1162 *J. Chem. Eng. Data* **2000,** *45,* 1162−1166

Phase Behavior of Poly(L-lactide) in Supercritical Mixtures of Carbon Dioxide and Chlorodifluoromethane

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Phase behavior data are presented for poly(L-lactide) (L-PLA: MW = 2000 g·mol^{-1}), a biodegradable polymer, in supercritical solvent mixtures of carbon dioxide (CO_2) and chlorodifluoromethane (HCFC-22). Experimental cloud point curves, which were the phase boundaries between single and liquid−liquid phases, were measured using a variable-volume view cell apparatus for various CO_2 compositions up to about 82 mass % (on a polymer-free basis) and for temperatures up to about 393.15 K. The location of the phase transition boundaries between liquid (L) and liquid−vapor (LV) and between liquid−liquid (LL) and liquid−liquid−vapor (LLV) was also investigated as a function of solvent composition for the L-PLA dissolved in mixed solvents of CO_2 and HCFC-22. The cloud point curves exhibited a lower critical solution temperature phase behavior. As the CO_2 content in the solvent mixture increased, the cloud point pressure at a fixed temperature increased significantly. Addition of CO_2 to HCFC-22 caused a lowering of dissolving power of the mixed solvent. A lower critical end point (LCEP) was estimated from the cloud point curve and the L-to-LV and LL-to-LLV phase transition curves. The LCEPs were shifted to lower temperatures as the CO_2 content in the mixed solvent increased.

Introduction

Supercritical fluids (SCFs) have been used as solvents in a variety of polymer processes such as extractions and separations, fractionations, and reactions. Particularly, SCF technology has recently gained great attention in the particle formation of biodegradable polymers for sustained delivery devices in pharmaceutical industries.[1−3] SCF solvents are an attractive alternative to incompressible organic liquid solvents, since they can have liquidlike dissolving power while exhibiting transport properties of a gas. Phase behavior data for polymer−SCF systems are required for efficient operation and design of SCF polymer processes.

The selection of SCF solvents to dissolve polymers is often challenging for processing applications because it is difficult to find a good SCF solvent that will dissolve the polymer at relatively moderate conditions. Carbon dioxide (CO_2) is the favorite solvent in SCF processes because it has a relatively low critical temperature and pressure and because it is inexpensive, nonflammable, nontoxic, and readily available. However, it is generally not a good solvent for dissolving high molecular weight polymers with the exception of fluoro-polymers[4] and siloxane polymers.[5,6] On the other hand, chlorodifluoromethane (HCFC-22) has been known to be a good solvent for polar polymers.[7,8] In our previous work,[9] it was observed that biodegradable polymers such as poly(L-lactide) (L-PLA) and poly(D,L-lactide-*co*-glycolide) were insoluble in nonpolar CO_2 solvent but were soluble in polar HCFC-22 solvent. For example, the L-PLA (MW = 2000 g·mol^{-1}) polymer was not completely soluble in CO_2 even for very low polymer concentrations less than 0.03 mass % at pressures as high as 80 MPa and at temperatures up to 373.15 K. On the other hand, it was readily soluble even in saturated liquid HCFC-22 at temperatures below about 343.15 K.

Chlorodifluoromethane hydrogen-bonds to molecules such as esters but does not hydrogen-bond to itself. It should be a better solvent for ester-containing polymers such as L-PLA. Therefore, the enhanced solubility of L-PLA in HCFC-22 can be attributed to hydrogen bonding between HCFC-22 and L-PLA.[9] The addition of polar HCFC-22 to CO_2 provides enhanced polar interactions between L-PLA and the mixed solvent that are expected to lead to increased solubility. Moreover, HCFC-22 has a much higher density than that of CO_2, when compared at similar conditions of temperature and pressure. The addition of HCFC-22 to CO_2 increases the solvent density and thus facilitates the solubilization of L-PLA in the mixed solvent.

Consequently, CO_2 is a poor solvent for L-PLA, while HCFC-22 is an excellent solvent for the same polymer. Thus, one can adjust the dissolving power of the solvent for L-PLA by utilizing a mixture of CO_2 and HCFC-22 as an SCF solvent. This work is focused on determining the feasibility of dissolving L-PLA in CO_2 + HCFC-22 solvent mixtures. Tom et al.[10] measured the solubility of L-PLA (MW = 10 000) in the solvent mixtures of CO_2 and HCFC-22 ranging from 10 to 40 mass % HCFC-22, using a flow-type apparatus. They reported very low solubility data of less than 0.08 mass % in CO_2 + HCFC-22 solvent mixture at temperatures of 328.15 K and 338.15 K and at pressures up to 20 MPa.

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10.1021/je0001678 CCC: $19.00

In this work we present the phase behavior data for the L-PLA polymer in supercritical mixtures of CO_2 and HCFC-22. The cloud point pressures were measured using a high-pressure variable-volume view cell apparatus and were characterized as a function of CO_2 composition in the solvent mixture. The CO_2 composition in the solvent mixture ranged widely from 9 to 82 mass %. In addition, liquid (L) to liquid−vapor (LV) and liquid−liquid (LL) to liquid−liquid−vapor (LLV) phase transitions were also measured as a function of solvent composition for the L-PLA dissolved in the CO_2 + HCFC-22 mixed solvents. The phase behavior data produced in this work would be useful for establishing operating conditions in the particle formation of L-PLA by SCF processes.

Experimental Section

Materials. L-PLA was purchased from Polysciences Inc. and used without further purification. It has the viscosity average molecular weight of 2000 $g\cdot mol^{-1}$, which is derived from the intrinsic viscosity and the Mark−Houwink equation. CO_2 and HCFC-22 were obtained from Myung-Sin General Gas Co. (Yangsan, Kyungnam, Korea) and Solvay Fluorides Inc. (Greenwich, CT), respectively, and their certified purities were 99.99 mass %. They were used as received without further purification.

Apparatus and Procedure. The phase behavior of the L-PLA polymer in supercritical mixtures of CO_2 and HCFC-22 was measured using a variable-volume view cell apparatus. A main feature of using the variable-volume cell apparatus is that the concentration of the system is kept constant during the experiment. A detailed description of the experimental apparatus and procedure is given in our previous publication[9] and elsewhere.[8,11] The apparatus consists of a view cell equipped with a sapphire window and a movable piston, a pressure generator (High-Pressure Equipment Co. model 50-6-15), a borescope (Olympus model R080-044-000-50), a video monitor, and a magnetic stirring system. The view cell has dimensions of 16 mm i.d. by 70 mm o.d. and an internal working volume of about 31 cm^3. The system pressure is measured using a high-precision pressure gauge (Dresser Heise model CC-12-G−A-02B, ±0.05 MPa accuracy, ±0.01 MPa resolution) and a piezoresistive pressure transmitter (Keller Druckmesstechnik, type PA-25HTC/8585−1000). The system temperature is measured by an RTD (Pt-100 Ω) probe inserted into the cell and is monitored with a high-precision digital thermometer (ASL model F250, ±0.01 °C accuracy).

The experiment for measuring a cloud point was performed by the following procedure. A certain amount of the L-PLA polymer was loaded into the cell. The amount of the L-PLA loaded into the cell was determined using a sensitive balance (AND model HM-300) measurable to ±0.1 mg. To remove any entrapped air present in the cell, the cell was purged at least three times with low-pressure CO_2 gas of less than 0.3 MPa at a very slow rate so that the polymer in the cell was not disturbed and loss of polymer was avoided. HCFC-22 and CO_2 were charged into the cell using high-pressure sample cylinders. HCFC-22 was first charged because its vapor pressure was lower than that of CO_2. The composition of each component in the solvent mixture was determined by weighing HCFC-22 and CO_2 sample cylinders before and after charging them into the cell using a balance (Precisa model 1212 M SCS) with an accuracy of ±1 mg.

The solution in the cell was compressed by moving the piston located within the cell using the pressure generator and agitated by the magnetic stirrer until it became a single phase. The cell was then heated to a desired temperature. Once the system reached thermal equilibrium and the solution was maintained at a single phase, the pressure was then slowly reduced until the solution became cloudy. Enough time was allowed to ensure thermal equilibrium during the pressure reduction. The pressure was reduced at a rate of about 0.05 $MPa\cdot min^{-1}$ when approaching the cloud point pressure. At fixed polymer and solvent concentrations and temperature, the cloud point was defined as the pressure at which it was no longer possible to visually observe the stirring bar.[7] For obtaining consistent measurements, every measurement was repeated at least twice at each temperature. The polymer concentration was kept constant arbitrarily around 3 mass % in order to exclude the effect of the polymer concentration on the phase behavior. The temperature of the system was raised in about 10 K increments and the above procedure was repeated, thus creating a pressure−temperature ($P-T$) cloud point curve at fixed polymer and solvent concentrations. The maximum temperature was set to about 393.15 K to avoid thermal degradation of O-rings and polymers.

Table 1. Experimental Data of Cloud Points of L-PLA (1) (MW = 2000) in $w_2CO_2 + (1 - w_2)$HCFC-22

$100w_2$[a]	$100w_1$[b]	T/K	P/MPa	$100w_2$[a]	$100w_1$[b]	T/K	P/MPa
0.00	2.88	344.35	3.60	44.00	3.26	305.05	9.25
		353.05	5.95			315.35	13.90
		363.35	8.72			324.35	17.40
		372.75	10.90			328.05	18.95
		382.05	13.05			338.15	22.40
		392.65	15.62			350.85	26.97
7.43	2.78	333.85	3.98			362.45	30.70
		342.45	6.53			372.85	33.60
		352.95	9.70			383.05	36.30
		362.85	12.53			393.45	38.15
		373.35	15.20	51.59	2.81	302.45	12.62
		382.35	17.37			315.85	18.22
		392.55	19.70			325.05	22.55
15.17	3.10	325.35	3.97			333.75	25.72
		333.75	6.70			342.55	28.90
		344.45	10.03			354.05	33.02
		355.45	13.20			363.65	35.87
		364.55	16.10			373.35	38.65
		372.65	18.10			383.55	41.22
		382.65	20.60	66.43	2.60	315.35	30.25
		391.85	22.75			324.55	34.42
31.59	3.16	309.75	5.07			335.15	38.18
		316.75	8.10			343.85	41.50
		324.05	10.93			352.95	44.45
		333.95	14.50			362.95	47.75
		344.75	18.05			372.85	50.65
		353.85	21.07			382.65	53.40
		362.25	23.50	82.28	2.82	323.95	56.55
		372.85	26.42			334.35	60.65
		382.15	28.97			343.45	63.75
		392.35	31.35			353.25	66.55
						363.35	69.15
						372.05	71.45

[a] Mass fraction of CO_2 in a mixed solvent on a polymer-free basis. [b] Mass fraction of total.

After the cloud point was measured, the pressure was reduced further to measure the phase transition boundaries of L-to-LV and LL-to-LLV of the solution. The pressure of the phase transition was defined as the initial pressure at which the first vapor bubble was observed in the solution. When the solution was at temperatures below its critical point, it was orange or reddish in color. Near the critical point, the entire solution became cloudy and extremely opaque and brought out the color of light cobalt blue. Upon reaching the critical point of the solution, the temperature was changed in about 0.2 K increments and the phase transition was observed. At the critical point of the solution, no bubble appeared from the solution even though the pressure decreased.

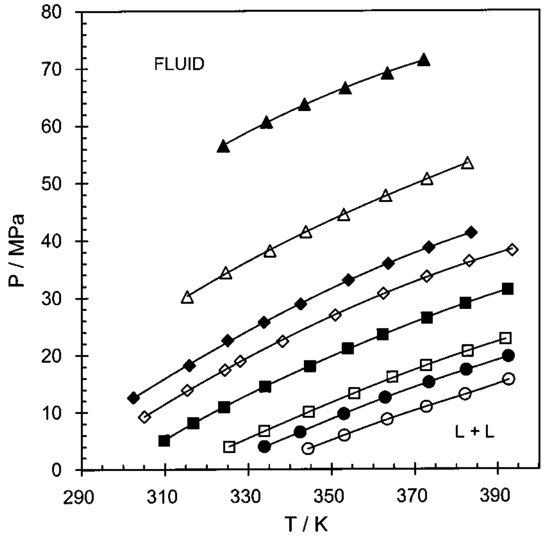

Figure 1. $P-T$ isopleths of cloud points of L-PLA (MW = 2000) in a CO_2 + HCFC-22 mixed solvent. Compositions of CO_2 in the mixed solvent: (○) 0.0 mass %; (●) 7.43 mass %; (□) 15.17 mass %; (■) 31.59 mass %; (◇) 44.00 mass %; (◆) 51.59 mass %; (△) 66.43 mass %; (▲) 82.28 mass %.

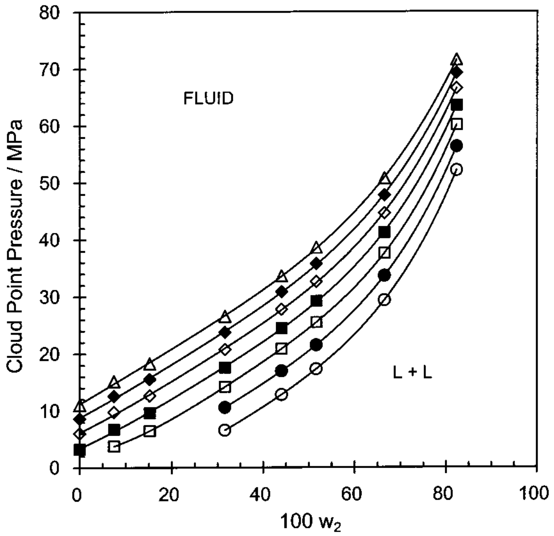

Figure 2. Effect of CO_2 composition (w_2) in a mixed solvent on the cloud point pressures of L-PLA (MW = 2000) at various temperatures: (○) 313.15 K; (●) 323.15 K; (□) 333.15 K; (■) 343.15 K; (◇) 353.15 K; (◆) 363.15 K; (△) 373.15 K.

Results and Discussion

The phase behavior of L-PLA (MW = 2000) in a mixed solvent of CO_2 and HCFC-22 was investigated as a function of solvent composition. The experimental cloud point data are given in Table 1. Figure 1 shows the $P-T$ isopleths of the cloud points of L-PLA in the mixed solvents of CO_2 and HCFC-22 for various CO_2 compositions up to about 82 mass % (on a polymer-free basis). The polymer concentration in the solution was fixed at (2.93 ± 0.19) mass % of total, to eliminate the effect of the polymer concentration on the cloud points. Above each cloud point is the single-phase region, and below the point is the liquid−liquid two-phase region. The cloud point curves had similar slopes for all the CO_2 compositions. The cloud point pressure increased as the temperature increased, indicating that the system exhibited a typical lower critical solution temperature (LCST) behavior. In other words, as the temperature increased, a higher pressure was needed to obtain a single-phase solution from a two-phase solution.

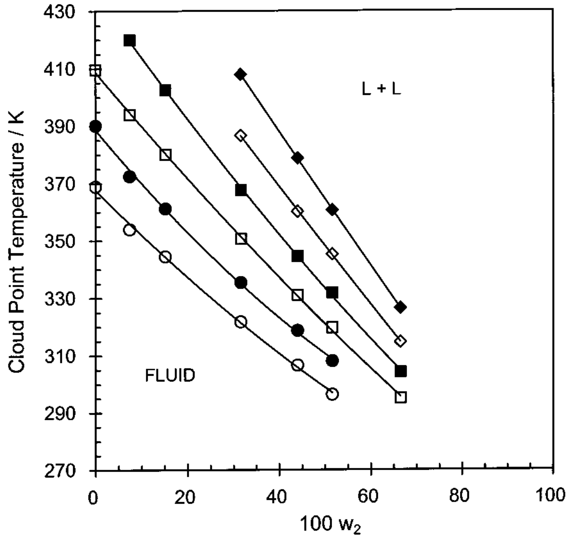

Figure 3. Effect of CO_2 composition (w_2) in a mixed solvent on the cloud point temperatures of L-PLA (MW = 2000) at various pressures: (○) 10 MPa; (●) 15 MPa; (□) 20 MPa; (■) 25 MPa; (◇) 30 MPa; (◆) 35 MPa.

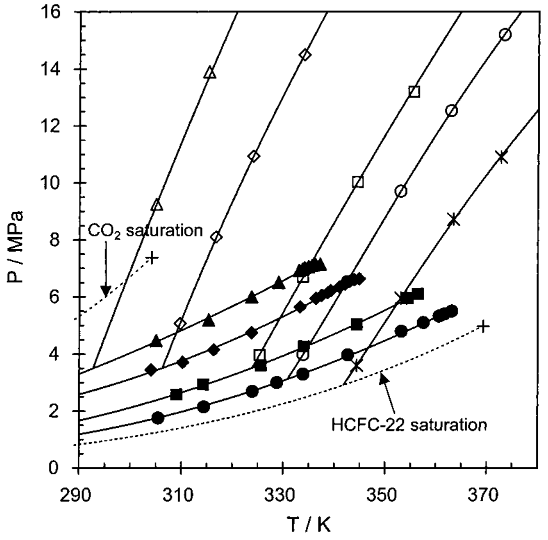

Figure 4. Phase transitions of L-PLA (MW = 2000) in a CO_2 + HCFC-22 mixed solvent. Compositions of CO_2 in the mixed solvent: (∗) 0.0 mass %; (●, ○) 7.43 mass %; (■, □) 15.17 mass %; (◆, ◇) 31.59 mass %; (▲, △) 44.00 mass %. The open symbols are the cloud point data, and the filled symbols are the L-to-LV and LL-to-LLV phase transition data.

CO_2 is not a good solvent to dissolve the L-PLA polymer. In our work the L-PLA (MW = 2000) was observed to be not completely soluble in pure CO_2 at pressures as high as 80 MPa and at temperatures up to 373.15 K. On the other hand, HCFC-22 is a good solvent for the L-PLA polymer due to the hydrogen bonding between the hydrogen atom in HCFC-22 and the ester group in the L-PLA.[9] The cloud point pressure of the L-PLA in pure HCFC-22 solvent was as low as about 16 MPa even at 393.15 K, as shown in Figure 1. However, the cloud point pressure at a fixed temperature increased significantly with increasing CO_2 content in the solvent mixture. Addition of CO_2 to HCFC-22 caused a decrease of dissolving power of the solvent. As the CO_2 composition in the solvent increased, the cloud point curve was shifted to lower temperatures so that the single-phase region of polymer−solvent miscibility shrunk.

The $P-T$ isopleths of the cloud points given in Figure 1 were further characterized by drawing the cloud point

Table 2. Experimental Data of Phase Transitions of L-PLA (1) (MW = 2000) in $w_2CO_2 + (1 - w_2)$HCFC-22

$100w_2$	$100w_1$	T/K	P/MPa	phase transition
7.43	2.78	305.45	1.76	LV[a]
		314.45	2.15	LV
		323.95	2.69	LV
		328.75	3.00	LV
		333.85	3.30	LLV[b]
		342.65	3.97	LLV
		353.15	4.80	LLV
		357.45	5.10	LLV
		360.55	5.33	LLV
		361.55	5.40	LLV
		363.05	5.50	CP[c]
15.17	3.10	309.05	2.58	LV
		314.25	2.94	LV
		325.55	3.60	LLV
		333.95	4.27	LLV
		344.35	5.03	LLV
		354.35	5.95	LLV
		356.35	6.10	CP
31.59	3.16	304.05	3.45	LV
		310.25	3.72	LLV
		316.35	4.15	LLV
		323.75	4.75	LLV
		333.25	5.65	LLV
		336.35	5.95	LLV
		337.45	6.05	LLV
		338.65	6.15	LLV
		339.25	6.22	LLV
		340.95	6.35	LLV
		342.05	6.45	LLV
		342.95	6.55	LLV
		343.85	6.60	LLV
		344.85	6.63	CP
44.00	3.26	305.05	4.47	LLV
		315.35	5.20	LLV
		323.75	6.00	LLV
		329.05	6.51	LLV
		333.05	6.93	LLV
		333.75	6.98	LLV
		334.15	7.02	LLV
		334.85	7.06	LLV
		335.55	7.10	LLV
		336.25	7.13	LLV
		337.15	7.15	CP

[a] Liquid (L) to liquid–vapor (LV) phase transitions. [b] Liquid–liquid (LL) to liquid–liquid–vapor (LLV) phase transitions. [c] Critical point of solution.

pressures and temperatures as a function of solvent composition. Figure 2 shows the effect of CO_2 composition in the mixed solvent on the cloud point pressures at several temperatures. It was obtained by fitting the cloud point curves at different CO_2 compositions with polynomial equations and then by determining the pressures corresponding to desired temperatures from the curve fits. The correlation coefficients of the curve fits, which expressed the goodness of the fits, were greater than 0.999 for all cases. The cloud point pressures increased sharply with increasing the CO_2 composition in the solvent mixture.

Similarly, the cloud point temperatures at different CO_2 compositions and pressures were obtained by making polynomial fits of the cloud point temperatures of Table 1 as a function of the pressure for each CO_2 composition and then by determining the temperatures corresponding to desired pressures from the curve fits. Figure 3 shows the effect of CO_2 composition in the mixed solvent on the cloud point temperatures at various pressures. The cloud point temperatures decreased as the CO_2 content in the mixed solvent increased.

Figure 4 shows the L-to-LV and LL-to-LLV phase transition curves for the L-PLA dissolved in the CO_2 + HCFC-22 mixed solvents. The saturation curves of pure CO_2 and HCFC-22, which are obtained from Daubert and Danner,[12] are also given along with the phase transition and cloud point data. The experimental values of the L-to-LV and LL-to-LLV phase transitions are given in Table 2. The last point in each set of the phase transition data indicates the mixture critical point. For each CO_2 composition, the intersection of the LL-to-LLV curve with the cloud point curve corresponds to the lower critical end point (LCEP) of the solution, at which the fluid to LL phase transition ends. The LCEP was not measured experimentally, but it was determined by estimating the intersection point of the cloud point and LL-to-LLV phase transition curves using extrapolation of their polynomial fits. The L-to-LV phase transitions occur at temperatures below the LCEP, while the LL-to-LLV phase transitions occur at temperatures between the LCEP and the mixture critical point. The LCEPs were shifted to lower temperatures as the CO_2 content in the mixed solvent increased.

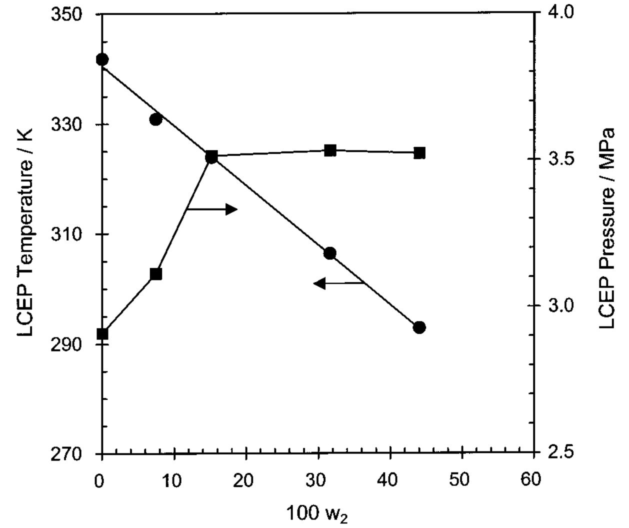

Figure 5. Effect of CO_2 composition (w_2) in a mixed solvent on LCEP temperatures and pressures for an L-PLA (MW = 2000)/CO_2 + HCFC-22 mixed solvent system.

Figure 5 illustrates the estimated values of the LCEP temperature and pressure at different CO_2 compositions in the mixed solvent. The LCEP temperature decreased almost linearly with increasing the CO_2 composition in the mixed solvent. However, as the CO_2 composition in the mixed solvent increased, the LCEP pressures increased at CO_2 compositions less than about 15 mass % and were kept constant at CO_2 compositions more than about 15 mass %.

Conclusions

The phase behavior of L-PLA (MW = 2000) in a mixed solvent of CO_2 and HCFC-22 was investigated as a function of solvent composition. The cloud points of the L-PLA in the mixed solvents of CO_2 and HCFC-22 at various CO_2 compositions up to about 82 mass % were measured using a high-pressure experimental apparatus equipped with a variable-volume view cell. The polymer concentration in the solution was fixed at (2.93 ± 0.19) mass %. The cloud point curves exhibited an LCST-type phase behavior. As the CO_2 content in the solvent mixture increased, the cloud point pressure at a fixed temperature increased significantly due to a lowering of the dissolving power of the solvent.

For the L-PLA dissolved in the CO_2 + HCFC-22 mixed solvents, the L-to-LV and LL-to-LLV phase transitions were measured and the LCEPs were estimated. The LCEPs were shifted to lower temperatures as the CO_2 content in the mixed solvent increased. The LCEP temperatures decreased almost linearly with an increase of the CO_2 composition in the mixed solvent. However, the LCEP pressures increased at CO_2 compositions less than about 15 mass % and were kept constant at CO_2 compositions more than about 15 mass %.

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Received for review June 6, 2000. Accepted August 28, 2000. This work was supported by Grant No. 981-1103-011-2 from the Basic Research program of the KOSEF.

JE0001678