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Solubilities in Supercritical Fluids: The Application of Chromatographic Measurement Methods

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ABSTRACT

New methods are described for the measurement of the solubilities of solids in supercritical fluids. These methods utilize instrumentation developed for capillary supercritical fluid chromatography consisting of deactivated, small diameter, fused silica tubing, coupled with detection methods based upon on flame ionization and mass spectrometric detectors. The methods involve (a) direct solubility determination where the fused silica capillary is used as an equilibrium cell, and (b) a pressure of threshold solubility technique which resembles chromatography and uses a programmed pressure increase and sensitive detection to determine the onset of solute migration. Results are also presented which suggest that solubilities can be determined, within certain limitations, from actual chromatographic experiments. The methods are illustrated using aromatic hydrocarbons and complex mycotoxins of the trichothecene group.

INTRODUCTION

Supercritical fluids continue to find new applications in extraction, chemical fractionation, chemical analysis (chromatography), as reaction media, and in novel methods for the production of new materials (1-3). The primary property of a supercritical fluid which leads to such versatility is the continuously variable solvent power of the fluid. The potential applications, coupled

with present limitations of theoretical methods for prediction of supercritical fluid solubilities (and other properties), have resulted in widespread laboratory investigations. Typically these studies involve an initial qualitative assessment of the application and some measurement of solubility. For supercritical carbon dioxide, a relative wealth of available experimental data now exists. For complex systems, or those requiring higher pressures and temperatures, or more reactive fluids (e.g., ammonia, water, etc), experimental difficulties have hindered progress.

A number of micro-scale systems for characterization of supercritical fluid systems are currently being developed and applied in our laboratory. Many of these methods are based upon instrumentation and approaches developed for capillary supercritical fluid chromatography (4-13). Such micro-scale methods utilize extremely small volumes (<< 1 ml) and incorporate on-line methods for continuous or periodic chemical analysis. The advantages of this approach include greatly reduced cost and experimental set-up time, the ease with which a wide range of experimental variables may be evaluated (e.g. pressure, temperature, solvent composition, residence time), and an almost negligible risk associated with work on this scale. The on-line analysis methods are sensitive, typically requiring sample flow rates of <5 µl/min, allowing characterization of even thermally labile or nonvolatile components (including those for which conventional analytical methods are often inadequate), and minimizing consumption of the solvent and quantity of the material required for study. In addition, these methods allow measurements over a wide concentration range with extension to highly dilute solutions. The recent availability (14) of instrumentation for capillary supercritical fluid chromatography (SFC) should serve to widen interest in these methods.

In this report we describe three new approaches for the measurement of solid solubilities in supercritical fluids. These methods are based upon capillary SFC and related instrumentation. The methods have been illustrated using aromatic hydrocarbons and a group of more complex polar compounds, mycotoxins of the trichothecene group. The present results illustrate what appears to be typical solubility behavior for solids in supercritical fluids and demonstrate new methods for the study of fluid phase equilibria in dilute solutions.

EXPERIMENTAL

Direct Solubility Measurements from Capillary Cells

The apparatus used for these studies is shown in Figure 1 and is nearly identical to that described previously for supercritical fluid chromatography-mass spectrometry (SFC-MS) (4-6,9,11,13)). In brief, a pressure regulated high pressure syringe pump operated at room temperature delivers solvent through a 0.2 µl HPLC injection valve to a constant temperature oven. The oven contains a capillary

sample holder, one end of which is directly connected to an injection valve and the other end to a quadrupole mass spectrometer through a direct fluid injection (DFI) interface (6,9,11). The capillary sample holder (up to 2 m long) ensures that equilibrium is rapidly achieved due to the large sample surface area obtained by coating the solute on the inside of the 100 μm ID fused silica capillary. The capillary was deactivated by silylation at 350°C with a mixture of 80% hexamethyldisilazane (HMDS) and 20% trichloromethylsilane to ensure that an inert (but nonpolymeric) surface was produced. The solute was then coated onto the walls of the capillary using a standard procedure similar to that used in coating the inside of a capillary chromatographic column with stationary phase (7). To accomplish this, the solutes were dissolved in dichloromethane to a concentration of approximately 2 mg/ml. The solution was then forced into the capillary until the entire length was filled with solution. One end of the column was capped and the solvent removed over a period of several hours by evacuating the tube from the other end of the capillary. This procedure was assumed to result in the deposition of a uniform, solvent free film of the sample on the inner surface of the capillary to a depth of approximately 50 monolayers. The coated column was then placed in the oven of the SFC-MS instrumentation (Figure 1).

The transfer line in the DFI probe was also a deactivated fused silica capillary, 70 cm long by 100 μm ID. A restrictor (80 mm long by 7 μm ID fused silica capillary) at the end of the probe controlled flow and ensured a negligible (<.10 bar) pressure drop along the capillary and transfer line. In order to coat any possible remaining active sites in the transfer line with the solute and minimize any film thickness inhomogeneities, insuring that the solution is in equilibrium with the solid solute while passing down the transfer line, the system was first "conditioned" by heating the probe and oven to the desired temperature,then raising the pressure of the solvent until a good signal was obtained on the spectrometer. The pressure was then reduced, causing the material in the transfer line to drop out of solution and coat the surface.

For solubility measurements, temperature was held constant and the solvent pressure raised stepwise from a selected starting value. Sufficient time was allowed between steps for the system to reach equilibrium (< 5 min) before data were acquired. The mass spectrometer was operated in the chemical ionization (CI) mode with ammonia as the reagent gas (6,11). Under these conditions the trichothecenes studied produced primarily $(M + 18)^+$ ions with abundances proportional to the mass flux entering the detector (13). The spectrometer was equipped with an Extrel Model 271 dual electron ionization (EI)/CI source, which allowed switching modes electronically and permitted measuring the solvent-flow rate by monitoring the solvent signal in the EI mode. Therefore, at each pressure step the solute signal was measured in the CI mode and the solvent signal recorded in the EI mode. A Teknivent data system controlled mass spectrometer scanning and data acquisition.

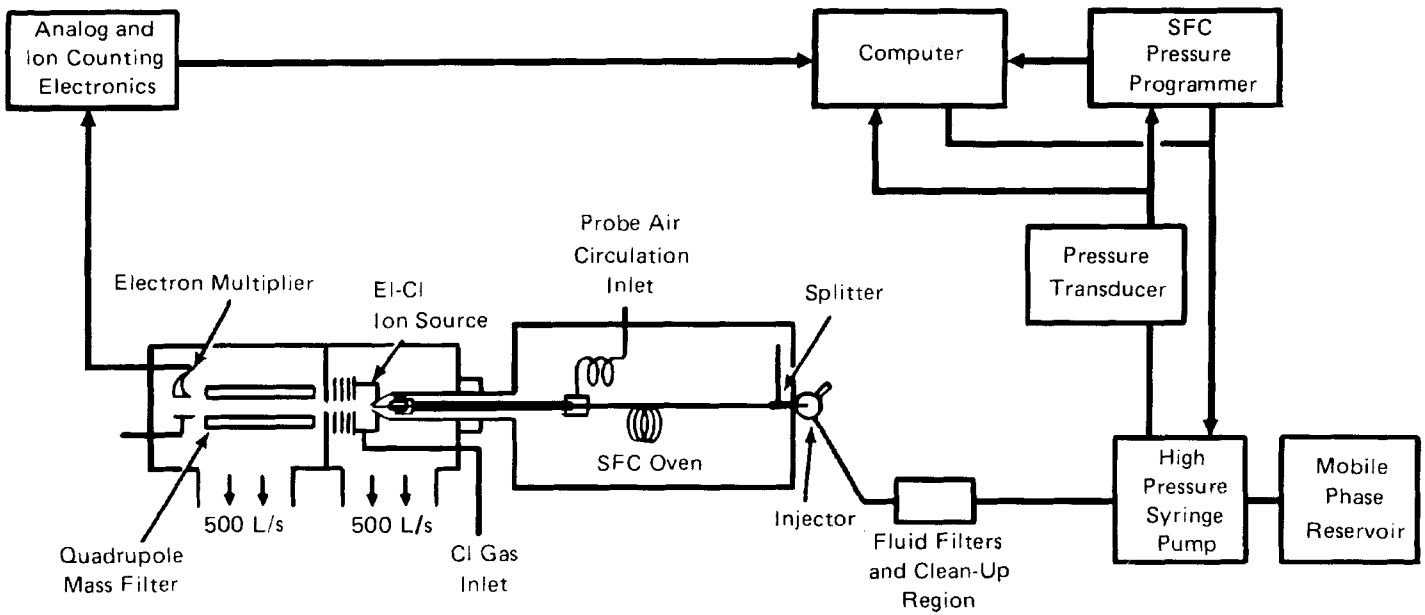

Figure 1. Schematic illustration of the instrumentation for solubility measurements using direct fluid injection-mass spectrometry.

This procedure was continued until the sample was exhausted. The system was then calibrated for an absolute response factor using a 0.2 µl HPLC injection valve to inject a solvent blank into the system, followed by injection of a standard solution containing a known amount of the solute. These injections allowed determination of the absolute response of the system for each experiment. The solvent flow rate was calibrated by recording the EI solvent signal; then withdrawing the probe and measuring the absolute flow from the restrictor with a flow meter at the same temperature. The solute concentrations were calculated from the ratio of solute signal to solvent signal corrected for the appropriate mass spectrometric response factors.

Pressure of Threshold Solubility Measurements

The instrumentation used for threshold pressure measurement is similar to that used for capillary supercritical fluid chromatography with flame ionization detection. A schematic diagram of this instrumentation is shown in Figure 2. The apparatus utilized a modified Varian 8500 syringe pump controlled with a microcomputer to maintain accurate pressure control and generate programmed pressure ramps. A pressure transducer (Setra Systems, Model 204) monitored pressure during threshold pressure determinations (accuracy ± 0.3 bar), and the precision and stability of the pressure control was ± 0.1 bar. Constant temperature conditions (± 0.5°C) were provided by a Hewlett-Packard 5700 gas chromatograph oven. Detection of the dissolved solute was with a flame ionization detector. A 6 m x 100 µm ID length of deactivated fused silica capillary tubing was used as the sample cell. Deactivation was accomplished as described for the capillary-equilibrium studies. Sample solutions were introduced into the capillary tubing at ambient temperatures with a 0.06 µl Valco C14W HPLC injection valve. The capillary tubing was connected to the injection valve through a splitter device which allowed an 1:80 split flow into the capillary tubing so that the actual sample volume injected was ~ 0.7 nl. The linear velocity of the supercritical carbon dioxide was controlled to approximately 1.5 cm/sec by connecting the terminal end of the 100 µm capillary tubing with a short length (25 mm) of 5 µm ID fused silica restrictor column.

Threshold pressure measurements were made by injecting a solution of the solute at a selected oven temperature. Solutions were prepared in methylene chloride at approximately 20 mg/ml concentration. The pressure of the carbon dioxide was held slightly above the critical pressure (~ 75 bar) during injection and elution of the solvent band. The pressure was then slowly increased, typically at 2.0 or 4.0 bar/minute. The pressure was recorded when the solute band was eluted. To correct for transit time through the capillary, the flow rates were determined and corrected for variations in the linear velocity of the supercritical carbon dioxide due to pressure ramp rate (12) by injecting a volatile solvent and measuring its elution time at various pressures and calculating integrated

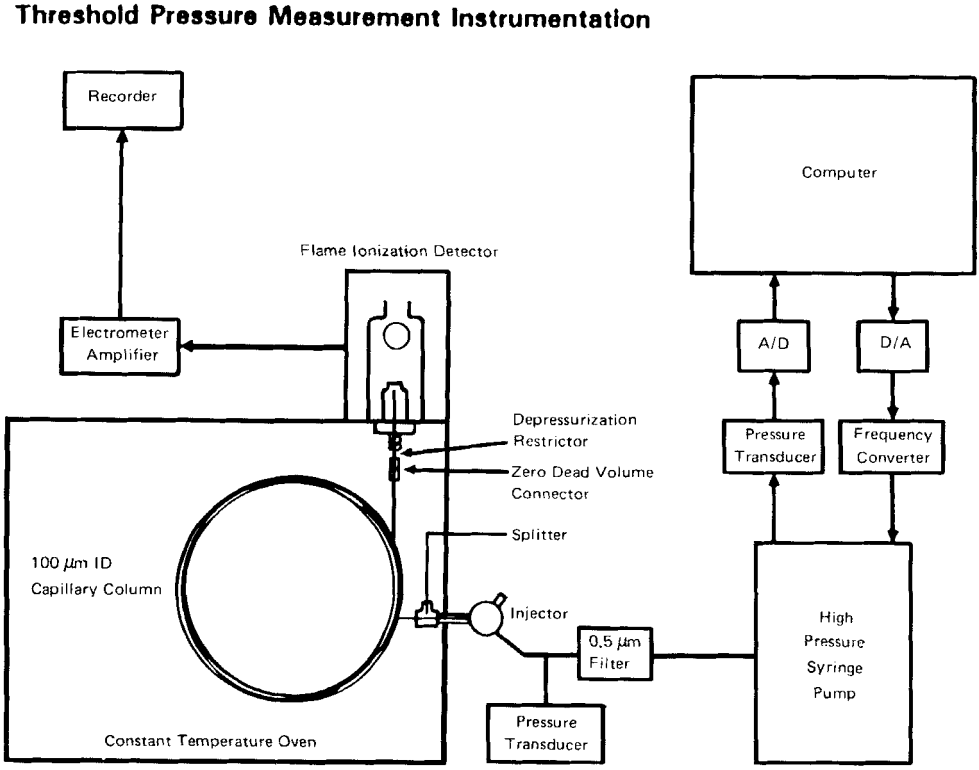

Figure 2. Schematic illustration of instrumentation used for pressure of threshold solubility measurements with flame ionization detection and for capillary supercritical fluid chromatography.

elution times as described previously (12). The solutes included pyrene, benzo[e]pyrene, diacetoxyscirpenol (DAS), deoxynivalenol (DON), and T-2 Toxin (T-2).

Capillary Chromatography Measurements

The experimental apparatus and technique has been described in detail elsewhere (7,10,13) and is similar to that described above, except an open tubular capillary column coated with a polymeric stationary phase was used. The retention factors of selected solutes under isothermal conditions at various pressures were obtained using capillary columns coated with a cross-linked 5%-phenyl polymethylphenylsiloxane stationary phase and carbon dioxide as the mobile

phase. The retention times of the solute as a function of carbon dioxide pressure were determined by a reporting integrator with an accuracy of 0.1 second.

RESULTS AND DISCUSSION

Capillary-Equilibrium Cell Measurements

The fused silica capillary-equilibrium cell provides relatively rapid measurements of solubility (< ~ 10 min per datum) because of the continuous nature of the experiment and the large surface area of the coated capillary, which assures rapid equilibrium is attained. Direct fluid injection-mass spectrometric analysis allows continuous monitoring of the abundances of the solute and solvent with virtually no restriction on the nature of the system (4,6,10,11). Up to five orders of magnitude change in solubility could be measured from a single column loading. The maximum solubility observed in these studies was about 3.3×10^{-3} mole fraction, and may still be considered relatively dilute. One practical restriction of the capillary-equilibrium technique is the limitation to relatively dilute systems, so that the solute is not exhausted from the cell after only a few measurements. As the solute coating on the deactivated fused silica approaches a monolayer, surface effects become significant and reliable equilibrium measurements are not feasible. This situation is characterized by continuously decreasing solute concentration; such measurements were disgarded and the capillary recoated with solute.

Figures 3 and 4 show solubility measurements, as log mole fraction (χ)vs. the calculated density for the pure solvent obtained from a cubic equation of state for diacetoxyscirpenol (DAS), T-2 toxin (T-2), and deoxynivalenol (DON) in N_2O and CF_3Cl (freon-13), respectively. Table 1 lists the three supercritical fluid solvents, their critical parameters, liquid densities and solubility parameters at liquid densities. Table 2 gives the melting points and molecular weights of the trichothecene mycotoxins (15). Solubilities were reported at 98°C in N_2O, Figure 3 and 89°C in CF_3Cl, Figure 4, which correspond to a reduced temperature (temperature/critical temperature) of 1.2. DAS and T-2 are significantly less polar than DON (although the melting points are roughly equivalent) and thus have much greater solubilities in nitrous oxide under most conditions. In all cases dramatic increases in solubility were observed as density was increased.

Qualitatively these results show a nearly linear relation between log mole fraction and density for dilute solutions. Interestingly, comparison of N_2O and CF_3Cl data shows that the divergence from this trend occurs at much lower concentrations for CF_3Cl. This observation is consistent with the fact that CF_3Cl is generally an inferior solvent compared to N_2O or CO_2. This coincides with the observed effects upon solvent properties seen in solvatochromic studies (16), where solvent properties of CF_3Cl change more gradually with density than N_2O or CO_2.

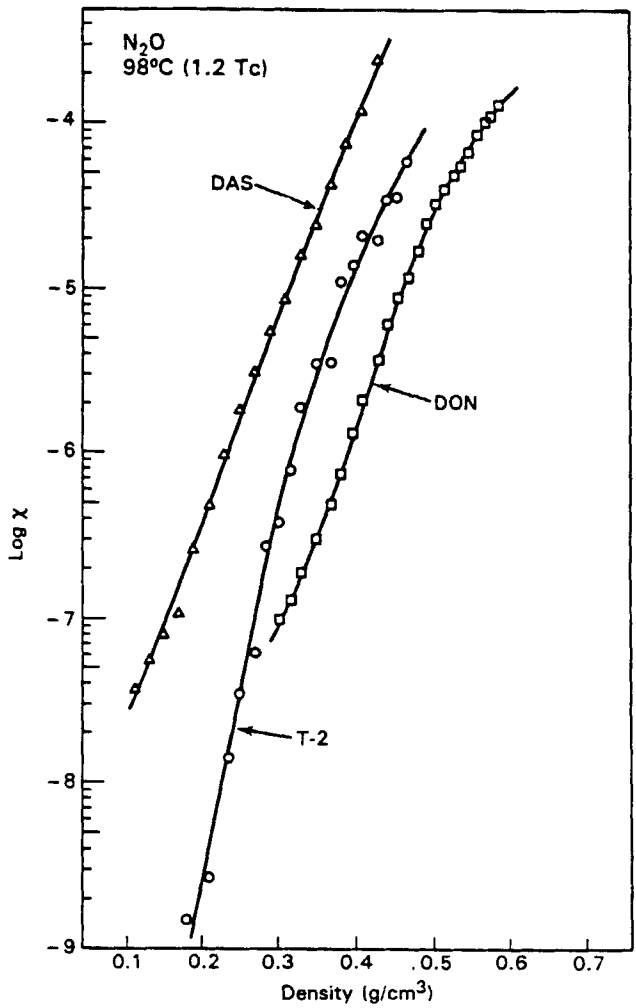

Figure 3. Solubility (log mole fraction) as a function of nitrous oxide fluid density for three trichothecenes at 98°C.

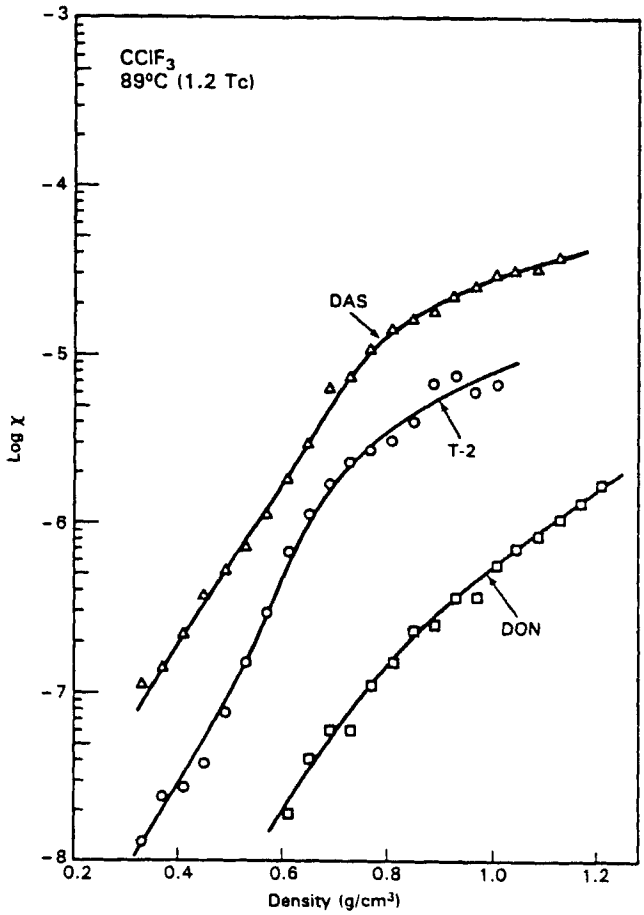

Figure 4. Solubility (log mole fraction) as a function of freon-13 fluid density for three trichothecenes at 89°C.

TABLE 1: Properties (33) of Supercritical Solvents used in this Work

Solvent	T_c (°K)	P_c (MPa)	ρ_c (g/cm^3)	ρ_l (g/cm^3)[a]	Solubility Parameter[b] (cal/cm^3)$^{1/2}$
CO_2	304	7.36	0.46	1.24	10.7
N_2O	310	7.24	0.45	1.22	10.6
CF_3Cl	302	3.86	0.58	1.57	7.7

[a] Density of subcritical liquid at atmospheric pressure.
[b] Determined as described in Reference 17.

TABLE 2. Physical Properties of Trichothecene Mycotoxins[a]

Trichothecene	Molecular Formula	Molecular Weight	Melting Point
Deoxynivalenol (DON)	$C_{15}H_{20}O_6$	296	151-153°C
Diacetoxyscirpenol (DAS)	$C_{19}H_{26}O_7$	366	162-164°C
T-2 Toxin (T-2)	$C_{24}H_{34}O_9$	466	151-152°C

[a] Reference 15.

A marked increase in solubility with temperature at a fixed density is also observed. The proportional increase is not the same for all of the solutes, with DON showing a larger effect than the less polar solutes. The relative solubilities were DAS > T-2 > DON, but the observed temperature dependence suggests that the order might change at sufficiently high temperatures. Figure 5 compares solubilities for DAS at a reduced temperature of 1.1 in N_2O and CO_2. Relative solubilities can also be compared by relating density to the solubility parameter of the fluid, as described by Giddings (17). In comparing solubility in CO_2 with

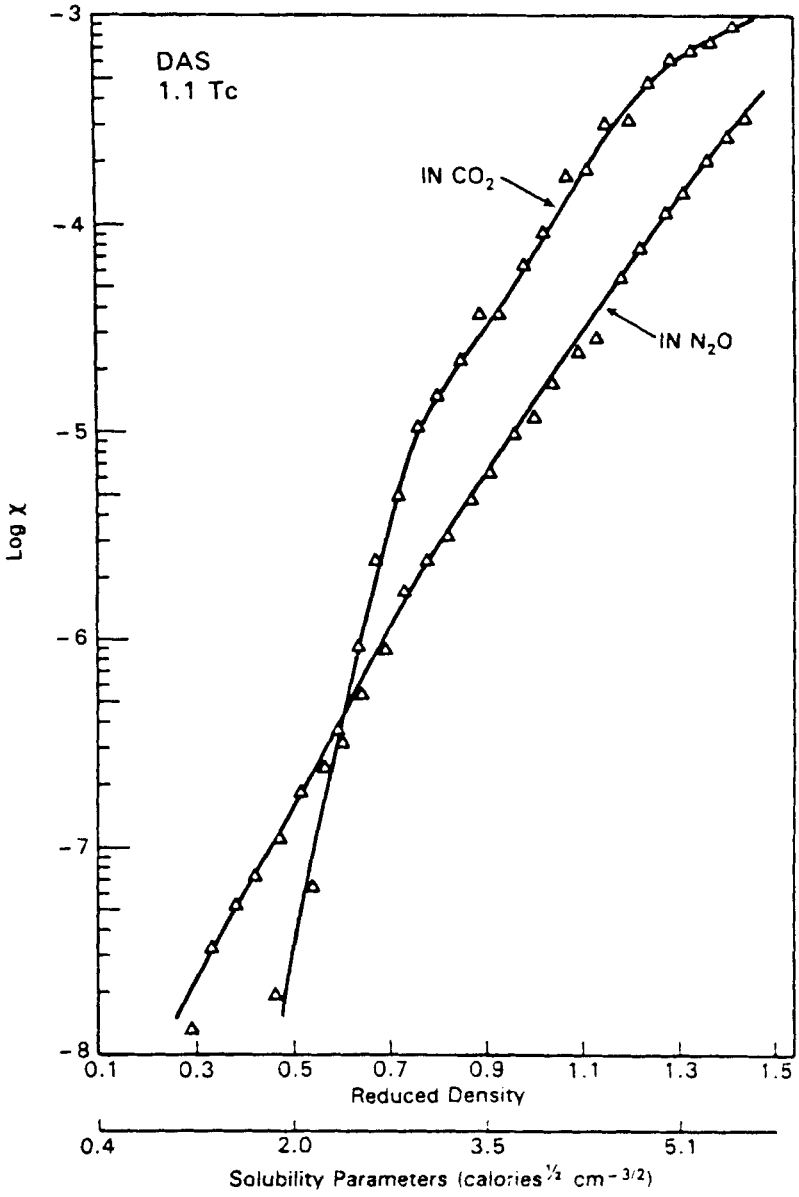

Figure 5. Comparison of DAS solubility (mole fraction) in carbon dioxide and nitrous oxide as a function of reduced density and fluid solubility parameter at a reduced temperature of 1.1.

solubility in N_2O, it should be noted that for a given pressure the reduced densities and solubility parameters of the two fluids will be nearly the same since their critical parameters are similar (Table 1).

Solubilities are quite different between the CF_3Cl and N_2O supercritical solvents. Figure 6 gives the solubilities of DAS and DON in the two fluids as a function of solubility parameter (which is directly proportional to density for a particular fluid). It can be seen that solubility increases more rapidly in N_2O than in CF_3Cl as the solubility parameter increases. This is consistent with the observed effects upon solvent properties observed in solvatochromic studies (16) where we have observed the solvating properties of CF_3Cl to change much more gradually with density than N_2O. It can also be seen from Figures 3 and 4 that solubilities become more similar at low densities as the contribution due to vapor pressure becomes significant. Similar data for other fluids and temperatures and in multicomponent mixtures will be reported elsewhere (18).

Pressure of Threshold Solubility Measurements

The concept of "threshold pressure" was originated by Giddings and coworkers (17, 19) and refers to the pressure at which detectable migration (or solubility) occurs. Consideration of the solubility data for the trichothecenes shows that the threshold pressure would obviously be dependent upon the sensitivity of the analytical methodology used to establish migration. Thus, physically useful threshold pressure measurements are obtained only when (a) the detector sensitivity is relatively constant or predictable from compound to compound, and (b) when the range of solubilities of interest is limited to relatively dilute solutions. The first limitation is necessary to allow meaningful comparison of the threshold pressures between compounds. The second arises from the fact that relative solubilities in dilute solutions are often nearly invariant with pressure at constant temperature (e.g., see Figures 3 and 4), and the sensitivity of the analytical technique readily allows measurements in this regime. Since solubility varies strongly with pressure, minor changes or variations in detector sensitivity are not likely to be the limiting factor in determining the quality of threshold pressure measurements.

An example of a threshold pressure measurement is given in Figure 7 which shows flame ionization detector response to T-2 toxin at 62°C (T_R = 1.1) in supercritical carbon dioxide. After injection of the T-2 toxin in the sample solvent (methylene chloride) and elution of the solvent, the pressure was increased at a rate of typically 2 or 4 bar/min until elution of the solute was observed (peak at right). At higher pressure ramp rates the rise in solute signal is typically quite sharp due to the rapid increase in solubility with pressure. Response to an arbitrary

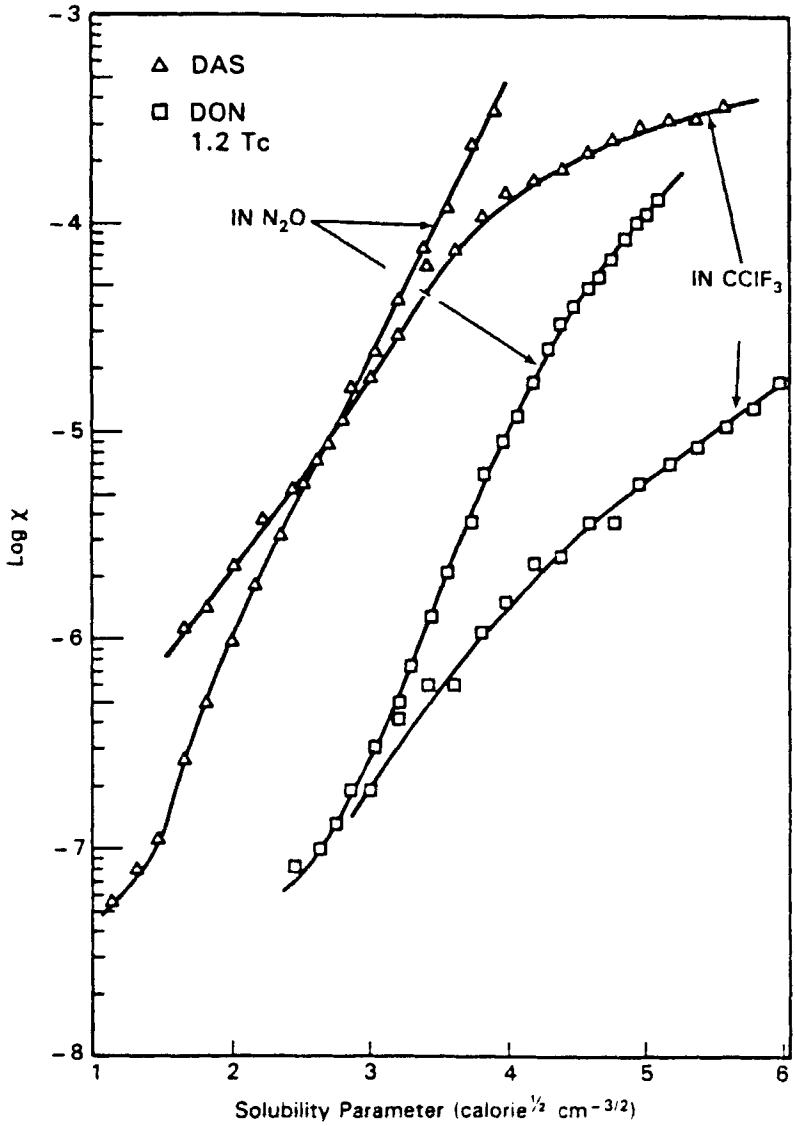

Figure 6. Comparison of solubilities of DAS and DON in nitrous oxide and freon-13 as a function of solubility parameter.

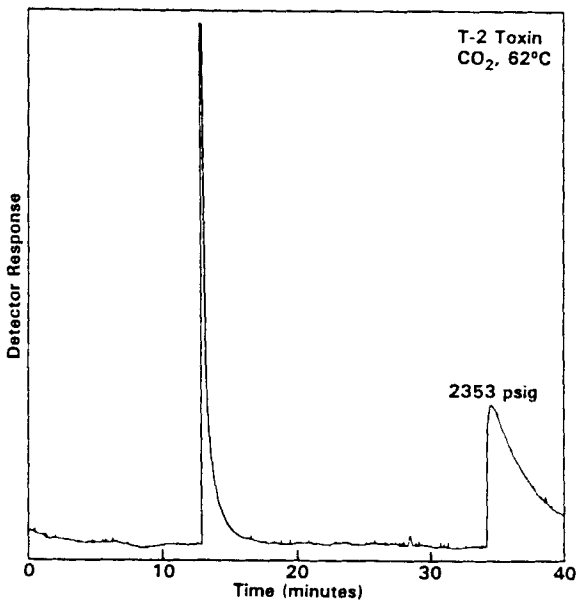

Figure 7. Example of data obtained during a pressure of thresnold solubility measurement for T-2 toxin for a pressure ramp rate of 4 bar/min with carbon dioxide at 62°C.

intensity level is considered the uncorrected threshold pressure. The pressure at the time of elution is then corrected for flow rate (i.e., transit time through the column) and the actual pressure of threshold solubility calculated. Comparison of threshold pressure measurements with actual solubility measurements for the trichothecenes indicates that the threshold solubility concentration corresponds to a mole fraction of DAS or T-2 in the range of 0.5 -3 x 10^{-5} (for a detector signal-to-noise ratio of about 50:1.)

Tables 3 and 4 give threshold pressure measurements for two polycyclic aromatic hydrocarbons and the three trichothecenes at various temperatures for supercritical carbon dioxide. The measurements in Table 3 for pyrene and benzo[e]pyrene show that the threshold pressure appears to pass through a maximum as temperature is increased for pyrene, while a steadily increasing value was observed for benzo[e]pyrene. For benzo[e]pyrene the decreased solvent density leads to lower solubility in the fluid at constant pressure as temperature is increased. This is manifested as an increased threshold pressure. For pyrene a more

TABLE 3. Threshold Pressure Measurements in Carbon Dioxide

	Pressure (Bar)	
Temperature	Pyrene	Benzo[e]pyrene
45°C	64.1 ± 1.1	84.1 ± 0.1
55°C	70.8 ± 0.1	92.0 ± 0.2
75°C	63.2 ± 0.2	106.8 ± 0.7
100°C	61.8 ± 0.3	117.1 ± 1.0
125°C	49.0 ± 0.2	125.2 ± 1.0

TABLE 4. Trichothecene Threshold Pressure Measurements in Carbon Dioxide

	Pressure Bar		
Temperature	DAS	T-2	DON
62°C (TR = 1.1)	125.1 ± 0.5	120.0 ± 2.0	--
92°C (TR = 1.2)	122.8 ± 1.1	157.2 ± 0.5	197.1 ± 1.1
125°C (TR = 1.3)	--	--	166.9 ± 0.2

complicated case is observed because of its greater volatility. Initially the threshold pressure increased because of decreased solvent density, but above ~ 60°C the threshold pressure decreased because of the large increase in vapor pressure.

Somewhat similar trends can be seen in Table 4 for the trichothecenes. The higher molecular weight T-2 gave an increased threshold pressure when temperature was increased, while the lower molecular weight DAS had a nearly constant value. The DON showed a decreased threshold pressure at elevated temperatures. It should be noted that for both the aromatic hydrocarbons and the trichothecenes that the retention behavior in SFC shows a very similar dependence upon pressure and temperature (12); however, the trichothecenes show changes in elution order with DON usually eluting from the chromatographic column between DAS and T-2 (13).

The pressure of threshold solubility measurements are relatively rapid and provide information on relative solubilities and separations in dilute supercritical fluid solutions. While such threshold measurements are more easily obtained than the capillary-equilibrium cell studies described previously, they are more limited because of the fixed migration concentration measured (i.e., the threshold solubility). In principle, such measurements can be extended by injection of large volumes of solute so that a continuous measurement of solubility vs. pressure can be obtained during the programmed pressure increase (since the flow rate is readily measured in addition to the solute concentration). In this limit, the technique would be the same as the capillary-equilibrium measurements, with the difference due to the method of solute deposition in the capillary (i.e., static off-line coating vs. a dynamic solute injection/coating process). In practice, this is difficult because of the need to evaporate substantial quantities of liquid solvents while avoiding immediate transfer of the solute to the detector. A possible solution to this problem may be to utilize a supercritical fluid for solute introduction to the capillary.

Solubility Measurements from Chromatographic Studies

The ability to measure supercritical fluid solubilities at a selected pressure and temperature by a chromatographic process would be generally valuable since it would be rapid and would circumvent the limitations of threshold solubility measurements to more dilute solutions. Any such measurements must take into account the chromatographic phase partitioning process. Recent work with highly deactivated and nonselective stationary phases in capillary SFC has suggested that, in the absence of adsorption and specific chemical interactions with the stationary phase, fluid phase solubility is the major determinant of retention (20). Our interest here was to use available solubility data to predict retention in SFC, with the implicit assumption that, if successful, the alternative prediction of relative solubilities would also be feasible.

Retention in SFC is determined by solute solubility in the fluid and solute interaction with the stationary phase. The functional relationship between retention and pressure at constant temperature has been described by Van Wasen and Schneider (21). The trend in retention is shown to depend on the partial molar volume of the solute in the mobile and stationary phases coupled with the isothermal compressibility of the fluid mobile phase.

A simple relationship between solubility and chromatographic retention was derived from which solute retention behavior can be examined on the basis of theory and experiment in order to gain some insight into the complicated dependence of retention on the thermodynamic and physical properties of the solute and the fluid.

The solubility of a pure, incompressible solute in a fluid over the pressure region of interest has been discussed in a simple form by Gitterman and Procaccia (22). The combination of solute solubility in a fluid with the equation for retention as a function of pressure allows one to determine the effect of solubility on solute retention.

In SFC the basic assumption of infinitely dilute solutions of the solute in the mobile and stationary phases is generally valid. The concentration of the solute in these respective phases is $C_i = X_i/V_m$, where X_i is the mole fraction of solute (i) and V_m is the molar volume of the pure mobile or stationary phase (21). Solute retention is calculated from a dimensionless retention factor, k, where,

$$k = (C_i^{stat}/C_i^{mob}) \cdot (V^{stat}/V^{mob}) \quad (1)$$

C_i^{stat} and C_i^{mob} are the concentration of solute (i) in the stationary and mobile phases, respectively, V^{stat} and V^{mob} are the volumes of the stationary and mobile phase. Substituting for concentration into equation 1,

$$k = (X_i^{stat}/X_i^{mob}) \cdot (V_m^{mob}/V_m^{stat}) \cdot (V^{stat}/V^{mob}) \quad (2)$$

or alternatively:

$$\ln k = \ln (X_i^{stat}/X_i^{mob}) + \ln (V_m^{mob}\, V^{stat}/V_m^{stat} V^{mob}) \quad (3)$$

At equilibrium, the solute chemical potential in the respective phases are equal, $\mu_i^{stat} = \mu_i^{mob}$ (23). Therefore,

$$\mu_i^{stat} = \mu_i^{mob} = \mu_i^{o\ stat} + RT \ln X_i^{stat} = \mu_i^{o\ mob} + RT \ln X_i^{mob} \quad (4)$$

where μ_i^o is the chemical potential at the chosen standard state at infinite dilution of solute (i) in the two phases. Rearranging equation 4,

$$\ln (X_i^{stat}/X_i^{mob}) = (\mu_i^{mob} - \mu_i^{stat})/RT \quad (5)$$

Substituting equation 5 into 3,

$$\ln k = (\mu_i^{mob} - \mu_i^{stat}) / RT + \ln (V_m^{mob} V^{stat}/V_m^{stat} V^{mob}) \quad (6)$$

An assumption can be made that the second term on the right-hand side of equation 6 is independent of pressure except for V_m^{mob}, the molar volume of the fluid mobile phase. Therefore, differentiation of equation 6 with respect to pressure at constant temperature yields,

$$(\partial \ln k/\partial P)_T = 1/RT \quad (\partial \mu_i^{mob}/\partial P)_T - (\partial \mu_i^{stat}/\partial P)_T + (\partial \ln V_m^{mob}/\partial P)_T \tag{7}$$

The partial molar volume of a solute is defined as $(\partial \mu_i/\partial P)_T$ (23) and on rearranging the second term in equation 7 is seen to be the isothermal compressibility of the fluid mobile phase (24). Thus on substitution equation 7 reduces to,

$$(\partial \ln k/\partial P)_T = 1/RT\ \bar{V}_i^{mob} - \bar{V}_i^{stat} - K \tag{8}$$

where $\bar{V}_i^{mob}$ and $\bar{V}_i^{stat}$ are the partial molar volume of the solute (i) in the mobile and stationary phases at infinite dilution, respectively, and K is the isothermal compressibility of the fluid mobile phase.

The solubility of a solid in a supercritical fluid has been described by Gitterman and Procaccia (22). The region of interest chromatographically will be for infinitely dilute solutions whose concentration is far removed from the lower critical end point (LCEP) of the solution. Therefore the solubility of the solute in a supercritical fluid at infinite dilution far from the critical point can be approximated as,

$$(\partial \ln X_i^{mob}/\partial P)_T = 1/RT \quad V^S - \bar{V}_i^{mob} \tag{9}$$

where V^S is the molar volume of the pure solid solute (22). Solving equation 9 for $\bar{V}_i^{mob}$:

$$\bar{V}_i^{mob} = -RT\ (\partial \ln X_i^{mob}/\partial P)_T + V^S \tag{10}$$

Equation 10 can be substituted into equation 8 and upon rearrangement,

$$(\partial \ln k/\partial P)_T = (V^S - \bar{V}_i^{stat})/RT - (\partial \ln X_i^{mob}/\partial P)_T - K \tag{11}$$

Equation 11 gives the relationship between retention, solubility and pressure at constant temperature for infinitely dilute solutions within the limitations of the assumptions. The dependence of k on pressure described by Equation 11 consists of three terms. The first term is a constant whose value depends on the partial molar volume of the solute in the stationary phase. The second term can be determined experimentally from bulk solubility measurements of the solute in the supercritical fluid mobile phase. The last term, the solvent isothermal compressibility, can be reasonably predicted from a two-parameter, cubic equation of state (EOS) such as the Redlich-Kwong EOS or the Peng-Robinson EOS (25,26).

The isothermal compressibility of the pure fluid solvent mobile phase was determined using the Redlich-Kwong EOS to evaluate the derivative $(\partial V_m^{mob}/\partial P)_T$ in equation 12,

$$(\partial \ln V_m^{mob}/\partial P)_T = (1/V_m^{mob}) \cdot (\partial V_m^{mob}/\partial P)_T = -K \tag{12}$$

The molar volume of the pure fluid solvent was determined in a similar fashion allowing the isothermal compressibility of the fluid to be calculated.

Therefore from equation 11, the trend in retention as a function of pressure at constant temperature can be determined and is related to the solubility of the solute in the supercritical fluid, the isothermal compressibility of the solvent and the partial molar volume of the solute in the stationary phase at infinite dilution.

Solute retention as a function of pressure has been determined experimentally for a wide number of solutes over a range of temperatures and pressures (21, 27-29). The trend in retention of a solute with pressure can be correlated by the simple thermodynamic relationship given in equation 11. The solubility of naphthalene in CO_2 has been reported by McHugh and Paulaitis at 35°C, 55.0°C, 60.4°C, and 64.9°C (30). The slope $(\partial \ln X_i^{mob}/\partial P)_T$ at 35°C and 64.9°C was obtained by interpolation between the data points while the data was extrapolated to lower pressures using the method outlined by Kurnik et al. (31). This allowed modeling of retention for a wider range of pressure. The solute partial molar volume in the stationary phase was assumed constant and independent of pressure (32). These assumptions allow one to calculate the trend in solute retention based on the solubility of the solute in the mobile phase. Figure 8 gives the calculated retention obtained using equation 11 compared to experimental data. The simple thermodynamic model allows satisfactory calculation of retention data particularly since the assumptions allow only one adjustable parameter (which corresponds to the absolute magnitude of k).

On closer examination of equation 11, one can deduce that as the isothermal compressibility of the solvent becomes less important (temperature and pressure further removed from the critical temperature and pressure), $(\partial \ln k/\partial P)_T$ is proportional to the solubility of the solute in the fluid phase. Therefore, if solubility is found to be a linear function of density, then retention will mirror this behavior and also be a linear function of density. Furthermore, as conditions are further removed from the critical pressure and temperature of the solvent, it is more likely that a constant slope ($(\partial \ln k/\partial P)_T$ = constant) will be obtained. Such a relationship is commonly observed in SFC (12).

The simple thermodynamic relationship developed above has been shown to adequately describe the features of solute retention as a function of pressure at constant temperature for supercritical fluid chromatography within a set of constraints involving solute or solvent interactions with the stationary phase. The approach provides a relationship between solute solubility in the fluid mobile phase and solute retention in SFC. The trend in solute retention is also dependent on isothermal compressibility and the partial molar volume of the solute in the stationary phase. The results clearly suggest the use of

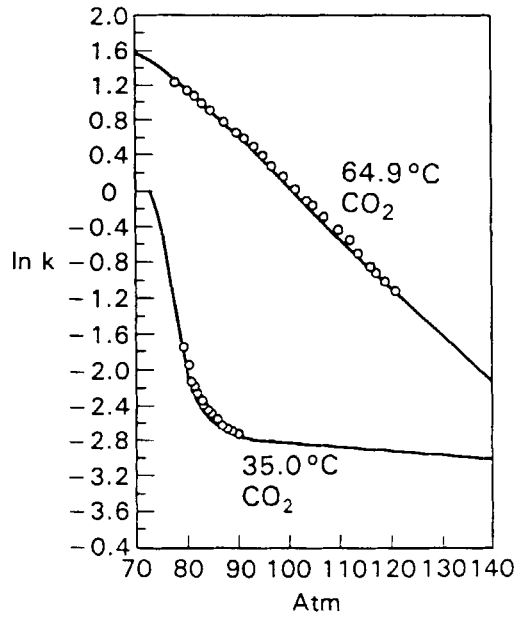

Figure 8. Comparison of experimental and calculated retention factors for naphthalene in carbon dioxide at 35°C and 64.9°C.

chromatographic methods, within certain constraints, for the measurement of solubilities in supercritical fluids. Such measurements require either accurate data on the partial molar volume of the solute in the stationary phase or a solubility measurement at the given temperature. Further developments may serve to generalize this approach to include liquids and polar systems and provide an approach for measurement of partial molar volumes of solutes in various condensed phases.

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