Solubilities of Substituted Phenols in Supercritical Carbon Dioxide

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The binary (solute + CO_2) equilibrium solubilities of six substituted phenols (2,5-dimethyl phenol, 2,3-dimethyl phenol, 2,4,6-trimethyl phenol, 2,3,5-trimethyl phenol, 4-phenyl phenol, and 4-*tert*-butyl phenol) were determined at a temperature of 308 K in the pressure range of 10.1 to 28.0 MPa. Solubility data were obtained using a dynamic approach with a simple and reliable apparatus. The mole fraction solubilities of substituted phenols ranged from 5.14×10^{-5} to 2.56×10^{-2}. Solubilities of three ternary (two solutes + CO_2) systems were investigated at a temperature of 308 K in the pressure range of 10.1 to 28.0 MPa. In the 4-phenyl phenol + 2,3,5-trimethyl phenol and 4-phenyl phenol + 2,4,6-trimethyl phenol systems, the solubility of 4-phenyl phenol was enhanced relative to its binary solubility by 22.9 % and 217 %, respectively. The 2,3,5-trimethyl phenol and 2,4,6-trimethyl phenol did not exhibit any solubility enhancements in the two ternary systems. Accurate solubilities could not be measured for the 2,5-dimethyl phenol + 4-*tert*-butyl phenol ternary system due to the existence of a liquid phase under the conditions studied.

Introduction

Supercritical fluid carbon dioxide (SCF CO_2) is an attractive solvent for a variety of SCF processes.[1−3] The application of SCF CO_2 to any process requires knowledge of accurate solubility information for all components in the system. For this reason, the solubility of compounds in SCF CO_2 has been investigated. The data have been compiled by several researchers.[4−6] However, solubility data are still extremely scarce for several classes of compounds. This lack of accurate solubility data is often cited as one of the main factors hindering the progress of SCF technology.[4,7−10]

Furthermore, the majority of the experimental studies have dealt with binary systems (solute + SCF CO_2). On the other hand, solubility data derived from mixed solute systems are relatively scarce. The study of mixed solute systems is important since real systems of practical interest are multicomponent in nature. It has been reported that solubility of a solute in the presence of cosolutes can be considerably different from its binary solubility.[11−21] In most cases, solubility enhancements have been observed. Binary solubility may provide only a limited picture, and this may have implications in the process design of a commercial plant and on its operating and capital costs. To promote a more widespread use of SCFs in the industry, there is a great need for reliable solubility determinations for pure and mixed solute systems.

Phenols are an important class of compounds used in the manufacture of polymers, plastics, dyes, and fragrances and serve as intermediates in the synthesis of medicines and agricultural chemicals.[22,23] However, there is very little information in the literature regarding the solubility of phenols in SCF CO_2.[24−28]

In this study, we investigated the solubilities of six industrially important substituted phenols in binary and ternary systems (two solutes + SCF CO_2) at 308 K in the pressure range of 10.1 to 28.0 MPa. The selected substituted phenols include 2,5-dimethyl phenol (2,5-DMP), 2,3-dimethyl phenol (2,3-DMP), 2,4,6-trimethyl phenol (2,4,6-TMP), 2,3,5-trimethyl phenol (2,3,5-TMP), 4-phenyl phenol (4-PP), and 4-*tert*-butyl phenol (4-tBuP). In addition, the effect of impurities and the purity of the sample on the solubility measurements of 2,3-DMP have also been investigated.

Experimental Section

Materials. "Bone-dry" industrial-grade CO_2 (> 99.9 %) was obtained from Superior Water & Welding. Histological-grade methanol was obtained from Fisher and was used for sample dilutions. Reagent-grade potassium monobasic phosphate was obtained from Fisher. HPLC-grade methanol and HPLC-grade acetonitrile were obtained from Fisher. The sources, purities, and melting points of the substituted phenols used in the study are shown in Table 1. All chemicals were used as received without further purification.

Apparatus. Figure 1 is the schematic diagram of the apparatus designed and built in-house to perform solubility measurements using a dynamic method.[29,30] Liquid CO_2 from a cylinder with a siphon attachment was directed into a high-pressure syringe pump (Isco model 260D), which was used to compress CO_2 to the desired operating pressure. A digital pressure gauge (Omega; DPG-5000), calibrated against a NIST certified pressure gauge (accuracy ± 0.1 %), was used to monitor the pressure of the system. During the experiment, the pressure of the system was maintained constant to within ± 0.1 MPa. A heating coil (10 m, 1/16 in. stainless steel tube) ensured that solvent reached the desired temperature prior to entering the equilibration cell. The equilibration cell was an empty HPLC column (10 cm × 4.6 mm or 15 cm × 4.6 mm) with stainless steel filters at each end. A gas chromatograph oven (Varian 1400) was used to maintain the temperature of the system (within ± 1 K). The temperature was controlled externally and calibrated against NIST traceable thermometers.

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Table 1. Sources, Purities, and Melting Points (T_m) of the Substituted Phenols

substance	source	purity	T_m/K
2,3-dimethyl phenol	Aldrich	∼97 %	346−348
2,5-dimethyl phenol	Aldrich	99+ %	348−350
2,3,5-trimethyl phenol	Aldrich	99 %	365−368
2,4,6-trimethyl phenol	Aldrich	99 %	341−344
4-*tert*-butyl phenol	Aldrich	99 %	371−374
4-phenyl phenol	J. T. Baker	99 %	439−440

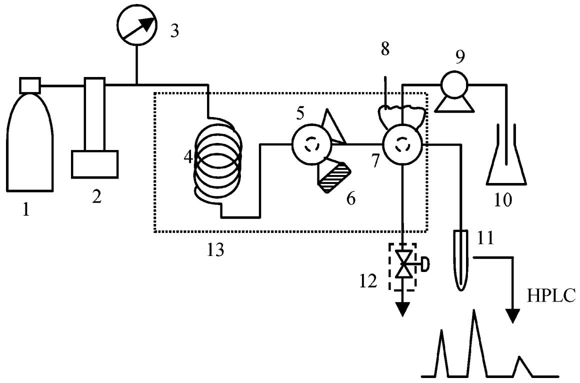

Figure 1. Schematic diagram of the solubility apparatus: 1, CO_2 cylinder; 2, CO_2 pump; 3, pressure gauge; 4, heating coil; 5, switching valve; 6, equilibration cell; 7, sampling valve; 8, sample loop; 9, solvent pump; 10, solvent reservoir; 11, analyte collection; 12, heated micrometering valve; 13, oven.

A switching valve (6-port Rheodyne model 7100) directed the pressurized CO_2 to flow either through the equilibration cell (equilibration mode) or to bypass the equilibration cell and purge the rest of the system (bypass mode). A microsampling valve (6-port Rheodyne model 7110) with a sample loop was used to obtain a fixed volume of the saturated solution (120 μL) for off-line analysis (sample mode). Both valves were manually controlled. A Milton Roy mini-pump was used to flush the sample loop and the microsampling valve with the trapping solvent. A heated micrometering valve was used to maintain the pressure of the system and to manually control the flow of SCF CO_2. It also functioned as a vent.

To ensure that only solid−fluid equilibria existed under the experimental conditions used for solubility studies, the phase behavior of all the systems was checked visually using a phase monitor (Supercritical Fluid Technologies, Inc.). The phase behavior study involved the visual determination of the lower critical end point[21] for each system and verifying the absence of a liquid phase due to depression in the melting point of the solutes.

Method. In a typical experiment, the equilibration cell was packed with ground solid solute (∼700 mg), and glass wool plugs were placed at both ends to prevent clogging of the filters. For ternary solubility studies, equal amounts of the selected solutes were weighed, mixed, and ground to obtain a uniform composition of the solid mixture before packing into the equilibration cell.

Operating in the bypass mode, the system was initially purged with CO_2 at low pressure and then brought up to the desired system temperature and pressure and allowed to stabilize. Prior to sampling, the system was switched to equilibration mode. In the equilibration mode, the SCF CO_2 flowed through the equilibration cell, and the saturated SCF CO_2 solution exiting the equilibration cell flowed through the sample loop of the microsampling valve and was depressurized across a heated micrometering valve. After about 35 to 60 s (sufficient time to obtain an equilibrated sample), the microsampling valve was switched to sample mode. The sample loop with saturated SCF CO_2 solution was depressurized into a trapping solvent (1 to 2 mL of methanol) and collected off-line in a collection tube. The system was immediately returned to bypass mode using the switching valve. The loop was rinsed with 3 to 4 mL of methanol to collect any precipitated solute. The contents of the collection tube were then transferred and diluted volumetrically with methanol for analysis by HPLC.

Calibration of the Sampling Loop. The sampled volume included both the sampling loop and the associated dead volume in the microsampling valve. This volume was calibrated by filling the microsampling valve with a stock solution of known solute concentration and washing the loop contents into a collection tube for dilution and HPLC analysis. The resultant peak area was compared to a standard to determine the concentration followed by the calculation of the loop volume.

Solubility of the solutes is expressed here as mole fraction solubility (y):

$$y = \frac{\text{no. of moles of solute}}{\text{total no. of moles of saturated solution in sampling loop}} \tag{1}$$

The total number of moles of the saturated solution in the sampling loop is calculated from the volume of the loop and the density of the saturated SCF CO_2 solution. For solid solubilities below 1 mol %, the density of the saturated solution is essentially the same as the density of the solvent.[30,31] Density values for SCF CO_2 were taken from those reported by Schmitt and Reid.[32]

The bypass mode prevented sample carryover problems between runs as the system was purged with CO_2. To confirm that there was no carryover, blank extractions were conducted in the bypass mode by sampling the CO_2 flowing through the sampling loop followed by HPLC analysis of the diluted trapping solvent.

Analysis. The collected samples were analyzed by HPLC. An HPLC pump (Waters; model 590), an injection valve (Rheodyne; model 7125) with 20 μL injection loop volume, a UV−Vis detector (Waters; model 490), an integrator (Dionex; model 4270), and an HPLC column (Spherisorb ODS-2; 5 μm; 25 cm × 4.6 mm) were used. For all the solutes except 2,3-DMP, the column was operated at a flow rate of 1.0 $mL\cdot min^{-1}$ using a mobile phase of 0.010 M KH_2PO_4 (pH = 4.27) and methanol (40:60). The wavelength of detection for 2,5-DMP, 2,4,6-TMP, and 4-tBuP was 265 nm. For 2,3,5-TMP and 4-PP, the detector was set at 280 nm. For 2,3-DMP, the column was operated at a flow rate of 1.0 $mL\cdot min^{-1}$ using a mobile phase of 0.010 M KH_2PO_4 (pH = 4.27) and acetonitrile (50:50), and the detector was set at 274 nm. The stock solutions for all the analytes were prepared in methanol. Area−concentration calibration curves were used to determine the concentration of the collected analytes. A new calibration curve was generated each time an analysis of the sample solutions was conducted.

Results and Discussion

Verification of the Method. The phase behavior investigation of all the solute systems, with the exception of the 2,5-DMP + 4-tBuP ternary system, confirmed that the conditions used for solubility measurements in the present study were well above the critical region of CO_2 and that the data presented represent solid−fluid equilibria with no liquid phase present.

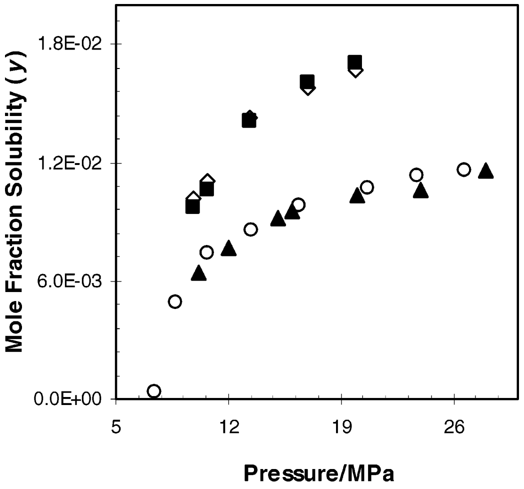

Figure 2. Solubility isotherms of naphthalene and 2,5-DMP in supercritical CO_2 at 308 K. Naphthalene solubility: ■, this work; ◇, ref 29. 2,5-DMP solubility: ▲, this work; ○, ref 28.

Naphthalene is often used as a calibration standard to validate the accuracy of the experimental method.[12,27] To test the reliability and accuracy of our solubility measurement technique, the solubility of naphthalene in SCF CO_2 was determined at 308 K over a pressure range of 9.8 to 19.9 MPa and compared to that reported by McHugh and Paulaitis.[29] Each mole fraction solubility of naphthalene plotted in the figure is an arithmetic average of three replicate measurements with a relative standard deviation of 2 % or less.

In addition, our experimental solubility data of 2,5-DMP at 308 K in the pressure range of 10.1 to 28.0 MPa was compared with that reported by Iwai et al.[28] As evident from Figure 2, there is good agreement between the literature data and the data presented in this work. Each experimental mole fraction solubility of 2,5-DMP plotted in Figure 2 is an arithmetic average of three replicate measurements with a relative standard deviation of 3 % or less. These results also served to validate the method employed in this study.

Binary Solubility. Solubility measurements were carried out at CO_2 (liquid) flow rates ranging from 0.8 to 2.5 $mL\cdot min^{-1}$. Variation of the flow rate within this range was found to have no effect on the observed solubilities, thereby confirming that solubility measurements were made under equilibrium conditions. Experimentally measured solubilities of the six substituted phenols at 308 K in the pressure range of 10.1 to 28.0 MPa are listed in Table 2. In Table 2, each reported solubility data point is an average of at least three replicate measurements with relative standard deviation within 5 %. To avoid bias, replicate solubility measurements for each condition were performed on separate days. The standard deviation of these measurements is also presented in Table 2.

Examination of solubility data at a constant temperature reveals the expected trend of increasing solubility with increasing pressure. The rate of increase in solubility is higher at lower pressures and is less pronounced at higher pressures. The increase in solvent power with the increase in pressure can be explained in terms of the increase in the solvent density.[33,34]

The selected substituted phenols exhibited solubilities ranging from 5.14×10^{-5} to 2.56×10^{-2} mole fraction and were in the following order: 2,4,6-TMP > 2,3-DMP ≈ 2,5-DMP > 4-tBuP > 2,3,5-TMP > 4-PP. The variation in solid solubilities in SCF CO_2 is mainly due to two factors: the vapor pressures of solutes and the intermolecular interactions between the solute and solvent. In general, the vapor pressure (volatility) of solid solutes exerts primary influence on the solubilities and also on the selectivities in CO_2. The observed differences in the solubility of the substituted phenols correlated with the relative melting points and thus the vapor pressure of the solutes; the higher the melting point, the lower the solubility. Similar trends have been reported in the literature.[35,36]

Although the melting points of 4-tBuP and 2,3,5-TMP are very close, solubility of 4-tBuP was slightly higher than 2,3,5-TMP, which could be because of the differences in the nature of the substituents present on the phenol. Among the isomers, the dimethyl phenol isomers have similar solubility; whereas, in the case of trimethyl phenol isomers, there is an order of magnitude difference in solubility. Solubility of isomers in SCF CO_2 has been studied by several researchers, and it has been suggested that solubility is related to the melting point.[37,38] The results obtained in the present study conform to the general behavior of the isomers.

Effect of Impurities on Solubility of 2,3-DMP. The purity of the samples used for solubility measurements may be critical as it can affect the accuracy of the solubility data. The influence of the impurities on the component solubility is determined by their nature and volatility. There are reports in the literature which suggest that the presence of impurities, even in the range of 0.1 to 5 wt %, results in orders of magnitude changes in solute solubility.[39,40] The 2,3-DMP reagent used in this study was ~97 % pure and contained several impurities (~50 different components, observed as chromatographic peaks). This system served as a real multicomponent system and presented an opportunity to study the effect of impurities on the solubility measurements. A comparison of solubility data obtained from 97 % pure 2,3-DMP with that of 99 % pure 2,3-DMP is represented in Figure 3. Despite the presence of several impurities, there was no change in the solubility of 2,3-DMP. It is likely the impurities were substantially less volatile and therefore did not result in any significant change in the 2,3-DMP solubility.

Ternary Solubility. Three ternary systems (4-PP + 2,3,5-TMP, 4-PP + 2,4,6-TMP, and 2,5-DMP + 4-tBuP) were investigated. At a temperature of 308 K, ternary solubility data were determined at seven different pressures in the range of 10.1 to 28.0 MPa. To compare the ternary solubility with the binary solubility, solubility enhancement (SE) was calculated at each pressure condition. SE is defined as the percent relative increase of the ternary solubility relative to the binary solubility of the component at the same temperature and pressure:[21]

$$SE = (y_{\text{ternary}} - y_{\text{binary}})/(y_{\text{binary}}) \times 100\ \% \qquad (2)$$

In each of the ternary systems, at least one of the solutes exhibited enhanced solubility relative to its binary solubility. According to Dobbs and Johnston,[41] solubility enhancements in most ternary systems follow a pattern where the solubility of a given solid increases relative to that in its binary system in proportion to the solubility of the other solid in the system (the entrainer effect). This effect is usually negligible unless the solubility of the "other solid" exceeds 0.5 mol %.

4-PP + 2,3,5-TMP Ternary System. The solubility data for a 50:50 wt % mixture of 4-PP and 2,3,5-TMP are presented in Table 3. In this table, each reported solubility data point is an average of at least three replicate measurements with relative standard deviation within 5 %. The ternary solubility data exhibited trends similar to binary data (i.e., an increase in solubility with an increase in pressure at constant temperature). The tabulated results also show the corresponding solubility

Table 2. Solubilities of Substituted Phenols in SCF CO$_2$ (Binary Systems) at 308 K

P	2,5-DMP	2,3-DMP	2,3,5-TMP	2,4,6-TMP	4-tBuP	4-PP
MPa	$10^3\,y^a$	$10^3\,y^a$	$10^3\,y^a$	$10^3\,y^a$	$10^3\,y^a$	$10^3\,y^a$
10.1	6.40 (± 0.19)	6.18 (± 0.14)	2.41 (± 0.09)	14.7 (± 0.5)	3.09 (± 0.05)	0.0514 (± 0.0012)
12.0	7.70 (± 0.13)	7.91 (± 0.07)	3.06 (± 0.04)	17.6 (± 0.6)	4.15 (± 0.05)	0.0633 (± 0.0036)
15.1	9.20 (± 0.26)	9.86 (± 0.21)	3.71 (± 0.06)	20.9 (± 0.2)	5.19 (± 0.04)	0.0755 (± 0.0033)
16.0	9.51 (± 0.33)	9.90 (± 0.25)	3.82 (± 0.08)	21.7 (± 0.8)	5.39 (± 0.08)	0.0836 (± 0.0042)
20.0	10.4 (± 0.3)	12.3 (± 0.3)	4.27 (± 0.09)	24.4 (± 1.3)	6.30 (± 0.09)	0.104 (± 0.004)
24.0	10.6 (± 0.4)	14.8 (± 0.4)	4.61 (± 0.04)	25.6 (± 0.9)	6.93 (± 0.05)	0.122 (± 0.005)
28.0	11.6 (± 0.2)	15.5 (± 0.2)	4.88 (± 0.04)		7.44 (± 0.12)	0.136 (± 0.007)

[a] y = mole fraction solubility (± standard deviation).

Table 3. Solubilities of 4-PP + 2,3,5-TMP in SCF CO$_2$ (Ternary System) at 308 K

P	4-PP		2,3,5-TMP	
MPa	$10^3\,y^a$	SE^b/ %	$10^3\,y^a$	SE^b/%
10.1	0.0547	6.36	2.27	−5.91
12.0	0.0682	7.67	2.89	−5.53
15.1	0.0895	18.6	3.55	−4.34
16.0	0.103	22.9	3.73	−2.48
20.0	0.127	21.7	4.24	−0.85
24.0	0.146	19.7	4.55	−1.09
28.0	0.164	21.1	4.85	−0.56
average		16.9		−2.97

[a] y = mole fraction solubility. [b] SE = solubility enhancement.

Table 4. Solubilities of 4-PP and 2,4,6-TMP in SCF CO$_2$ (Ternary System) at 308 K

P	4-PP		2,4,6-TMP	
MPa	$10^3 y^a$	SE^b/%	$10^3\,y^a$	SE^b/%
10.1	0.137	166	14.3	−2.98
12.0	0.188	197	17.4	−1.42
15.1	0.239	217	20.7	−1.23
16.0	0.260	211	21.2	−2.26
20.0	0.296	184	23.6	−3.27
24.0	0.346	184	25.3	−1.11
average		193		−2.04

[a] y = mole fraction solubility. [b] SE = solubility enhancement.

enhancements relative to the binary solubility data. Under the conditions studied, the solubility of 4-PP in the presence of 2,3,5-TMP was enhanced up to 22.9 %. Relative to the binary solubility, the solubility of 2,3,5-TMP in the presence of 4-PP was slightly lower with an average solubility enhancement of −2.97 %. This difference is still within the limits of experimental precision and is attributed to experimental error rather than an actual change in solubility behavior. The low solubility enhancements observed in this study for 4-PP indicate weak solute−solute interactions, which are probably governed by dispersive forces.[21]

4-PP + 2,4,6-TMP Ternary System. The solubility data for a 50:50 wt % mixture of 4-PP and 2,4,6-TMP are presented in Table 4. In this table, each reported solubility data point is an average of at least three replicate measurements with relative standard deviation within 5 %. The tabulated results also show the corresponding solubility enhancements relative to the binary solubility data. In the presence of 2,4,6-TMP, the solubility of 4-PP is enhanced up to 217 %. There was no discernible change in the solubility of 2,4,6-TMP, and the average solubility enhancement (−2.04 %) was within the limits of the experimental error. This result supports Dobbs and Johnston's postulate that a more soluble solute (2,4,6-TMP solid; solubility > 0.5 mol %) causes a more significant increase in the solubility of a less soluble component (4-PP) rather than vice versa.

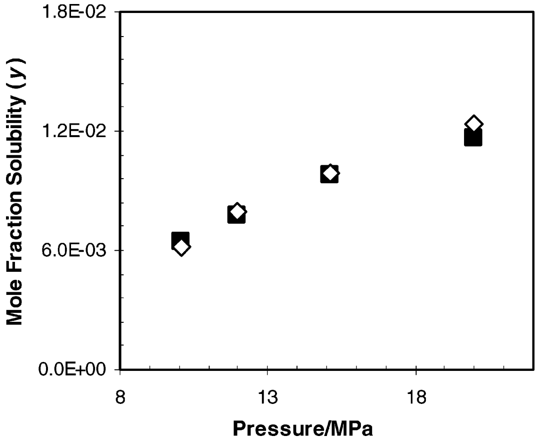

Figure 3. Comparison of solubility isotherms of 2,3-DMP at 308 K: ■, 99 % pure 2,3-DMP; ◇, 97 % pure 2,3-DMP.

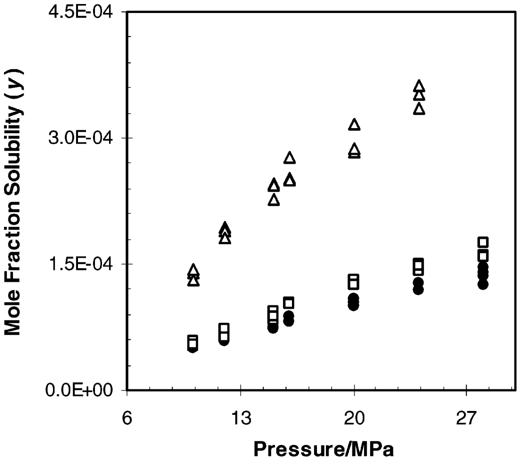

Figure 4. Comparison of binary solubility and ternary solubility of 4-PP at 308 K: ●, binary solubility; □, ternary solubility in (4-PP + 2,3,5-TMP); △, ternary solubility in (4-PP + 2,4,6-TMP).

In both the 4-PP + 2,3,5-TMP and the 4-PP + 2,4,6-TMP ternary systems, the negligible solubility enhancement for 2,3,5-TMP and 2,4,6-TMP, respectively, can be attributed to the low solubility of 4-PP. Figure 4 shows a comparison of binary solubility of 4-PP with ternary solubility of 4-PP in the two ternary systems. In this figure, the data from replicate solubility measurements have been presented.

2,5-DMP + 4-tBuP Ternary System. The ternary system containing a 50:50 wt % mixture of 2,5-DMP + 4-tBuP exhibited unusually high solubilities leading to clogging of the micrometering valve, inconsistent flow rates, and irreproducible results with high percent RSDs. The solubility of 2,5-DMP was enhanced up to 3207 %, and that of 4-tBuP was enhanced up to 1559 % relative to their individual binary solubilities.

This degree of solubility enhancement is unrealistic in mixed solid systems that display solid−fluid equilibria, and it seemed unlikely that the high solubilities observed are merely due to the interactions between solutes. Phase behavior study of this mixture using a view cell apparatus revealed the existence of a liquid phase under the conditions studied. It is likely that physical removal of solute liquid phase by the flow of CO_2 through the equilibration cell led to high apparent solubilities and irreproducible measurements.

Conclusions

Equilibrium solubilities of six substituted phenols in SCF CO_2 were measured by the dynamic solubility method in the pressure range of 10.1 to 28.0 MPa at 308 K. The solubility database provided by this investigation can be very useful for correlation of data, development of predictive models, and design of SCF processes such as extraction, synthesis, separation, and purification.

The study of the 2,3-DMP system consisting of several impurities provided a good example of a real multicomponent system. The solubility behavior of 2,3-DMP in the presence of the less soluble impurities was similar to the two ternary systems studied, where the solubility of the more soluble solute was unaffected by the presence of a less soluble cosolute. The effect of the more soluble 2,3-DMP on the solubility of the less soluble impurities, however, could not be studied because of the lack of knowledge of the impurities and/or the availability of suitable standards.

The solubility enhancements observed in the 2,3,5-TMP + 4-PP and 2,4,6-TMP + 4-PP ternary systems conform to the entrainer effect. The solubility enhancements of 4-PP in the two ternary systems vary greatly as a result of the differences in the solubilities of 2,3,5-TMP and 2,4,6-TMP. Accurate solubilities could not be measured for the 2,5-DMP + 4-tBuP ternary system due to the existence of a liquid phase under the conditions studied.

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