SUPERCRITICAL FLUIDS

1. Introduction

Supercritical fluids (SCFs) have gained considerable attention for a variety of processes and technologies since the early 1970s. The supercritical region of a pure fluid, which may be defined as the area above both the critical pressure and critical temperature, is shown in Figure 1. A unique feature of supercritical fluids may be demonstrated by beginning with a subcritical liquid at point A on Figure 1. If the liquid is depressurized isothermally in a view cell from point A to point E, the presence of a meniscus is observed as the vapor pressure line is crossed. However, if the liquid takes the path of A–B–C–D–E, the fluid then passes from a liquid phase to a gas and no meniscus is seen. On this path, if one were looking only inside the view cell, one could not tell whether the component was in the gas, liquid, or fluid state. This A–B–C–D–E pathway is used in supercritical drying to avoid collapse of delicate microstructures by the strong surface tension forces that arise at liquid–vapor interfaces. Other common applications of supercritical fluids, such as extraction operate near point C, where the density and diffusivity of the fluid is relatively high while the viscosity remains low. Changing the conditions to point D or E results in a lower density while retaining good transport properties. This variability in solvent power allows a single supercritical fluid solvent to replace multiple solvents in some processes.

Frequently, the term compressed fluid, a more general expression than supercritical fluid, is used. A compressed fluid can be either a supercritical fluid, a near-critical fluid, an expanded liquid, or a highly compressed gas, depending on temperature, pressure, and composition.

From a historical point of view, supercritical fluids have been the subject of research since the early 1800s, perhaps as early as 1822, when Baron Cagniard de la Tour discovered the critical point of a compound (1). The phenomenon of solubility enhancement in dense gases was discovered in the late 1870s, when the effects of pressure on the solubility of the potassium iodide–ethanol system were observed (2). The technology progressed slowly until the late 1970s and early 1980s, when a number of processes were commercialized and research intensified. Several books provide an excellent overview (1,3–9) and the field has continued to expand such that entire books are now devoted to specific areas of supercritical fluids, eg, chromatography (10), extraction (11), reactions (12–14), and materials processing (15,16).

The supercritical fluid carbon dioxide, CO_2, is of particular interest. This compound has a mild (31°C) critical temperature and pressure (7.38 MPa); it is nonflammable, essentially nontoxic, and, especially when used to replace Freons and certain organic solvents, environmentally friendly. Moreover, it can be obtained from existing industrial processes without further contribution to the greenhouse effect. Carbon dioxide is fairly miscible with a variety of organic solvents, and is readily recovered after processing owing to its high volatility. It is a small linear molecule and thus diffuses more quickly than bulkier conventional liquid solvents, especially in condensed phases, eg, polymers. Finally, CO_2 is the second least expensive solvent after water.

Water has an unusually high (374°C) critical temperature owing to its polarity. At supercritical conditions water can dissolve gases, eg, O_2 and nonpolar organic compounds. This phenomenon is of interest for oxidation of toxic wastewater and hydrothermal synthesis. Many of the other supercritical fluids commonly available are listed in Table 1, which is useful as an initial screen for a potential supercritical solvent. The ultimate choice for a specific application, however, is likely to depend on additional factors, eg, safety, flammability, phase behavior, solubility, and expense.

2. Properties of Supercritical Fluids and Their Mixtures

2.1. Solvent Strength of Pure Fluids. The density of a pure fluid is extremely sensitive to pressure and temperature near the critical point, where the reduced pressure, P_r, equals the reduced temperature, $T_r, = 1$. This is shown for pure carbon dioxide in Fig. 2. Consider the simple case of the solubility of a solid in this fluid. At ambient conditions, the density of the fluid is 0.002 g/cm^3. Thus the solubility of a solid in the gas is low and is given by the vapor pressure over the total pressure (ideal gas behavior). The solubilities of liquids are similar. At the critical point, the density of CO_2 is 0.47 g/cm^3 and at slightly supercritical pressures ($P_r \geq 1.2$), the density can easily exceed 0.70 g/cm^3. This value is comparable to that of organic liquids. The solubility of a solid can be 3−10 orders of magnitude higher in this more liquid-like CO_2.

The solvation strength of a given supercritical compressed fluid is related directly to the fluid density (17). Thus solvent strength may be manipulated over a wide range by making small changes in temperature and pressure. In general, the greater the density, the greater the ability of a given compressed fluid to solvate a component. One means of expressing solvent strength is by the solubility parameter, δ, which is the square root of the cohesive energy density and can be defined rigorously (18). A plot of the solubility parameter for CO_2 versus pressure resembles that of the density versus pressure (Fig. 2). Although the solubility parameter of CO_2 is larger than that of propane, a substantial portion of the value results from the large quadrupole moment exhibited by CO_2. The dispersion component of the solubility parameter is actually less than that of ethane. Another measure of the strength of van der Waals forces, the polarizability per volume, is also very small for CO_2: below that of ethane at comparable conditions. This makes CO_2 more like a fluorocarbon than a hydrocarbon with respect to solvent strength.

A particularly attractive and useful feature of supercritical fluids is that these materials can have properties somewhere between those of a gas and a liquid (Table 2). A supercritical fluid has more liquid-like densities, and subsequent solvation strengths, while possessing transport properties, ie, viscosities and diffusivities, that are more like gases. Thus, an SCF may diffuse into a matrix more quickly than a liquid solvent, yet still possess a liquid-like solvent strength for extracting a component from the matrix.

Physical properties of pure supercritical fluids may be found in many of the standard reference textbooks and journals (19). There are also computerized databases available for thermodynamic and physical properties, eg, NIST Chemistry WebBook (Free), DIPPR, DETHERM, NIST Standard Reference Databases 4 (also known as SUPERTRAPP), 12 (Pure Fluids), and 14 (Mixtures).

2.2. Phase Behavior. One of the pioneering works detailing the phase behavior of ternary systems of carbon dioxide was presented in the early 1950s (23) and consists of a compendium of the solubilities of >260 compounds in liquid (21–26°C) carbon dioxide. This work contains 268 phase diagrams for ternary systems. Although the data reported are for liquid CO_2 at its vapor pressure, they yield a first approximation to solubilities that may be encountered in the supercritical region. Various additional sources of data are also available (1,4,9,24). An understanding of the phase behavior of a particular system of interest is important because complex results can sometimes occur. A dramatic example, which occurs frequently for solubilities in supercritical systems, is retrograde behavior. Figure 3 clearly shows the presence of a retrograde region. For an isobaric system at some pressure, eg, 12.7 MPa (1841.5 psi), an increase in temperature of a solution of ethylene and naphthalene from 300 to 320 K results in an increase in the equilibrium solubility of naphthalene. This behavior is typical of liquid solvent systems. For the same increase in temperature (300–320 K), but at a pressure of 8.1 MPa (1174.5 psi), the solubility of naphthalene decreases by nearly an order of magnitude. Because this latter behavior is the opposite of typical liquid solvents, it is termed retrograde solubility.

Either pressure or temperature may be used to control the solubility of solids in the vicinity of the mixture critical point. The appearance of the retrograde region occurs because of two competing effects of temperature. The first is on the vapor pressure of the solute; the second on the density of the supercritical solvent. At the higher pressures the dominant temperature effect is on the vapor pressure, giving positively sloped isobars. Near the critical pressure the density is more sensitive to temperature than at the higher pressures (see Fig. 2). At these near-critical pressures, the relatively rapid density decrease with increasing temperatures dominates the effect on solute vapor pressure, leading to negatively sloped isobars and retrograde behavior.

The following generalizations can be made in terms of the solubilities of solutes in a supercritical phase. Solute solubilities in supercritical fluids can approach those of liquid solvents as the SCF density increases. Solubilities typically increase as the pressure is increased. Increasing the temperature can cause increases, decreases, or no change in solute solubilities, depending on the temperature effect on solvent density and/or the solute vapor pressure. Also, at constant SCF density, a temperature increase always increases the solute solubility.

To increase the solvation ability of CO_2 further, especially for high molecular weight or polar compounds, both nonpolar and polar cosolvents or modifiers may be added from 0 to 20 mol % (26). The cosolvent interacts more strongly with the solute than does CO_2. Small amounts of alkane cosolvents have been shown to increase significantly the solubility of hydrocarbons in supercritical CO_2 (27). Figure 4 shows that addition of as little as 3.5 mol % methanol to CO_2 increases the solubility of salicylic acid [69-72-7] (25) by an order of magnitude. In most practical applications, the SCF phase will contain more than two components whether or not a cosolvent has been purposely added. Because of the high sensitivity of solubility to the composition of the solvent, it is always important to characterize the phase behavior of the actual system of interest. Compressed gases and fluids have the ability to dissolve in and expand organic liquid solvents at pressures typically between 5 and 10 MPa (725–1450 psi). This expansion nearly always decreases the liquid's solvent strength. If enough compressed fluid is added, eventually the mixture solvent strength is comparable to that of the pure compressed fluid. In Fig. 5, an organic solid is dissolved in toluene. As more compressed CO_2 is added to the solution, indicated by higher pressure, the mole fraction of the solute decreases (28). The decrease is partly a result of dilution, but it is clear that as the pressure exceeds ~5 MPa (725 psi), a dramatic change in the solute solubility occurs. For phenanthrene, there is a decrease of nearly two orders of magnitude. At ~6 MPa (870 psi), the mixture solvent strength approaches that of pure liquid CO_2. This expansion behavior has become the basis for a wide range of precipitation and crystallization techniques based on SCFs. These are discussed in more detail in subsequent sections.

2.3. Transport Properties of Supercritical Fluids. While solubility and phase behavior are sufficient for process feasibility, an increase in commercialization spurred activity in measurement and modeling of transport properties of supercritical fluids and their mixtures. Some of the earliest viscosity data came from attempts to increase the viscosity of CO_2 for enhanced oil recovery (29). Viscosity of mixtures where the primary component is a supercritical fluid can be reasonably correlated with existing theories of gas viscosity and the viscosity behavior with temperature and pressure mirrors that of the pure supercritical fluid solvent (30). Data for a few typical cosolvents at 2 mol% in CO_2 are shown in Figure 6, where it can be seen that viscosity is roughly proportional to the molecular weight of the cosolvent within a homologous series. A separate class of mixtures of interest includes polymer melts with dissolved supercritical fluids, wherein the supercritical fluid is the minor component. The viscosity of such a mixture is dramatically reduced compared to the pure polymer melt, yet viscoelastic scaling behavior common to polymer rheology is maintained including both temperature and concentration superposition.

Diffusivity and mass transfer of solutes in supercritical fluids plays a large role in equipment selection and sizing for processes. Diffusivity can also be correlated well by existing gas theories (eg, Chapman-Enskog) with the exception of those very near the critical point. For infinitely dilute solutes in supercritical fluids, the diffusion coefficient is typically near 10^{-8} m^2/s. Near the critical point, the divergence of some solvent properties hinders an accurate measurement of diffusivity. These same properties cause difficulties in operating the process (eg, pumping the SCF) and as a result processes are typically designed to avoid operations at or very near the critical point of the solvent. Data for the diffusivity variation of CO_2 in four different polymers as a function of pressure are available (31).

2.4. Polymers and Supercritical Fluids. With the exception of a few polymers, eg, polydimethylsiloxane and some specially synthesized fluoropolymers, most high molecular weight polymers do not dissolve in neat CO_2 (32,33). However, although not soluble in a particular supercritical fluid, polymers can uptake a significant amount of the fluid (34) and this has created an entire subarea of SCF technology where the SCF acts as a diluent rather than a solvent. Initial interest arose from gas separation with polymeric membranes from which early sorption data were obtained at temperatures up to 35°C and for pressures up to the vapor pressure of CO_2 at 25°C (35–37). Subsequently, the potential for supercritical CO_2 to be used as a polymer processing aid (38,39) gave rise to a plethora of studies over a wider range of conditions encompassing sorption, swelling, viscosity, and interfacial tension measurements (40). It is now well accepted that a small amount of dissolved CO_2 can reduce the shear viscosity of a polymer melt significantly and CO_2 is a promising candidate to replace CFCs as physical blowing agents for extruded polymer foams.

As the concentration of compressed fluid is increased in the polymer phase, the sorption and subsequent swelling of an amorphous polymer can cause a glass-to-rubber (or glass-to-liquid) phase transition. The glass-transition temperature (T_g) of a polymer can be depressed to below the normal T_g by 30°C or more (36, 41). Certain polymers can exhibit an isobaric liquid-to-glass transition with a temperature increase, defined as retrograde vitrification (42) (Fig. 7). Continuing to increase the temperature results in a normal transition from a glass to a liquid state. The retrograde vitrification is caused by an increase in the solubility of CO_2 in the polymer at the lower temperatures. The T_g behavior may be exploited in polymer processing to process polymers at much lower temperatures than without CO_2. A crystalline or semicrystalline state in polymers can be induced by thermal changes from a melt or a glass, by strain, by organic vapors, or by liquid solvents (43). Polymer crystallization can also be induced by supercritical CO_2 (44). The plasticization can increase the polymer segmental motions so that crystallization is kinetically possible. Because the amount of gas (or fluid) sorbed into the polymer is a direct function of the pressure, the rate and extent of crystallization may be controlled by controlling the SCF pressure. It is generally believed that CO_2 sorbs into the amorphous regions of a polymer and not the crystalline regions. As a result, the net effect of treating a semicrystalline polymer (eg, whether an increase or decrease of crystallinity occurs) is often unpredictable and requires experimentation.

2.5. Dispersions in Supercritical Fluids. The ability to design surfactants for the interface between water (or organics) and SCFs offers new opportunities in protein and polymer chemistry, separation science, reaction engineering, environmental science for waste minimization and treatment, and materials science. The design of surfactants for conventional reverse micelles and water-in-oil microemulsions is reasonably well understood for SCF alkane solvents (45–50). Microemulsions are thermodynamically stable and transparent dispersions of one phase within another. For CO_2, surfactant design is more difficult because the properties of CO_2 are much different from those of water or nonpolar organic solvents. Unlike water, carbon dioxide has no dipole moment. Even when highly compressed, CO_2 has far weaker van der Waals forces than hydrocarbon solvents, making CO_2 more like a fluorocarbon or fluoroether. Because of carbon dioxide's weak solvent strength, both lipophilic (high molecular weight) and hydrophilic materials are often insoluble in CO_2. It is possible, however, to form dispersions of either hydrophilic or lipophilic phases in a CO_2-continuous phase. Organic-in-CO_2 dispersions may be stabilized using surfactants containing CO_2-philic tails, such as fluorinated compounds (51). After a decade of study on emulsions and surfactants, a stable microemulsion containing a water-like core was formed within a CO_2-continuous phase (52). The surfactant was an ammonium carboxylate perfluoropolyether (PFPE), $CF_3O(CF_2CF(CF_3)O)_3$ CF_2COO —NH_4^+, commercially available in the COOH form, which has an average molecular weight of 740. The number of moles of water per mole of surfactant reached 20 in the one-phase region. CO_2 based emulsion and dispersion technology has now been applied for polymer synthesis, nanoparticle synthesis, biocatalysis, and other novel chemistries (53).

3. Modeling of Phase Behavior

Modeling of supercritical phase behavior requires advanced-phase equilibrium thermodynamic methods explicitly accounting for the effect of pressure on the solution. Especially in the region of the critical point, extreme nonidealities occur and high compressibilities must be addressed. In multicomponent mixtures, eg, when cosolvents are used, basic identification of the equilibrium phases is a nontrivial issue. Significant progress has been made in molecular modeling and computer simulations of supercritical fluids and their mixtures such that molecular level insight into solubility and self-assembly in supercritical fluids is now attainable. Typically, however, these models and techniques are not *predictive* in that it is not possible to design an extraction or reaction system without a significant amount of experimental data. Several review papers and books discuss modeling of systems comprised of SCFs and solid or liquid solutes (1,3,4,8,9,18,54,55).

One of the simplest cases of phase behavior modeling is that of solid–fluid equilibria for crystalline solids, in which the solubility of the fluid in the solid phase is negligible. Thermodynamic models are based on the principle that the fugacities (escaping tendencies) of component i, f_i, are equal for all phases at equilibrium under constant temperature and pressure (56). The solid-phase fugacity, f_2^s, can be represented by the following expression at temperature T:

$$f_2^s = P_2^s \Phi_2^s \exp\left[\int_{P_2^s}^{P} \frac{v_2^s}{RT} dP\right] \tag{1}$$

where P_2^s is the vapor pressure and the superscript s denotes saturation; Φ_2^s is the fugacity coefficient at the saturation pressure (usually unity); and v_2^s is the solid molar volume, which is frequently assumed to be pressure independent. Equating the fugacity of the pure solid to the fugacity of the solid in the fluid phase, the following equation is obtained, after rearranging for the mole fraction of the solid component in the fluid phase.

$$y_2 = \frac{P_2^s}{P}\left[\frac{\Phi_2^s \exp\left(\dfrac{v_2^s(P-P_2^s)}{RT}\right)}{\Phi_2^F}\right] \tag{2}$$

The fugacity coefficient of the solid solute dissolved in the fluid phase (Φ_2^F) is typically obtained using cubic equations of state. The enhancement factor, E, shown as the quantity in brackets in equation 2, is defined as the real solubility divided by the solubility in an ideal gas. The solubility in an ideal gas is simply the vapor pressure of the solid over the pressure. Enhancement factors of 10^4 are common for supercritical systems. Notable exceptions, eg, the squalane−carbon dioxide system may have enhancement factors $> 10^{10}$. Solubility data can be reduced to a simple form by plotting the logarithm of the enhancement factor versus density, resulting in a fairly linear relationship (57).

Specific chemical interactions, eg, associations resulting from hydrogen bonding or donor−acceptor interactions, can have a pronounced effect on SCF solution-phase behavior. Hydrogen bonding among mixtures containing SCFs is important to understand because of the increased interest in near- and supercritical water (SCW) solutions, and in polar cosolvents and surfactants in other fluids, eg, CO_2 (58–61). The fluid density has been shown to have a significant effect on hydrogen bonding because of the compressible nature of supercritical fluids (62). Various equations of state have been developed to treat association in supercritical fluids. Most are based on the statistical association fluid theory (SAFT) (63). These models include parameters that describe the enthalpy and entropy of association. Detailed descriptions of association in supercritical water have been obtained using molecular dynamics and Monte Carlo computer simulations (64–67).

Liquid-supercritical fluid solutions comprise a subset of the larger field of vapor−liquid equilibria. A number of theoretical models have been proposed to describe the phase behavior of polymer−supercritical fluid systems. Among these the PC−SAFT equation of state (68,69) has emerged as one of the more accurate although the Sanchez-Lacombe equation of state (70) also captures the essential features of the phase behavior with a simpler mathematical form. Polymer−supercritical fluid systems have been well reviewed in the literature (1,71).

4. Experimental Techniques

The discussion on fluid properties stresses the importance of physical confirmation of the actual phase behavior, lest unexpected behavior is encountered. A number of different experimental techniques are available for determining phase behavior. These include dynamic flow-through cells, static systems using visual observations in a variable-volume view cell, static systems with sampling for analysis, and the use of static or dynamic optical transmission cells for ultraviolet (uv)−visible, Fourier transform infrared (ir) spectroscopy (ftir), and Raman spectroscopy for analysis (1,3). Perhaps the most useful tool for examining phase behavior is the variable-volume view cell (Fig. 8) containing a piston to separate the pressurizing fluid from the sample. Using this single apparatus allows both manipulation of temperature, pressure, or composition and visual inspection for the appearance of unexpected phases. Samples can be removed for analysis, phase volumes can be measured to determine mixture composition and molar volumes (72), and phase boundaries can be measured. Many different configurations of view cells have been proposed and some are commercially available from companies, eg, Thar Technologies and Supercritical Fluid Technologies, Inc. Some are capable of pressures in excess of 100 MPa (14,500 psi). The cell contents may be viewed safely through the sapphire window by use of a mirror, video camera, or boroscope.

5. Processes and Applications

5.1. Supercritical Fluid Chromatography (SFC). As analytical tools, SFC and related unified chromatography techniques continue to grow, especially when used in conjunction with supercritical fluid extraction. As in other SCF processes, density is the controlling factor. Many SCF chromatographic separations use a programmed density profile, similar to temperature ramping used in conventional gas chromatography. The mobile phase can be pure SCF or any proportion of SCF–liquid solvent that is miscible at column conditions and a homogeneous phase. The stationary phase is a packed or capillary column. Carbon dioxide is frequently used as the mobile phase and organic modifiers are added for better separations of polar compounds (73). Subcritical (or superheated) water has also gained a great deal of interest as a mobile phase (74). The SFC is regarded to have higher speed and selectivity than conventional methods. The higher speed results from high diffusion coefficients and low viscosity. The SFC is accepted for some standard analyses and several companies market commercial instruments.

This technique has been widely applied. Examples include food-related applications (75–79), analysis of natural products (80–83), analysis of synthetic oligomers and polymers (84), and chiral separations (85).

5.2. Separation Processes *Extractions.* Supercritical fluid extraction (SFE) technique uses a SCF to remove soluble substances from insoluble matrices or solutions. The SFE can be classified as off-line or on-line. In off-line SFE, the extraction and analysis steps are done separately; in on-line SFE, the extract is fed directly into an analytical instrument, eg, SFC thus reducing sample handling and cleanup steps (86). Some successful examples are SFE/GC (87), SFE/LC (88,89), and SFE/FT–IR (90).

Like SFC, SFE has been applied in a variety of areas, eg, food and natural products, pharmaceutical, environmental, polymer fields, and forensic science. It is the largest segment of commercial application of SCFs with > 100 plants operating worldwide as of 2000 (91). Some applications in these areas are described below.

Food and Natural Products. This area has been well reviewed (92) and there are many commercial operations, eg, extraction of hops (1) and the decaffeination of coffee (93). Supercritical fluid extraction can be used to remove toxic compounds, metals, and organometallics from food and has been applied successfully to extract a variety of organic compounds from herbs and other plants.

Pharmaceutical Application. Among the advantages of CO_2, no organic solvent residue and low processing temperature are of particular interest and importance in the pharmaceutical industry. The former feature lowers the cost of removing toxic solvent and reduces the potential risk introduced by solvent, while the latter is especially beneficial for thermally labile compounds. One example is the extraction of vitamin E (94,95).

Environmental Application. Using SFE to remove contaminants from soil is a very encouraging process in principle. Realistically, nonpolar volatile contaminants, hydrocarbons, aromatics, and some phenolics, are suitably extracted, while other more strongly bound compounds, eg, pesticides and metals, are much less extractable. These latter compounds often require the use of organic cosolvents or special chelating agents that increase the complexity and cost of SFE on a large scale. The SFE has been applied to determination of organochlorine pesticides (96) in soils (97), oil seeds (98), air (99), and tobacco (100). Complete extraction of triazine herbicides by SC CO_2 from soils requires addition of methanol (101–103). Generally speaking, SFE coupled with highly sensitive analytical methods is quite useful for environmental analysis. However, the use of SFE for remediation of contaminated sites remains underdeveloped.

Polymers. Supercritical fluid extraction is applied for extraction of unreacted monomer, oligomeric material, and additives from the polymer matrix. These applications benefit from the relatively high solubility of some low molecular weight monomers and oligomers in SC CO_2. As described above, polymers exposed to SC CO_2 exhibit various extents of swelling and enhanced chain mobility, which efficiently facilitates the transport of components into and out of the polymer matrix. Bruna (104) reviewed the applications of SFE in polymer technology. Researchers have used SC CO_2 to extract additives, eg, phthalates from poly(vinyl chloride) (PVC) (105,106) or simply to determine the total extractables in styrene−butadiene rubber (107).

Forensic Science. The applications of SFE and SFC in forensic science are known to very important. The main uses in this area are sample preparation and separation of drugs of abuse, especially opiates, cannabinoids, cocaine, and sedatives. The SCF technology has been used for both time-of-death-related drug analysis and for obtaining information relating to long-term drug abuse. It is also useful in identification of fingerprinting and explosives from both bombing events and gunshot residues. The commonly used identification technique for latent fingerprints makes use of the reaction of ninhydrin with amino acids present in eccrine sweat to give purple or fluorescent fingerprints with the help of 1,8-diazafluorene-9-one (DFO) (108). The main ingredient of ninhydrin and DFO currently used is 1,1,2-trichlorotrifluoroethane (CFC113), which is an ozone depleting substance. Hewlett (109) showed SC CO_2 is a suitable solvent to replace CFC113. For determination of explosives, SC CO_2 chromatography has the advantage over traditional techniques, eg, GC because most of residues are thermally unstable (108).

Membrane Filtration. In the membrane filtration area, there are two new SCF-membrane coupled separation processes: nanofiltration plus SCF extraction process and SCF assisted ultrafiltration.

Sarrade and co-workers (110,111) developed a new hybrid process that couples nanofiltration and SCF extraction. It was designed to develop synergistic effects of these two processes for better performance. Because CO_2 is used as a solvent, the process is environmentally friendly and products have high quality. The process also gives a high permeate flux because of the low viscosity of SC CO_2.

Ultrafiltration of highly viscous liquids (particularly oils) is difficult and expensive due to its low permeate flux and high energy consumption. Although increasing process temperature and adding surfactants can lower the liquid viscosity, they may cause degradation or contamination. So a new cross-flow ultrafiltration process, which takes advantage of the low viscosity, low surface tension, tunable solvation power of SC CO_2 has been recently demonstrated and showed excellent rejection of metals Fe, Zn, and Cu up to $> 99\%$ (110,111).

5.3. Reactions. An area of SCF technology with great interest is the application of SCF as an active participant in a reaction or as the solvent for reactants, catalysts, and/or products. The solvent properties of SCF, eg, solvent strength, viscosity, diffusivity, and dielectric constant can be controlled by varying pressure and temperature. Therefore, these changes can be used to affect reaction conditions and results.

SCFs and Green Chemistry. In the early 1990s, the U.S. Environmental Protection Agency (EPA) defined their green chemistry mission: "to promote innovative chemical technologies that reduce or eliminate the use or generation of hazardous substances in the design, manufacture and use of chemical products" (112). In practice, we expect a high conversion of reagents, minimization of waste produced, safe operation, and energy efficiency. The SC CO_2 is an attractive and environmentally benign reaction medium for chemical synthesis and has strong effects on homogeneous and heterogeneous metal catalysis. It can be used as a solvent or reagent and solvent simultaneously.

Carbon dioxide can be used to replace volatile organic chemicals (VOCs, ie, organic compounds that take part in atmospheric photoreactions, and therefore deplete the atmospheric ozone layer) in many processes. It has been reported (32) that SC CO_2 is possible to replace chlorofluorocarbon (CFC) solvents, which are one of the main causes of depletion of the ozone layer, in synthesis of fluoropolymers. It can also be a replacement of organic solvents for some purely hydrocarbon-based polymers with the aid of surfactants containing a CO_2-philic and a polymer-related part (113).

The use of SC CO_2 makes many processes safer because it is nonexplosive, nonflammable, and has good heat transport capacities relative to low density gases. These properties and its inertness to oxidation make it a good medium for many oxidation reactions, eg, the metal-catalyzed oxidation of alkenes with organic peroxides in SC CO_2 (114,115).

Replacing organic solvents with SC CO_2 often brings better catalytic performance, eg, as improved selectivity (116,117) and enhanced catalyst lifetime (118). Sometimes the use of SC CO_2 can change the course of the reaction.

In industry, product separation and catalyst recycling are often hard to handle. The SCFs offer a single-solvent approach to this problem. For example, in multiphase catalysis, biphasic water/SC CO_2 is designed to enhance catalyst–product separation and catalyst recycling (119).

Nanocrystal Synthesis and Assembly in CO_2. Sufactant-stabilized aqueous cores dispersed in the CO_2 phase [Water-in-Carbon dioxide (W/C) microemulsion] was shown to be a convenient medium for nanocrystal synthesis (53). Silver (120), copper (121), silver halide (122), CdS, and ZnS (123) have been synthesized in W/C microemulsions. Iridium and platinum nanocrystals can be synthesized by arrested precipitation directly in SC CO_2 (124). The synthesis of silicon and germanium nanocrystals that require elevated temperatures to achieve core crystallinity can take advantages of high temperatures of some SCF solvents (125,126).

The ability to disperse nanocrystals in liquid CO_2 at the vapor pressure can be used to deposit nanocrystal films. It can avoid some disadvantages of conventional methods, eg, drop-casting or spin-casting or Langmuir-Blodgett films. A successful example is FOMA–SH–capped gold nanocrystals (35-Å diameter) drop-cast from liquid CO_2 at the vapor pressure (127).

Polymerizations. The solvation power of SCFs can affect separation of the polymer from starting materials and polymer molecular weight fractionation. The supercritical CO_2 is the most extensively studied SCF for polymerization reactions.

The solubility of monomer and polymer determines the types of polymerization techniques used in polymer synthesis. For example, amorphous fluoropolymers can be synthesized homogeneously in SC CO_2. DuPont has recently invested to construct a Teflon FEP (Fluorinated Ethylene Propylene Resin) production facility in North Carolina (128). In the process, CO_2 is used to replace 1,1,2-trichloro-1,2,2-trifluoroethane or water and surfactant. In contrast, many other polymerization reactions in SC CO_2 are heterogeneous processes, eg, precipitation, dispersion, or emulsion polymerizations. Surfactants are usually used as stabilizers in CO_2 for the last two processes (129).

The main types of chain-growth polymerization include free-radical, cationic, anionic, and metal-catalyzed reactions. Most research in chain-growth polymerization in CO_2 focuses on free-radical polymerizations, eg, polymerizations of methyl methacrylate (MMA) (113), vinyl acetate (130,131), acrylamide (132), and 2,6-dimethylphenylene oxide (133). There are also a number of reports of cationic and metal-catalyzed polymerizations. Some examples are cationic polymerization of isobutylene (IB) (134), vinyl ethers (135, 136), and styrene (137), and transition metal catalyzed polymerization of bicyclo[2.2.1] hept-2-ene(norbornene) (138). There are no reports of anionic polymerizations in CO_2.

Researchers have successfully used step-growth reactions in CO_2 to produce polycarbonates (139), polyamides (140,141), silica gels (142), polypyrrole (143), and polyphenoxides (133). In some cases, SC CO_2 is a reaction medium and reagent simultaneously, eg, the copolymerization of propylene and CO_2 in SC CO_2 with a heterogeneous zinc catalyst (144).

Supercritical Water Reactions. When near its critical point, water shows very different properties from those of water at normal temperature and pressure. Its dielectric constant is much lower and hydrogen bonds become much weaker, which make SCW more like an organic solvent. Therefore, many organic substances exhibit high solubilities or are miscible with it. Many organic reactions can be conducted in a single phase with a SCW environment, consequently, high reaction rates can be achieved because interphase mass transfer can be avoided. In addition, when close to the critical point, the dissociation constant (K_w) is about three orders of magnitude higher than liquid water at normal temperature and pressure, which means much higher H^+ and OH^- ion concentrations. Therefore, it is an effective medium for acid- and base-catalyzed organic reactions (145).

Similar to CO_2, properties of water change continuously from the ambient to the supercritical state, so it is possible to control its properties by varying temperature and pressure and optimize it as a reaction medium, reactant, or catalyst in organic reactions.

In synthetic organic chemistry, near-critical or SC water has been used in a variety of reactions, eg, hydrogenation–dehydrogenation (146,147), carbon–carbon bond formation (148–150), rearrangement (147,151), hydration–dehydration

(152,153), dehydrohalogenation (154,155), hydrolysis (154,156), partial oxidation (157), H–D exchange (158,159), and others. One example of hydrolysis is a method of quick hydrolyzation of cellulose in SCW to recover glucose, fructose, and oligomers.

Oxidation of organic compounds have received a lot of attention due to concerns of environmental protection and remediation. The application of SCW in this area is often referred to as supercritical water oxidation (SCWO). It takes advantage of the complete miscibility of SCW with most organic compounds. Moreover, sufficiently high temperature (400–600°C) accelerates the reaction rate. Destruction of organic compounds with $> 95\%$ decomposition can be accomplished in several minutes or less (160). For example, the complete oxidation of 2,4-dichlorophenol in SCW was performed in a batch reactor for 5–10 min at temperature between 673 and 873 K (161).

Metal oxides and inorganic–organic hybrid compounds (162) can be prepared through hydrothermal synthesis. For example, hydrated metal ions are hydrolyzed and precipitated as crystalline metal oxides through dehydration at high temperatures.

5.4. Particle Formation. Particle size and distribution are two key factors for the performance of solid powder materials. Particles can be generated through milling and grinding of granular materials or synthesized from solution via crystallization, precipitation, and spray drying. The SCFs and dense gas technologies in general are used in these latter methods as powerful tools to control particle size, morphology, shape, and distribution. All of the same advantages described earlier apply to these processes. This area reflects some of the most creative uses of SCFs to date especially for encapsulating drugs in polymers to create controlled release formulations. Here, we describe the basic methods of using SC CO_2 and water to form particles.

Particle Formation by SC CO_2. There are two categories of particle generation methods using SCFs, one category involves only the SCF and the solute to be precipitated. Rapid expansion of supercritical solutions (RESS) is the only technique in this category. The second category involves a second liquid solvent in addition to the SCF and solute. There have been several techniques described that differ primarily in the way that the liquid solvent and SCF are contacted. Below, we discuss three of these: GAS (gas antisolvent) and related [including SAS (supercritical antisolvent), PCA (precipitation with compressed antisolvent), ASES (aerosol solvent extraction system), and SEDS (solution enhanced dispersion by supercritical fluids)]; PGSS (particle formation from gas saturated solutions); and DELOS (depressurization of an expanded liquid organic solution).

RESS. The SCF is the only solvent present in the RESS process. First, the active substance is dissolved into SC CO_2 (or other SCF) to reach equilibrium at some temperature and pressure. Then the solution is sprayed through a nozzle at very high velocity into a vessel at atmospheric pressure. The adiabatic expansion of SCF solution results in rapid drops in temperature and pressure, causing in turn very high solute supersaturation and catastrophic nucleation of particles. In recent research, RESS has been studied in micronization of various pharmaceuticals, eg, carbamazepine (163), ibuprofen (164), griseofulvin (165), and ß-sitosterol (166). In the polymer area, recent development in RESS include fluoropolymer coatings to protect historical buildings and civil infrastructures

(167,168). This process is limited due to the insolubility of most polymers in SC CO_2, although some researchers have worked with cosolvents to expand its applications in polymers.

GAS and Related Processes (SAS/PCA/ASES/SEDS). These all rely on essentially the same phenomena. As opposed to its relatively low solvating power, especially for polymers, CO_2 can dissolve appreciably in many organic solvents. In the GAS process, CO_2 is used as an antisolvent to reduce the solubility of the solute in an organic solvent. Typically, the active substance is dissolved in an organic solvent and then high pressure CO_2 is fed into it. The solubility of the active substance decreases substantially as the CO_2–solvent mixture dilates. The solution becomes supersaturated and the active substance is forced to precipitate or crystallize as micron-size particles.

In the SAS process, SC CO_2 is used as the antisolvent. Its main difference from GAS process is that SAS uses a nozzle to spray the solution and GAS does not (169). In the SAS process, the liquid solution and the antisolvent SC CO_2 are simultaneously, but separately, injected into the precipitation chamber. Reverchon (170) has reviewed this area. The process is completely suitable for use with polymers and biopolymers are gaining interest because of their potential for the drug-delivery applications.

Some specific examples include hydrocortisone-poly(vinylpyrrolidone) (PVP) (171), PMM (172), a class of hyaluronic acid-derived biopolymers (HYAFF11, HYAFF11p80, HYAFF11p75, HYAFF302) (173–175).

The SAS method has been modified and adapted by others who use slightly different acronyms. In PCA (176) and ASES (177) processes, the organic solution with the active substance is sprayed through a nozzle into a precipitation chamber filled with SC CO_2. Mass transfer between the solvent and SC CO_2 is enhanced greatly and fine particles are easily obtained. Some specific examples include PLA[poly(L-lactide)]/PLGA[poly(D,L-lactide-*co*-glycolide)] and their derivatives (178–181) by the ASES and nylon particles (182) by the PCA process.

In the SEDS process (183–187), one stream containing the active substance and another SC CO_2 stream are mixed and the mixture is sprayed into a vessel maintained at ambient pressure and temperature. The SEDS process allows more effective mixing and expansion of SC CO_2 and therefore enables formation of finer particles. Figure 9 shows scanning electron microscopy images of drug–mannitol mixtures processed with SEDS with different ratios (184). The drug used is 2,6-dimethyl-8-(2-ethyl-6-methylbenzylamino)-3-hydroxymethylimidazo-[1,2-*a*]pyridine mesylate.

PGSS. Polymers cannot be easily dissolved into compressed CO_2, but compressed CO_2 can be dissolved into molten polymers or polymer solutions. In the PGSS process (188–191), after compressed CO_2 is fed into molten polymers to reach equilibrium, the saturated polymer solution is sprayed into a precipitation chamber leading to particle formation. This technique is successfully used for impregnation of active ingredients in polymer matrices. The review by Yeo and Kiran (192) gives a list of polymers used in recent research.

DELOS. In the DELOS process (193), SC CO_2 is used as an organic solvent and a cosolvent. In the PGSS process discussed above, the substance of interest has to be in a molten or liquid state by heating, which is problematic for thermally degradable substances. In the DELOS process, the substance of interest is dissolved in an organic solvent and then is mixed with SC CO_2. Then, the mixed solution is sprayed into a vessel at ambient pressure to achieve fine particles. In this process, SC CO_2 is used as a cosolvent during the mixing and antisolvent and viscosity reducing agent during the spraying.

Particle Formation Using SCW. As mentioned above, hydrothermal synthesis using SCW is a successful technique. Powders through this technique are well crystallized and have fine grain size with controlled morphology and clean surface (194). Hydrothermal synthesis using SCW can be conducted in a batch or flow reactor (195). The batch method is used to synthesize highly crystalline products and large single crystals for which a long reaction time is required. This method has been used to produce fine particles of TiO_2 (196) and AlO(OH) (197).

The second method uses a flow reaction system with water. It is considered a promising process for formation of nano- and submicron-sized metal oxide particles because high reaction rates can be achieved. Some successful examples reported are syntheses of nano-sized phosphor (198), photocatalyst nanowire (199), magnetic materials (200–202), and dielectric materials (203).

5.5. Other Materials Processing. *Supercritical Impregnation of Polymers.* In this context, impregnation can be defined as the delivery of solutes to desired sites inside a polymer matrix with the aid of SC CO_2 (40). In general, one first exposes the polymer to SC CO_2-containing solutes for a period of time to transfer solutes from SC CO_2 phase to the polymer phase, then release CO_2 in a controlled manner and trap solutes in the polymer. When exposed to SC CO_2, polymers will exhibit various extents of swelling and enhanced chain mobility, which efficiently facilitate the transport of components. In general, lesser swelling means more difficult impregnation. At present, a lot of research on supercritical impregnation focuses on drugs, dyes, organic metallic complexes, and monomer and initiator impregnation (204).

In the dyeing processes of the textile industry, SC CO_2 as an alternative solvent has gained much interest to replace water-based processes. For example, the traditional dyeing process of PET fibers discharges waste water contaminated by dispersing agents, surfactants, and unused dyes. However, supercritical fluid dyeing (SFD) does not require any water, dispersing agents or surfactants, and does not involve drying after dyeing, which makes the process more environmentally friendly. Its high initial investment cost sets the barrier for its application in industry. However, it has strong potential in the application of hard-to-dye materials, eg, aramid, PE and PP fibers and films (204).

This process also allows synthesis of metallopolymer nanocomposites as follows: first SC CO_2 carries the organometallic compound to the polymer matrix and then the organometallic compound in the polymer is reduced or decomposed to metal by heat, chemical reagents, or radiations. There are reports on preparations of platinum nanoparticles in poly(4-methylpentene) and poly(tetrafluoroethylene), silver nanoparticles on the surface of polyimide film, silver nanoparticles in poly (ethylether ketone) and poly(styleneme-divinyl benzene) (205).

Finally, the technique of supercritical fluid impregnation can be used in the modification of polymers. An approach for chemical surface modification could be used to infuse monomer and initiator into a polymer matrix with the aid of CO_2 and afterward induce *in situ* polymerization within the polymer phase. Tang and co-workers (206,207) prepared electrically conductive polypyrrolepolystyrene composites by SC CO_2 impregnation. This technique is especially useful for synthesis of new polymer mixtures with thermally labile components or to produce biocompatible polymer surfaces.

SCF Cleaning and Drying. Applications of SC CO_2 in cleaning and drying benefit from its lack of surface tension, penetration efficiency, and low operating temperature to avoid distortion and degradation of delicate samples. The SCF cleaning and drying techniques have been used in textile cleaning, biological area, and microelectronic industry. The latter is described in detail below.

In dry cleaning of clothes, clothes are cleaned in a liquid solvent. “Dry” means that the exposure of clothes to water is minimized to prevent damage to hydrophilic fibers (13). The prevailing solvent used is perchloroethylene (also called perc or PCE), but perc spills can result in groundwater and soil contamination. Hydrocarbon solvents are also introduced for dry cleaning, but their flammability is a drawback. Environmentally friendly CO_2 was introduced to replace PCE or hydrocarbon solvents as a dry cleaning solvent in 1950s and has been commercialized. The controlled moisture in CO_2 does not damage hydrophilic fibers. In general, CO_2 dry cleaning is safer for clothes, workers, consumers, and the environment.

Critical point drying (CPD) is an established technique and can be used to dry all kinds of specimens, especially before examination with a SEM. A specimen and its solvent are maintained in CO_2 at SCF condition, and pressure releases in such a manner to avoid gas–liquid interface (160).

Large-Scale Polymer Processing Operations. Polymer foaming with CO_2 has been an active area recently because of restriction on the uses of ozone-depleting substances. Currently, three kinds of material, hydrogen-containing chlorofluorocarbons/fluorocarbons (HCFC/HFCs), hydrocarbons, and inert gases (eg, H_2O, CO_2, N_2) have the potential to replace the chlorofluorocarbon (CFC or Freon) physical foaming agents (40). Among these, CO_2 is the most preferable because of its unique features.

Carbon dioxide foaming has been used in industry for low value foam products (eg, packaging) while its applications in producing high value or high strength foams are still in progress. Carbon dioxide is being explored for products ranging from low density insulation ($<0.04\,g/cm^3$) to high density microcellular foams ($\sim 0.7\,g/cm^3$). Typical microcellular foams exhibit high impact strength, more importantly, they are light in weight, and consequently have higher mechanical strength/weight ratio than common structural foams. The challenges of CO_2 as a foaming agent are high pressure operation, dimensional instability during the foam-shaping process, and poor control of cell size and density. Some of these result from the high diffusivity of CO_2 compared to CFCs out of the foam.

In general, a foaming process consists of three steps: mix blowing agent into polymer melt to form homogeneous solution; increase temperature or decrease pressure to induce cell nucleation and phase separation; cells grow and coalesce to final foam morphology.

The foaming process can be carried out in a batch or continuous system. In batch foaming (208–210), preshaped samples are placed in a pressurized autoclave to achieve equilibrium, then bubble nucleation and growth are induced by pressure release or temperature increase. Figure 10 shows a polystyrene-based nanocomposite material foamed with CO_2 in a batch process at 120°C and 2000 psi.

Compared with batch foaming, a continuous extrusion process (212–218) is more attractive due to its high productivity, easier control, and flexible product shaping. A traditional extrusion process can be easily modified for foaming. For a typical extrusion foaming process, CO_2 is injected into the extruder barrel after melting the polymer resin, then the two components are mixed together to get a single phase by screw rotation and sometimes an in-line mixer. Usually, nucleation is initiated by the large pressure drop in the die. Foaming die temperature, pressure drop or pressure drop rate, and CO_2 concentration are key operating parameters in extrusion foaming (40).

5.6. Application in Microelectronic Engineering.

Supercritical CO_2 technologies have also been proposed for application in microelectronics processing (219). In traditional microelectronics processing, large volumes of water and solvents are used and toxic chemicals are released. To decrease the processing cost and abide by increasingly restrictive environmental regulations, the semiconductor industry is seeking alternatives. Carbon dioxide's unique features make it one of the best candidates for a more environmentally responsible replacement for organic and aqueous solvents used in many microelectronic processes. Some examples include drying, cleaning and photoresist stripping, developing, spin-coating, metal deposition, and silylation.

With the rapid development of the microelectronics industry, structures with smaller features are required. However, because of the surface tension of the rinse solution and spacing and aspect ratio of patterns, pattern collapse (deformation or bending) of structures becomes increasingly serious. By using SC CO_2 as the rinse liquid, cleaning can be controlled without presence of liquid−vapor interface. Some accomplishments are gained by using SC CO_2 technology to prevent collapse and some commercial systems are available (219,220).

Traditional photoresist stripping techniques produce a larger waste stream than other steps in the IC process, so photoresist stripping will probably be the first application of SC CO_2 in the process. A few companies are on the way to producing equipment for supercritical cleaning and resist stripping (219). Different from the commercialized CO_2 snow cleaning system that depends mainly on a physical mechanism for particle removal, SC CO_2 wafer cleaning and resist stripping also use chemical solvency mechanisms, often with the aid of a cosolvent. In addition, SC CO_2 has a high efficiency because it can rapidly penetrate crevices and boundary layers that snow cannot. Los Alamos's SCORR cleaning system (221) and Supercritical Systems Inc. (222) show successful results without damaging the underlying structures. Photoresist stripping without damage to the underlying low dielectric constant (low k) isolation material is an important advantage of SC CO_2 cleaning systems over conventional methods. With the aid of cosolvents, it can also remove organic particles, trace metals, and other contaminants. However, the high cost of SC CO_2 systems and requirements for continuous processing (CO_2 is batch) remain potential barriers for applications of SC CO_2 stripping technology.

Direct development of resists by CO_2 has the advantages of reducing chemical usage and processing steps (drying and developing become one step), therefore providing a "greener" and cheaper lithography. Some photoresists have been designed especially for direct development by CO_2 (223,224). Spin coating from liquid or SC CO_2 makes possible a green lithography platform incorporating spinning, developing, drying, and stripping of resists with the aid of cosolvents.

Chemical fluid deposition (CFD) of metals by SC CO_2 is gaining interest. Metals including copper and nickel have successfully deposited onto silicon through reduction of organometallic compounds with SC CO_2 as a carrier (225,226). In addition, it works on smaller features for which current CVD (Chemical Vapor Deposition) and PVD (Physical Vapor Deposition) technique are not viable (219).

Silylation of native oxide silicon surfaces can be conducted in a supercritical carrier solvent as a "greener" alternative to vapor or solution phase reactions (227). It can reduce the consumption of chemicals and improve surface coverage rate.

Although the high cost sets a barrier for application of SC CO_2 in microelectronic processing, it still has tremendous potential to become common in this area.

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Table 1. **Critical Properties for Common Supercritical Fluids**[a]

Solvent	CAS Registry Number	T_c, °C	P_c, MPa[b]	ρ_c, g/cm^3
ethylene	[74-85-1]	9.3	5.04	0.22
xenon	[7440-63-3]	16.6	5.84	0.12
carbon dioxide	[124-38-9]	31.1	7.38	0.47
ethane	[64-17-5]	32.2	4.88	0.20
nitrous oxide	[10024-97-2]	36.5	7.17	0.45
propane	[74-98-6]	96.7	4.25	0.22
ammonia	[7664-41-7]	132.5	11.28	0.24
n-nutane	[106-97-8]	152.1	3.80	0.23
n-pentane	[109-66-0]	196.5	3.37	0.24
isopropanol	[67-63-0]	235.2	4.76	0.27
methanol	[67-56-1]	239.5	8.10	0.27
toluene	[108-88-3]	318.6	4.11	0.29
water	[7732-18-5]	374.2	22.05	0.32

[a] T_c = critical temperature; P_c = critical pressure; ρ_c = critical density.

[b] To convert MPa to psi, multiply by 145.

Table 2. **Comparison of Properties of Gases, Supercritical Fluids, and Liquids**

Physical property	Gases	Supercritical fluids	Liquids
density, g/cm^3	0.001	0.2–1.0	0.6–1.6
diffusivity, cm^2/s	0.1	0.001	0.00001
viscosity, g/(cm·s)	0.0001	0.001	0.01

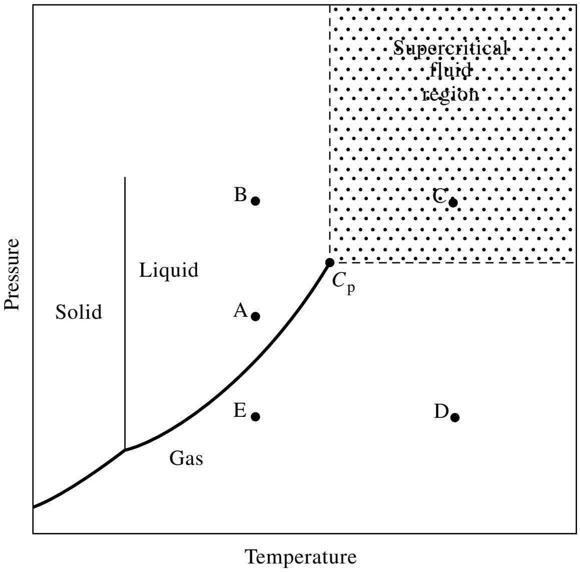

Fig. 1. Schematic pressure–temperature diagram for a pure material showing the supercritical fluid region, where C_p is the pure component critical point and dots A to E are points on the diagram (see text).

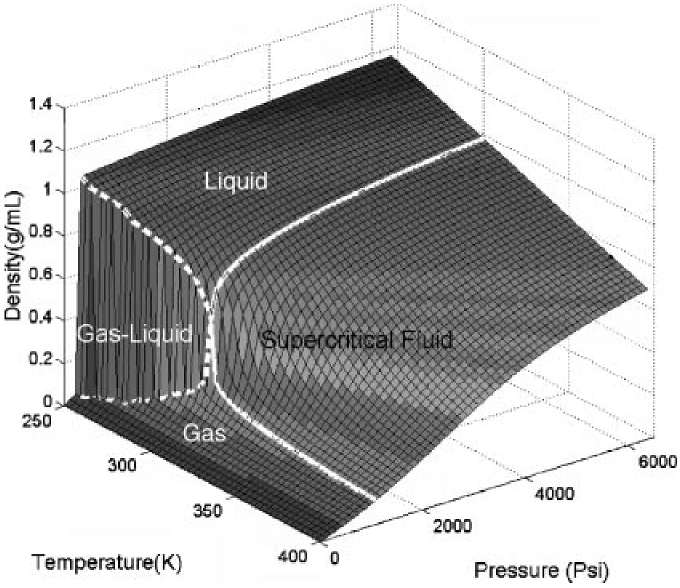

Fig. 2. Reduced density, ρ_r, versus reduced pressure, P_r, isotherms for pure carbon dioxide, where the numbers on the curves represent $T_r = T/T_c$ values. Critical properties may be found in Table 1.

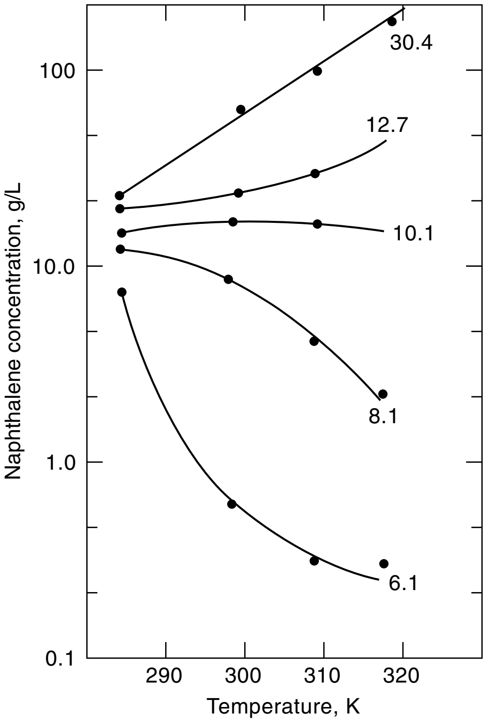

Fig. 3. Solubility isobars for solid naphthalene [91-20-3] in ethylene [74-85-1], where the numbers represent pressures in MPa (20–22). To convert MPa to psi, multiply by 145.

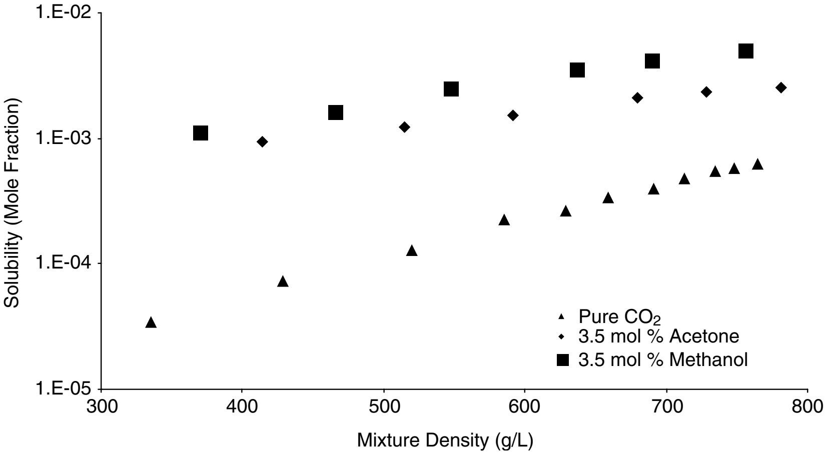

Fig. 4. Solubility of salicylic acid in CO_2 at 55°C with and without polar cosolvents, where (▲) represents pure CO_2; (◆), $CO_2 + 3.5$ mol % acetone; and (■), $CO_2 + 3.5$ mol % methanol (25). [Reprinted with permission from G. S. Gurdial, S. J. Macnaughton, D. L. Tomasko, and N. R. Foster, *Ind. Eng. Chem. Res.* **32**, 1488 (1993). Copyright © 1993 American Chemical Society.]

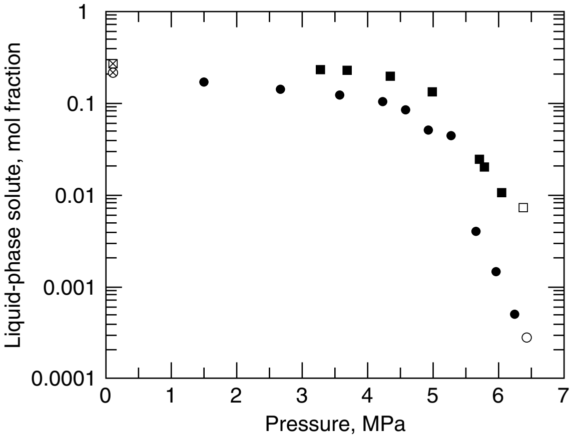

Fig. 5. Solubility of naphthalene (squares) and phenanthrene (circles) in mixtures of toluene expanded with carbon dioxide at 25°C (■, ●), in pure toluene (Θ, ⊗), and in pure CO_2 at 6.4 MPa (□,○) (28).

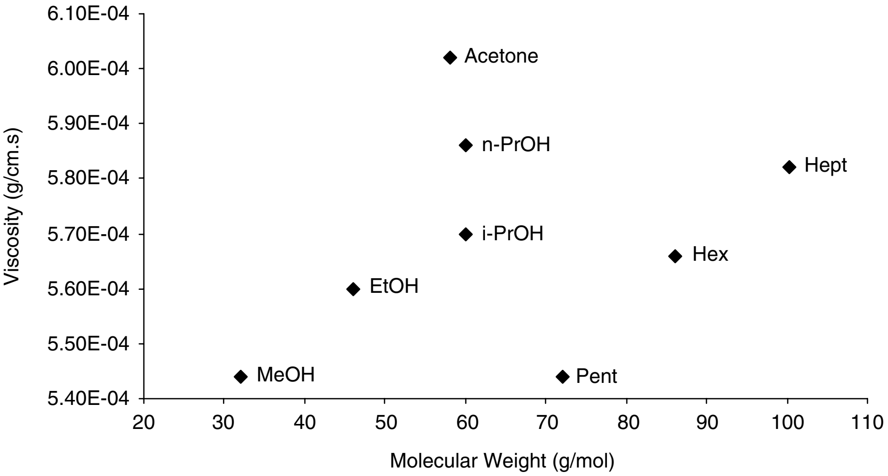

Fig. 6. Viscosity of 2 mol% cosolvent: CO_2 mixtures at 45°C and 12.0 MPa (30). [Reprinted with permission from K. D. F. Tilly, N. R. Macnaughton, and J. Stuart, *Ind. Eng. Chem. Res.* **33**, 681 (1994). Copyright © 1994 American Chemical Society.]

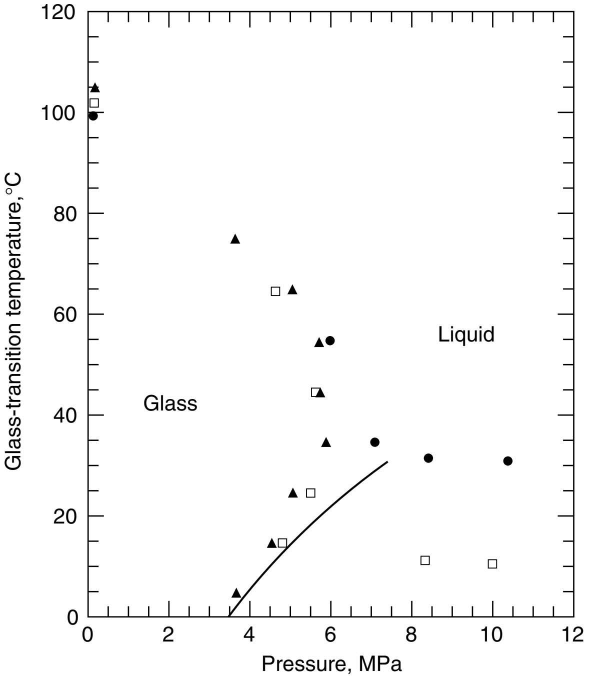

Fig. 7. Glass-transition temperatures of (▲) poly(methyl methacrylate) (PMMA); (□) poly(methyl methacrylate)-*co*-styrene (SMMA60); and (•) polystyrene (PS) as a function of carbon dioxide pressure, where the solid line represents CO_2 vapor pressure (41). To convert MPa to psi, multiply by 145.

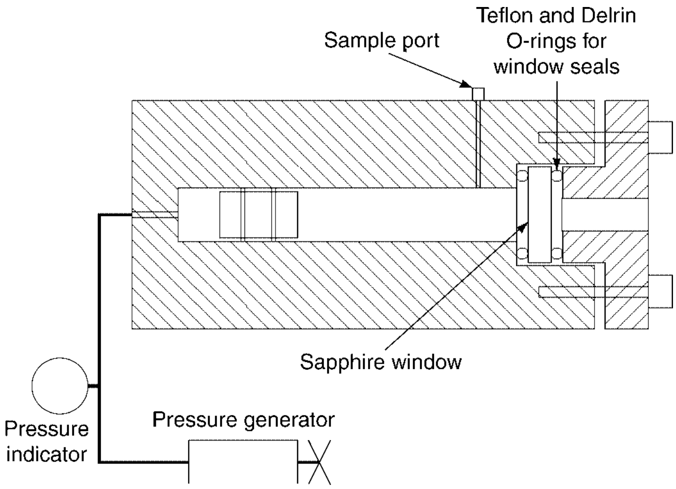

Fig. 8. Schematic drawing of a typical stainless steel variable-volume view cell having a movable internal piston. The outside diameter of the cell is 5.08 cm; the inside, 1.75 cm. Working pressure is 34 MPa (4930 psi) at room temperature.

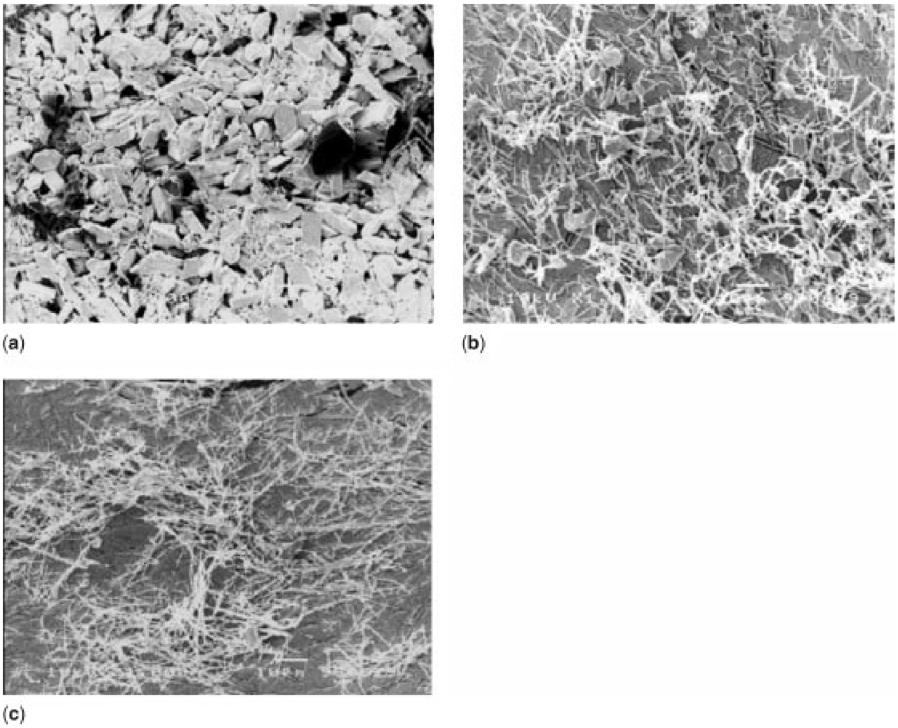

Fig. 9. Scanning electron microscopy graphs of drug–mannitol mixtures processed with SEDS. Drug/mannitol ratios: (**a**) 90:10, (**b**) 40:60, (**c**) 20:80. Scale bar represents 10 µm (184). [Reprinted from A. M. Juppo, C. Boissier, and C. Khoo, *Int. J. Pharmaceut.* **250**, 385 (2003). Copyright © 2003 with permission from Elsevier.]

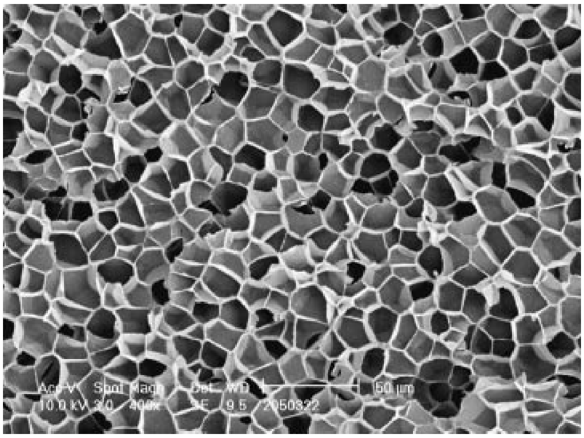

Fig. 10. Batch produced foam of a polystyrene–clay nanocomposite material. Scale bar: 50 µm; Cell size: 11.1 µm; Cell density: 6.25×10^8 cells/cm^3. [Reprinted with permission from Ref. 211.]