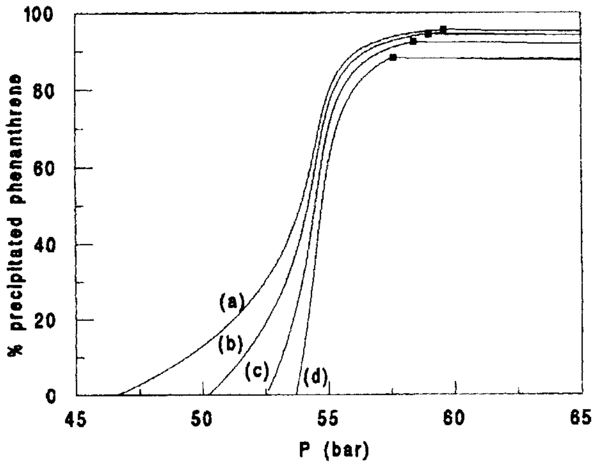

Figure 4. System CO_2-toluene-phenanthrene: percent of precipitated phenanthrene at $T = 298$ K and different initial solute mole fraction.

(a) = 0.17; (b) = 0.15; (c) = 0.125; (d) = 0.10; points indicate that precipitation cell becomes full of liquid phase.

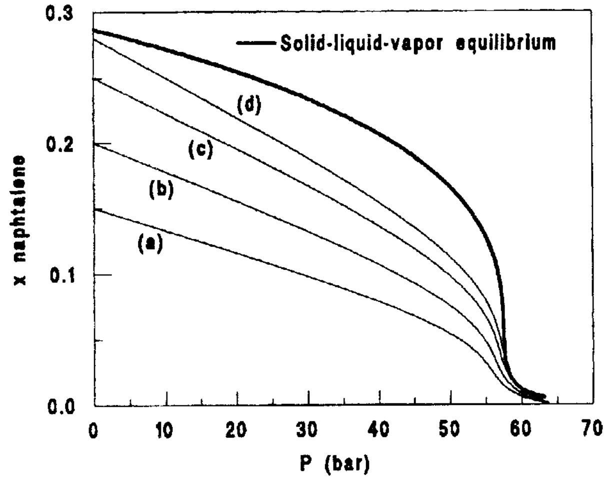

Figure 5a. System CO_2-toluene-naphthalene: S-L-V equilibrium and composition of the liquid phase during the pressurization at $T = 298$ K and different initial solute mole fraction.

(a) = 0.15; (b) = 0.20; (c) = 0.25; (d) = 0.28.

second case, it exhibits only one degree of freedom, which is saturated, for example, by assigning T.

With regard to the five-phase system, the following equilibrium equations can be written for each component in the two-liquid and in the vapor phases

$$x_1^{L1}\varphi_1^{L1}P = x_1^{L2}\varphi_1^{L2}P \quad (14)$$

$$x_2^{L1}\varphi_2^{L1}P = x_2^{L2}\varphi_2^{L2}P \quad (15)$$

$$x_3^{L1}\varphi_3^{L1}P = x_3^{L2}\varphi_3^{L2}P \quad (16)$$

$$x_4^{L1}\varphi_4^{L1}P = x_4^{L2}\varphi_4^{L2}P \quad (17)$$

$$x_1^{L1}\varphi_1^{L1}P = y_1\varphi_1^{G}P \quad (18)$$

$$x_2^{L1}\varphi_2^{L1}P = y_2\varphi_2^{G}P \quad (19)$$

$$x_3^{L1}\varphi_3^{L1}P = y_3\varphi_3^{G}P \quad (20)$$

$$x_4^{L1}\varphi_4^{L1}P = y_4\varphi_4^{G}P \quad (21)$$

The equilibrium equations for the two solutes between L1 and S1, S2 phases are given by

$$f_{30}^{S1} = x_3^{L1}\varphi_3^{L1}P \quad (22)$$

$$f_{40}^{S2} = x_4^{L1}\varphi_4^{L1}P \quad (23)$$

Again, fugacity coefficients are calculated by means of the PR EOS, as outlined above for ternary systems.

If only one liquid phase is present, the system exhibits two degrees of freedom; only Eqs. 16 to 21 have to be considered to solve the equilibrium problem.

The model has been tested on available S1-S2-L-V equilibrium data for the system CO_2-toluene-naphthalene-phenanthrene (Dixon and Johnston, 1991).

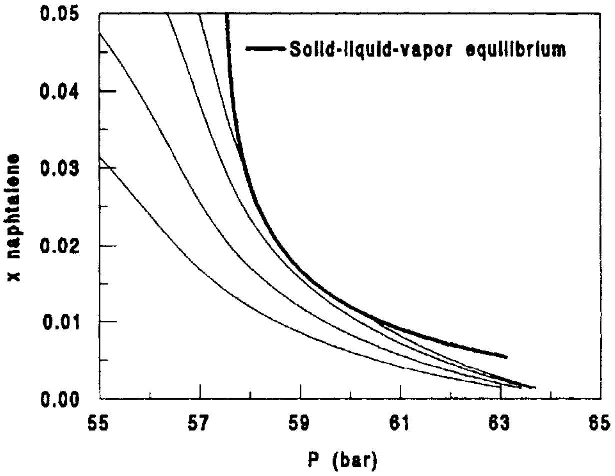

Figure 5b. Zoom of Figure 5a in the precipitation pressure range.

The values of the binary interaction parameters are the same as in the two ternary systems (Kikic et al., 1997a). For the pair naphthalene-phenanthrene, k_{ij} was calculated to represent solubility data of both in toluene. In particular, Dixon and Johnston (1991) reported that each solute acts as a cosolvent for the other one, leading to an increase of solubility in toluene of 17% for phenanthrene and 6% for naphthalene (on a molar basis) with respect to their solubility as unique solutes: we found that a value of $k_{ij} = -0.01$ represents this experimental evidence satisfactorily.

Comparison between experimental data (Dixon and Johnston, 1991) and calculations is shown in Figure 8, where the solubilities of naphthalene and phenanthrene in the liquid phase are reported as a function of pressure: the correlation is satisfactory. In their experiments, the referred authors did not detect the appearance of a second liquid phase. In our

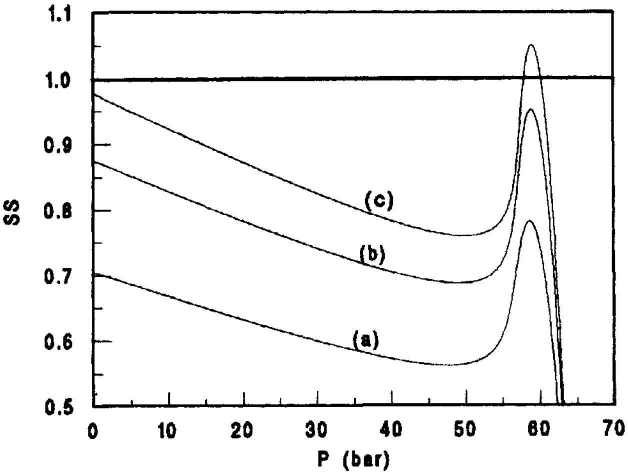

Figure 6. System CO_2-toluene-naphthalene: solute supersaturation (SS) in the liquid phase at $T = 298$ K.

Initial solute mole fraction: (a) = 0.2; (b) = 0.25; (c) = 0.28.

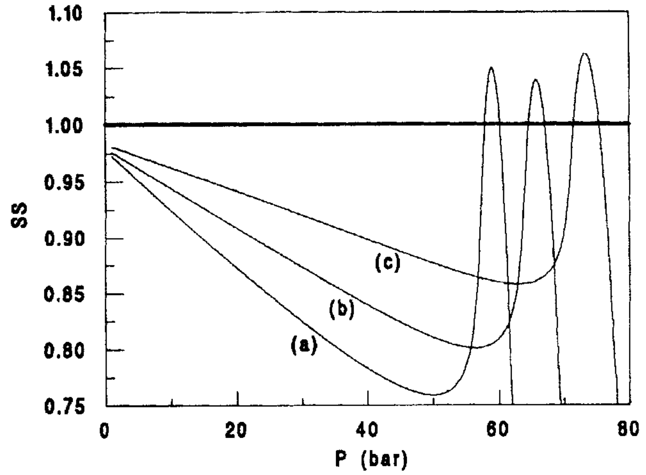

Figure 7. System CO_2-toluene-naphthalene: solute supersaturation at different temperatures and initial solute compositions.

(a): $T = 298$ K, $x_0 = 0.28$; (b): $T = 303$ K, $x_0 = 0.31$; (c): $T = 308$ K, $x_0 = 0.365$.

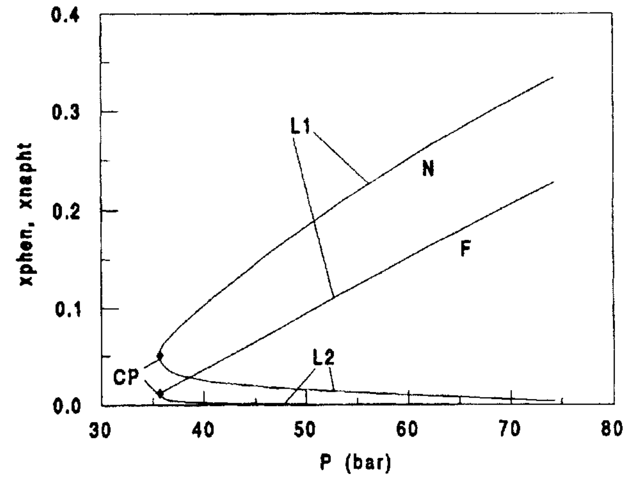

Figure 9. System CO_2-toluene-phenanthrene-naphthalene: mole fraction of phenanthrene (*F*) and naphthalene (*N*) in the two liquid phases at S1-S2-L1-L2-V equilibrium.

experiments a second liquid phase always appeared, and the precipitation started soon after. If the appearance of a second liquid phase were neglected, calculations would lead to unacceptable results. For example, at 298 K and pressure well above the vapor pressure of pure CO_2, a CO_2 mole fraction of about 0.5 would be evaluated for the liquid phase at S1-S2-L-V equilibrium.

Phenanthrene and naphthalene mole fractions in L1, L2 and V phases at equilibrium are reported in Figure 9. Note that on the low-pressure side L1 and L2 merge in a liquid-liquid critical point at $P = 36$ bar and $T = 278$ K. On the high-pressure side, L2 and V phases merge into a vapor-liquid critical point at $P = 74.3$ bar and $T = 305.75$ K. When comparing these calculations with those already discussed for the system CO_2-toluene-naphthalene (Kikic et al., 1997b), supported also by experimental evidence (Hong and Luks, 1992), one comes to the conclusion that the addition of phenanthrene has lowered the range of T and P in which a second liquid phase is detected.

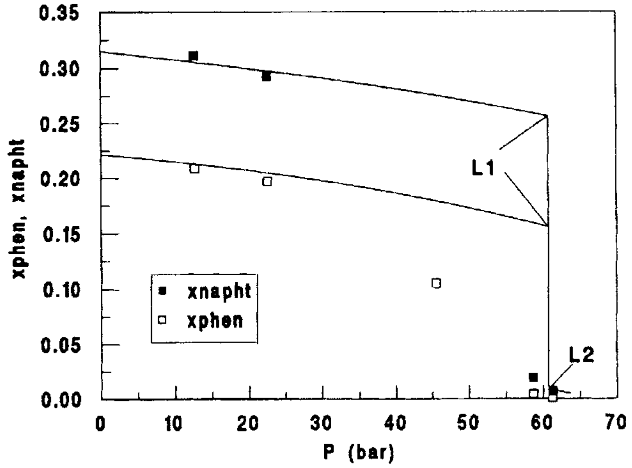

Figure 8. Composition of the liquid phase at S1-S2-L-V and S1-S2-L1-L2-V equilibria for the system CO_2-toluene-phenanthrene-naphthalene.

$T = 298$ K; experimental data by Dixon and Johnston (1991).

Four-component systems: process

We do not intend to pursue here the rigorous calculation of the composition profiles during the GAS batch process, starting from a solution of phenanthrene and naphthalene in toluene with a known composition.

Only a shortcut method was devised to simulate the amount of each precipitated solute as a function of pressure. We have assumed that precipitation occurs only after the appearance of the second liquid phase, which is richer in CO_2: in fact, only this second phase becomes supersaturated. Furthermore, we have verified that, at the conditions considered, the amount of toluene evaporated in the gas phase can be neglected; as a consequence, the mole ratio between each solute and toluene in the liquid phase remains constant until the precipitation occurs and is equal to its initial value $(x_{sol}/x_{tol})_{in}$. On the other hand, at any given pressure the equilibrium model reported above allows the calculation of the equilibrium mole ratio between each solute and toluene in the liquid phases $(x_{sol}/x_{tol})_{eq}$.

If, at a certain P

$$\left(\frac{x_{sol}}{x_{tol}}\right)_{eq}(T,P) > \left(\frac{x_{sol}}{x_{tol}}\right)_{in} \qquad (24)$$

the amount of toluene in solution is still enough to keep the solute in the liquid phase. When, as a consequence of CO_2 solubilization due to pressurization, the left term in Eq. 24 becomes equal to the right one, the solution has reached saturation. A further increase of P leads to supersaturation and precipitation. Under the hypothesis that precipitation occurs

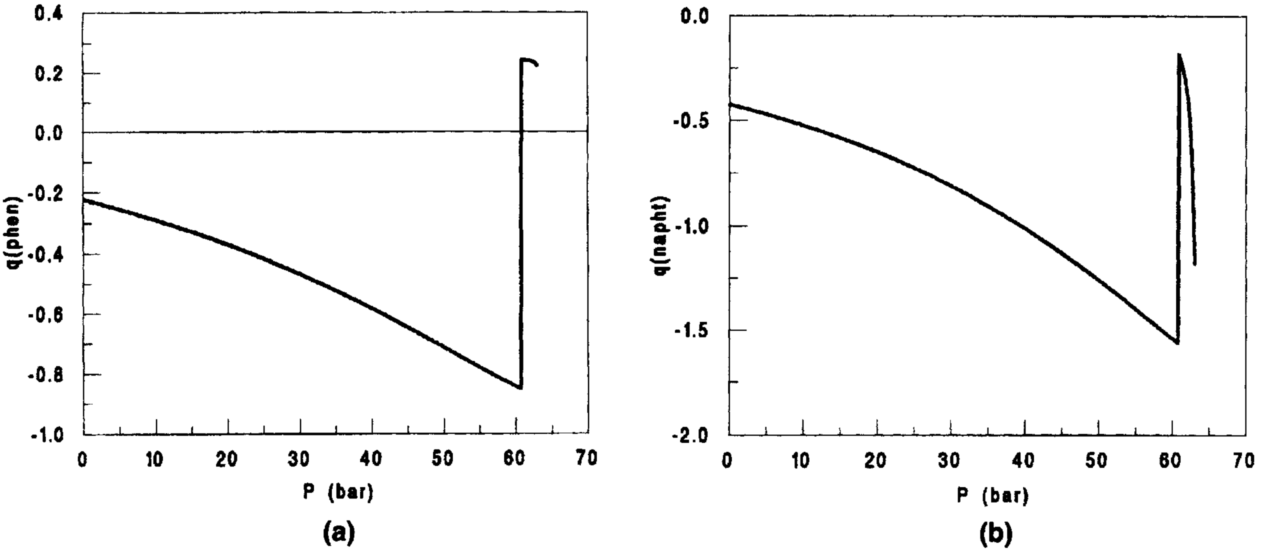

Figure 10. System CO_2-toluene-phenanthrene-naphthalene at $T = 298$ K.

(a) Phenanthrene supersaturation q(sol) as a function of pressure; (b) naphthalene supersaturation q(sol) as a function of pressure.

at equilibrium conditions and the solution does not become supersaturated, the amount q of precipitated solute per mole of solvent is given by the difference between the two terms of Eq. 24

$$q_{\text{sol}} = \left(\frac{x_{\text{sol}}}{x_{\text{tol}}}\right)_{\text{in}} - \left(\frac{x_{\text{sol}}}{x_{\text{tol}}}\right)_{\text{eq}} \tag{25}$$

According to this definition, the precipitation of a solute can start when q becomes positive.

In Figures 10a and 10b the values of q for phenanthrene and naphthalene are represented as a function of pressure (initial composition: $x_{\text{phen}} = 0.17$, $x_{\text{napht}} = 0.17$, $x_{\text{tol}} = 0.66$). At the beginning, q decreases with P for both solutes, since CO_2 dissolution and the subsequent dilution effect takes the solution away from saturation. The discontinuity in q occurs at 61 bar, when the second liquid phase appears. At this point, the solution becomes supersaturated in phenanthrene, but not in naphthalene (Figure 10b) and this situation does not change for a further increase in pressure. Therefore, pure phenanthrene is expected to precipitate. It can be concluded that the solution becomes supersaturated almost independently for each solute, and there is a range of initial composition where it is possible to achieve supersaturation only for one solute, which allows a complete separation.

Our experimental evidence confirms this result, even though a small amount of solid naphthalene was found in the cell, probably due to an entrainment effect (as explained previously).

Conclusions

The possibility of using the GAS technique to separate heavy compounds by crystallization from a liquid solution has been investigated for mixtures of naphthalene and phenanthrene, both theoretically and experimentally.

From a preliminary study on precipitation pressures, it was noted that naphthalene is not expected to precipitate, whatever the operating condition, while phenanthrene is expected to precipitate even when starting from a diluted solution. A model was developed to interpret these different behaviors. Supersaturation profiles as a function of pressure show that a phenanthrene solution can reach a high value of supersaturation even with low initial concentrations; on the other hand, a naphthalene solution can become supersaturated only in a narrow range of pressure, while starting from a composition very close to saturation.

These different behaviors were exploited to separate naphthalene from phenanthrene, starting from a solution of both at equimolar composition: almost pure phenanthrene was collected in the precipitation cell, while naphthalene with about 13% of phenanthrene was found in the expansion vessel. This result was interpreted with a simplified model of the four-component system.

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Literature Cited

Catchpole, O. J., S. Hochmann, and S. R. J. Anderson, "Gas Anti-Solvent Fractionation of Natural Products," *Proc. Int. Symp. on High Pressure Chem. Eng.*, Zürich (1996).

Chang, C. J., Y. Liou, and W.-E. Lan, "Relative Supersaturation Ratio and Separation Factor in Crystallization with High Pressure CO_2," *Can. J. Chem. Eng.*, **72**, 56 (1994).

Dixon, D., and K. P. Johnston, "Molecular Thermodynamics of Solubilities in Gas-Antisolvent Crystallization," *AIChE J.*, **37**, 1441 (1991).

Foster, N. R., S. L. J. Yun, A. Dillow, P. A. Wells, and F. P. Lucien, "A Fundamental Study of the Gas Anti-Solvent Process," *Proc. 4th Int. Symp. on Supercritical Fluids*, Sendai, Japan (1997).

Gallagher, P. M., M. P. Coffey, V. J. Krukonis, and M. Klasutis, "Gas Antisolvent Recrystallization: New Process to Recrystallize Compounds Insoluble in SCF," in *Supercritical Fluid Science and Technology*, K. P. Johnston and J. M. L. Penninger, eds., ACS Symp. Ser. No. 406, Chap. 22 (1989).

Hong, S.-P., and K. D. Luks, "Multiphase Equilibria of the Mixture Carbon Dioxide + Toluene + Naphthalene," *Fluid Phase Equil.*, **74**, 133 (1992).

Kikic, I., A. Bertucco, and M. Lora, "A Thermodynamic Description of Systems Involved in Supercritical Anti-Solvent Processes," *Proc. Int. Symp. on Supercritical Fluids*, Sendai (1997a).

Kikic, I., M. Lora, and A. Bertucco, "A Thermodynamic Analysis of Three Phase Equilibria in Binary and Ternary Systems for Applications in RESS, SAS and PGSS," *Ind. Eng. Chem. Res.*, **36**, 5507 (1997b).

Liang, M.-T., "The Application of Nucleation Theories to the Particles Formation in Expansion of Supercritical Solutions," *Proc. Int. Symp. on Supercritical Fluids*, Strasbourg, France (1994).

Liu, G.-T., and K. Nagahama, "Application of Rapid Expansion of Supercritical Solutions in the Crystallization Separation," *Ind. Eng. Chem. Res.*, **35**, 4626 (1996).

McHugh, M. A., and V. J. Krukonis, *Supercritical Fluid Extraction*, Butterworth (1993).

Nagahama, K., and G.-T. Liu, "Supercritical Fluid Crystallization of Solid Solution," *Proc. Int. Symp. on Supercritical Fluids*, Sendai (1997).

Shishikura, A., H. Takahashi, and K. Arai, "Novel Citric Acid Purification Process Using Compressed Carbon Dioxide," *Proc. Int. Symp. on Supercritical Fluids*, Boston (1991).

Shishikura, A., H. Takahashi, S. Hirohama, and K. Arai, "Citric Acid Purification Process Using Compressed Carbon Dioxide," *J. Supercrit. Fluids*, **5**, 303 (1992).

Shishikura, A., K. Kanamori, H. Takahashi, and H. Kinbara, "Separation and Purification of Organic Acids by Gas Antisolvent Crystallization," *J. Agric. Food Chem.*, **42**, 1993 (1994).

Yeo, S.-D., G.-B. Lim, P. G. Debenedetti, and H. Bernstein, "Formation of Microparticulate Protein Powders Using a Supercritical Fluid Antisolvent," *Biotechnol. and Bioeng.*, **41**, 341 (1993)

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