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Distribution Ratios of Lipase-Catalyzed Reaction Products in Ionic Liquid Supercritical CO₂ Systems: Resolution of 2-Octanol Enantiomers

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This paper presents vapor−liquid equilibrium (VLE) data for systems containing high-pressure CO₂, an ionic liquid, and products of an enzymatic reaction between succinic anhydride and (*R*,*S*)-2-octanol in the presence of a lipase. VLE experiments were used to calculate partition coefficients of reaction products between the ionic liquid-rich phase and the CO₂-rich phase. Experiments of extraction with CO₂ from an ionic liquid of (*S*)-2-octanol in conditions similar to those of the postreaction mixture were also carried out. The extraction at 11 MPa and 35 °C allows one to recover completely the unreacted enantiomer of 2-octanol with very high enantiomeric excess (98.42%).

1. Introduction

The resolution of optically active alcohols may be performed by enzymatic catalytic reactions. One of the pioneers in this area was Klibanov, who separated alcohols using esterase-catalyzed stereospecific transesterification in organic media.[1,2] Klibanov showed that enzymes required some water to maintain the catalytic activity but not the presence of bulk water. In fact, enzymes could work in nearly anhydrous organic solvents. Developments in using enzymes in nonaqueous solvents containing traces of water have stimulated research in achieving various kinds of enzymatic transformations and greatly enhance their technological application.[3]

One widely explored field in employing enzymes in nearly anhydrous organic solvents was the application of lipases in organic solvents for resolution of chiral alcohols through enantioselective acylation.[1,2,4–9]

Chiral alcohols were separated using different acylating agents. The most popular has been vinyl acetate. However, some authors used succinic anhydride because the hemiester formed in the lipase-catalyzed reaction is soluble in the aqueous phase while the unreacted compounds remain in the organic phase. This allows application of conventional separation methods for extraction of unreacted enantiomers.[4] This strategy was tested successfully by Bouzemi et al.[5] and Gutman et al.,[6] who used succinic anhydride for resolution of many aliphatic and aromatic alcohols in organic solvent media.

It is worth mentioning that secondary alcohols were already resolved via enzymatic catalysis in traditional media with good to excellent enantioselectivity. However, the weakest point of these processes was the product separation because these procedures required extra solvents for extraction.

The last year of the past century brought new solvents into biocatalysis: ionic liquids (ILs).[10–12] Because of their near-zero vapor pressure,[13] thermal stability,[14] and tunable properties with regard to polarity, hydrophobicity, and solvent miscibility behavior through appropriate modification of the cation and anion, ILs started to be used as alternatives to organic solvents.

ILs behave similarly to organic solvents in contact with enzymes, and ILs could replace organic solvents in many enzymatic processes.[15] Activities of enzymes in ILs are generally comparable with or higher than those observed in conventional organic solvents.[15–20] Furthermore, enhanced thermal[18,19] and operational stabilities[21] and regio- or enantioselectivities[12,15–26] of enzymes were observed. ILs have obvious potential as reaction media, and an important challenge is to use their unique solvent properties to develop efficient methods for product separation and IL recycling.

Efficient separation of reaction products from ILs can be achieved by employing supercritical fluids. After Brennecke and collaborators discovered that supercritical CO₂ (scCO₂) can dissolve up to approximately 0.6 mole fraction in 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF6]) while no IL is detected in the vapor phase,[27] the combination of IL and scCO₂ for reaction and separation started to gain interest.[16,17,25,26]

For example, Lozano et al.[17] presented the results of reactions between a model alcohol, 1-phenylethanol, and vinyl propionate at a 0.1 mL min⁻¹ flow at 15 MPa of CO₂ pressure, catalyzed by lipase CAL B (*Candida antarctica*) dissolved in 1-ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)amide ([emim]-[NTf₂]) and 1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)amide ([bmim][NTf₂]). In both ILs, the enantiomeric excess of the recovered product fraction (eeₚ) was above 99.9%.[17] An enzymatic reaction combined with extraction of products formed during the reaction of 1-phenylethanol with vinyl acetate and CAL B in [bmim][NTf₂], in a batch process, at 11 MPa at 40 °C, was studied by Reetz et al.[16] They very efficiently (eeₚ = 99.4%) separated enantiomers of 1-phenylethanol. Leitner and co-workers[25] also tested reactions in isooctane and in three ILs ([bmim][PF₆], 1-butyl-3-methylimidazolium tetrafluroborate ([bmim][BF₄]), and [bmim][NTf₂]). They performed processes in continuous mode with extraction of enzymatic reaction products. For model reaction 2-octanol + vinyl acetate, they achieved an enantiomeric excess of the recovered substrate fraction (eeₛ) above 99.9% and eeₚ = 99.6% at 50.9% conversion. They carried out the extraction using scCO₂ in two steps (first step, 9 MPa, 60 °C; second step, 20 MPa, 45 °C), obtaining high-purity products (eeₛ = 98.9% and eeₚ > 99.5%).[25]

The present work is a continuation of our study on the resolution of 2-octanol enantiomers in ILs via lipase-catalyzed reactions.[28] We performed the acylation of the model substrate (*R*,*S*)-2-octanol with succinic anhydride catalyzed by immobilized CAL B in nine 1-alkyl-3-methylimidazolium ILs, two quaternary ammonium ILs, two water-miscible organic solvents, and two water-immiscible ones, as is presented in Figure 1. We

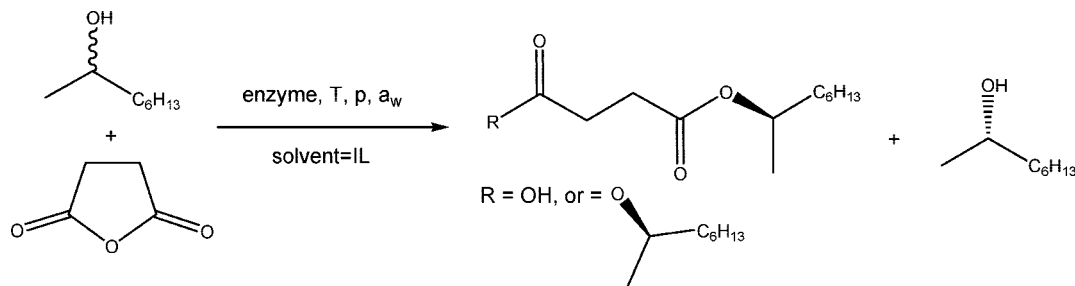* To whom correspondence should be addressed. Tel.: +351212948353. Fax: +351212948385. E-mail: rafal@dq.fct.unl.pt.

Figure 1. Enzymatic reaction scheme.

selected this system to develop an efficient way of separating enantiomers of nonbranched, aliphatic alcohols by a cyclic acylating agent. From previous reports about the resolution of secondary alcohols in ILs,[16,17,24,25,29–31] we expected to obtain an acidic hemiester. However, we found that the diester was also produced, in many cases at an even higher yield. The major reaction products were (R)-hemiester and (R,R)-diester. In the less polar solvents, the conversion of 2-octanol was higher but the enzyme was also less enantioselective and (S)-hemiester, (S,S)-diester, and meso-(R,S)-diester were detected as well.

In the course of enzymatic reactions, we achieved the highest ee_s's for transesterifications performed in 1-methyl-3-octylimidazolium hexafluorophosphate, [omim][PF$_6$], and 1-methyl-3-octylimidazolium dicyanamide [omim][N(CN)$_2$] at 35 °C (98.42% and 97.93%, respectively). High ee_s's were accompanied also by quantitative conversion of (R)-2-octanol.

On the basis of these results, [omim][PF$_6$] and [omim]-[N(CN)$_2$] were chosen as the optimal ILs to be studied. Thus, this paper presents vapor−liquid equilibrium (VLE) data for the ternary systems (CO$_2$ + IL + solute), where solutes are as follows: 2-octanol, 4-(octan-2-yloxy)-4-oxobutanoic acid (hemiester), or dioctan-2-yl succinate (diester). Separation factors between IL-rich and CO$_2$-rich phases for these solutes were calculated from VLE data for ternary systems and compared with results obtained for five component mixtures (IL + CO$_2$ + 2-octanol + hemiester + diester). Next, extraction of unreacted (S)-2-octanol from IL employing CO$_2$ was performed.

2. Experimental Section

In this section, descriptions of experimental apparatuses and techniques are provided.

A. Materials. Immobilized *C. antarctica* lipase B (Novozym 435) was a gift from Novo Nordisk Bioindustrial, Spain. (R,S)-2-Octanol (>97% purity) and Hydranal Coulomat A and C Karl Fischer reagents were from Riedel de Haën. Tridecane (>99% purity) was supplied by Aldrich. ILs [omim][PF$_6$] (≥98% purity) and [omim][N(CN)$_2$] (≥98% purity) were supplied by Solchemar. Tridecane was stored over molecular sieves (3 Å beads from Merck). Hemiester and diester were synthesized according to the procedure described in the literature.[28]

Carbon dioxide (99.99% purity) was supplied by Air Liquide and was used without further treatment.

To reduce the content of volatile compounds to negligible values, vacuum (0.1 Pa) and moderate temperature (50 °C) were applied to the IL samples for several days always immediately prior to their use.

Concentrations in IL + solute samples were chosen to cover the range of reactant and product concentrations found in enzymatic reactions.[28] The water content in the IL solutions was set to water activity (a_w) equal to 0.1. It was measured by Karl Fischer coulometric titration (Metrohm 831 KF coulometer).

B. VLE Apparatuses and Techniques. The apparatus used was previously described in the literature.[32–35] The main part of the phase equilibrium apparatus is a sapphire cell (SC) cylindrical tube with the following dimensions: height = 15 cm; internal diameter = 1.9 cm; external diameter = 3.2 cm. The SC was placed inside an air bath and initially connected to the vacuum pump to facilitate loading of 8.0 ± 0.1 mL of the sample with known concentration(s) of solute(s) in IL into SC using a syringe (S) as well as to eliminate the air that was present. Stirring of the contents was performed with a magnetic stirrer. The temperature was measured with a platinum-resistance thermometer with an accuracy of 0.03 K. The pressure was measured with an accuracy of 0.15% and a precision of 0.1%. In each experiment, the time allowed for phases to reach equilibrium was about 2 h, corresponding to stirring for 1 h and a rest period of another 1 h. The equilibration time depends on the amount of introduced CO$_2$ and was selected based on the previous experiments performed in our laboratory.[32,34,35] Later, a sample from either the top or bottom phase was taken through a HPLC valve into a sample loop. This was followed by an expansion of the loop contents into calibrated large volumes (474.9 mL). Measurement of the pressure in those volumes before and after the expansion allowed calculation of the CO$_2$ quantity in the sample using the equation of state for CO$_2$ presented in the literature.[36] The expansion volume includes cold traps that ensure precipitation of the other components, which were prepared for further analyses by gas chromatography (GC). The pressure drop during sampling (between 0.1 and 0.4 MPa) was balanced by introduction of CO$_2$ before the next sampling. The quantity of fresh CO$_2$ was calculated,[36] and the composition of samples was reckoned.

The measurement uncertainties used in the propagation of error calculations are temperature ± 0.1 K, pressure ± 0.07 bar, mass ± 0.001 g, and line volumes ± 0.1 mL. The reproducibility was ±0.0002 mole fraction for the vapor phase and ±0.0004 for the liquid phase. The larger deviation for the liquid phase is probably due to slightly higher drops of pressure in the sampling process from the liquid and to a generally stronger pressure dependence of equilibrium compositions in the liquid phase than in the vapor phase.

Preliminary VLE results for binary (n-butanol + CO$_2$) mixtures at various compositions were done to check the feasibility of the apparatus for VLE experiments. Obtained data were in agreement with published results.[37–39]

C. Extraction Installation and Technique. Figure 2 shows a schematic diagram of the apparatus used for extraction. A similar one was previously described by Serbanovic et al.[40] A sapphire-windowed cell (SC: 2.9 cm high, 2.4 cm internal diameter) is the core of this installation. Approximately 3 g of the reaction mixture after carrying out the enzymatic reaction was introduced into SC using the syringe (S), and the cell was placed into a water bath (TB). A temperature controller Julabo
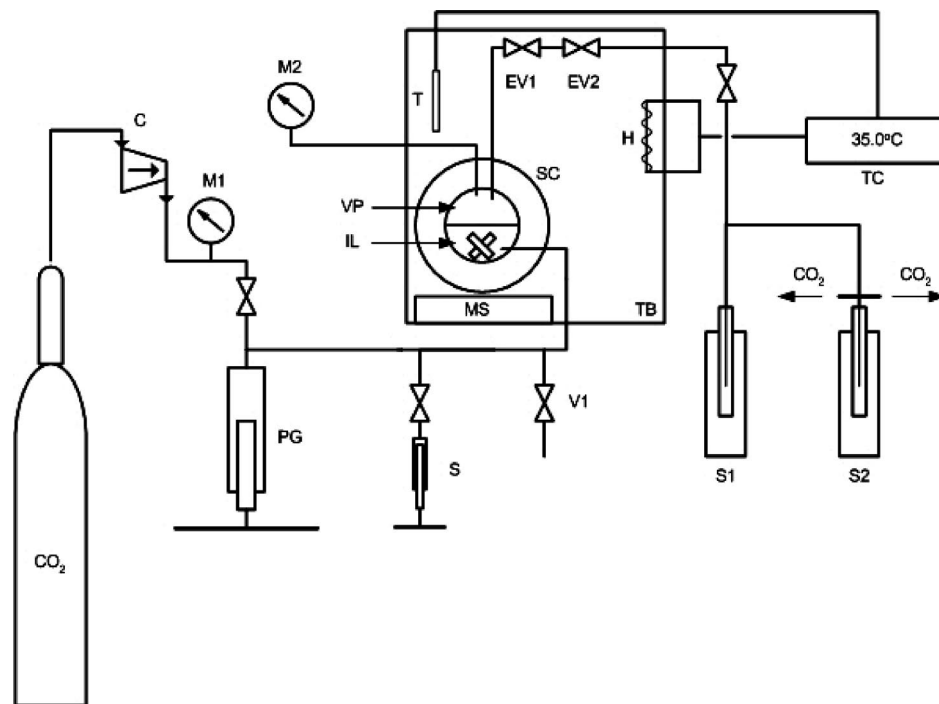
Figure 2. Flow diagram of extraction installation (C, CO_2 compressor; M1 and M2, pressure transmitters (manometers); PG, pressure generator; TB, thermostated bath; SC, sapphire-windowed cell; S, syringe; V1, safety valve; MS, magnetic stirrer; S1 and S2, extract collectors in a liquid nitrogen bath; EV1 and EV2, expansion valves; H, heating element; TC, temperature controller; T, temperature sensor; IL, ionic liquid-rich phase; VP, CO_2-rich phase).

PC (H) was used in order to maintain the required temperature (35 °C). The temperature stability during experiments was determined at level ±0.1 K. The SC was equipped with a magnetic bar driven by a magnetic stirrer (MS). The pressure in the system was measured by a manometer (M2): Amphenol B12, accuracy 0.1%.

CO$_2$ was initially pumped into the cell through a manual pressure generator (PG) of 60 mL capacity. The pressurized cell was left for 1 h for mixing. Afterward, by careful opening of venting valves EV1 and EV2, the extract started to be collected in two glass vessels (S1 and S2) placed in a liquid nitrogen bath. The drop of pressure was continuously compensated for by the introduction of fresh CO$_2$ from the PG. The internal volume of the PG was calibrated, and the quantity of CO$_2$ passed through the system was calculated on the basis of the number of turns of the piston. The samples collected in the glass vessels were analyzed by GC.

D. Enzymatic Reactions. Reactions were performed in plastic vials (reaction volume up to 1 mL) placed in an orbital shaker (400 rpm and 35 °C). Solvent (750 μL) was added to succinic anhydride (800 mM), followed by the addition of the amount of water required to reach $a_w = 0.1$, enzyme (40 g L^{-1}), and finally (R,S)-alcohol (400 mM) to start the reaction. Tridecane (2.91 mM) in acetonitrile was used as an external standard for GC analysis. Scales of a_w versus the water concentration were built by equilibrating solvents with saturated salt solutions or with water at 25 °C for a number of days to achieve values of 0.22 (potassium acetate) and 0.75 (sodium chloride), taken from the literature.[41–43] The water concentration was measured by Karl Fischer titration.

E. Analytical Methods. Experiments were followed by GC analysis performed with a Varian Chrompack CP-3800 gas chromatograph equipped with a 30 m × 0.32 mm i.d. fused silica capillary column, coated with a 0.25-μm-thick film of 5% phenyl groups dissolved in a dimethylpolysiloxane polymer, from Chrompack Co. Oven temperature program: 50 °C hold for 1 min, 50–240 °C ramp at 5 °C min^{-1}. Injection temper-

ature: 250 °C. Flame ionization detection (FID) temperature: 275 °C. Carrier gas: helium at 10.5 psi. Split ratio: 1:20. The data given are the average of at least two measurements. Retention times: tridecane, 8.48; 2-octanol, 17.01; hemiesters, 27.36; diesters, 36.69. Response factors: 2-octanol, 1.5; hemiesters, 1.3; diesters, 2.0. Tridecane (2.91 mM) in acetonitrile was used as the external standard for GC analysis.

3. Results and Discussion

A. VLE. VLE measurements were performed for ternary systems containing [omim][PF$_6$] or [omim][N(CN)$_2$] + CO$_2$ + an alcohol, hemiester, or diester). In the cases of experiments with 2-octanol and hemiester, the range of the initial concentration was from 38.9 to 206.7 mM of solute (2-octanol or hemiester) in IL. For the diester, the range was reduced for concentrations from 28.7 to 104.7 mM. These concentrations of solutes in ILs were selected according to typical concentrations of these solutes during the enzymatic reactions.[28] VLE measurements were performed at four different pressures (5, 7, 9, or 11 MPa) and at a temperature of 35 °C.

The water activity of samples used for experiments was controlled at a_w equal to 0.1, the value used in the enzyme-catalyzed reactions. This is an important factor because Najdanovic-Visak et al. discovered that a small addition of water dramatically changes the equilibrium in systems (ILs + alcohols).[44] Besides, a significant influence of water on the solubility of CO$_2$ + ILs was also reported in the literature.[45,46]

VLE data are presented in Table 1. The mole fraction of solutes in liquid (x) and vapor (y) phases are given by

$$x_{solute} = 1 - x_{CO_2} - x_{IL} \qquad (1)$$

and

$$y_{solute} = 1 - y_{CO_2} - y_{IL} \qquad (2)$$

Our experiments show that the concentration of IL in the fluid phase is not detectable at the experimental conditions. This is

Table 1. Experimental VLE Data for {CO$_2$ + IL ([omim][PF$_6$] or [omim][N(CN)$_2$]) + Solute (2-Octanol, Hemiester, or Diester)} Systems at 35 °C

[omim][PF$_6$]					[omim][N(CN)$_2$]				
p (MPa)	$C_{initial}$ (mM)	$10^4 y_{solute}$	x_{CO_2}	x_{IL}	p (MPa)	$C_{initial}$ (mM)	$10^4 y_{solute}$	x_{CO_2}	x_{IL}
2-Octanol									
5.0	206.7	12.0	0.6339	0.3446	5.0	199.7	6.0	0.6100	0.3733
	99.6	10.3	0.6470	0.3428		100.4	5.8	0.6192	0.3727
	50.0	7.3	0.6545	0.3406		50.3	4.9	0.6388	0.3573
7.0	200.8	24.8	0.8159	0.1736	7.0	195.8	18.7	0.7952	0.1962
	96.2	22.1	0.8222	0.1729		98.1	17.1	0.8026	0.1933
	47.3	15.8	0.8256	0.1720		48.3	13.2	0.8179	0.1802
9.0	192.4	34.7	0.8997	0.0948	9.0	189.3	26.4	0.8737	0.1212
	90.4	34.1	0.9034	0.0940		93.6	23.8	0.8797	0.1179
	43.7	24.6	0.9057	0.0931		45.3	19.7	0.8827	0.1161
11.0	185.2	56.1	0.9180	0.0776	11.0	183.7	37.5	0.8917	0.1040
	83.5	55.4	0.9212	0.769		88.8	35.2	0.8949	0.1032
	38.9	40.5	0.9233	0.0758		41.4	30.2	0.8986	0.1005
Hemiester									
5.0	198.8	1.3	0.6500	0.3305	5.0	205.7	0.8	0.6310	0.3530
	102.2	1.2	0.6618	0.3281		104.6	0.7	0.6466	0.3453
	50.0	0.9	0.6715	0.3238		51.3	0.4	0.6571	0.3392
7.0	197.2	1.5	0.8206	0.1694	7.0	204.6	1.0	0.8024	0.1891
	101.9	1.4	0.8262	0.1686		103.3	0.9	0.8086	0.1870
	49.4	1.3	0.8298	0.1678		50.4	0.7	0.8154	0.1826
9.0	195.1	1.8	0.8881	0.1058	9.0	203.1	1.4	0.8816	0.1133
	99.8	1.7	0.8917	0.1050		102.8	1.3	0.8869	0.1101
	48.8	1.7	0.8942	0.1043		48.8	1.0	0.8987	0.1000
11.0	192.6	2.0	0.9297	0.0665	11.0	201.0	1.7	0.9120	0.0842
	97.9	2.0	0.9319	0.0659		101.5	1.6	0.9139	0.0840
	48.0	1.9	0.9340	0.0650		46.8	1.4	0.9157	0.0835
Diester									
5.0	104.7	0.2	0.6551	0.3345	5.0	107.5	0.2	0.6362	0.3554
	51.0	0.2	0.6756	0.3196		52.2	0.1	0.6614	0.3348
	30.2	0.1	0.7056	0.2919		31.1	0.1	0.6957	0.3023
7.0	104.3	0.3	0.8220	0.1727	7.0	107.2	0.2	0.8113	0.1844
	50.6	0.2	0.8326	0.1649		52.0	0.2	0.8218	0.1762
	29.8	0.2	0.8651	0.1337		30.9	0.1	0.8451	0.1539
9.0	103.6	0.3	0.9062	0.0910	9.0	106.6	0.3	0.8836	0.1138
	50.1	0.3	0.9086	0.0900		51.6	0.2	0.8884	0.1104
	29.3	0.3	0.9120	0.0873		30.6	0.2	0.8995	0.0998
11.0	102.9	0.5	0.9317	0.0663	11.0	106.0	0.3	0.9185	0.0797
	49.4	0.4	0.9330	0.0660		51.1	0.2	0.9222	0.0770
	28.7	0.3	0.9356	0.0640		30.2	0.2	0.9310	0.0686

not surprising because the solubility of IL in CO$_2$ is extremely low.[27,47]

It should be noted that, according to Gibbs' phase rule, the number of degrees of freedom is 3 in the two-phase region of a ternary system, which means that, at fixed pressure and temperature, compositions of phases in equilibrium depend on the initial composition of the mixture. Taking this fact into consideration and analyzing the obtained results, the following conclusions can be stated:

(i) The solubility of CO$_2$ in the IL-rich phase decreases with an increase in the concentration of the solute.

(ii) The solubility of 2-octanol in the CO$_2$-rich phase is more than 1 order of magnitude higher than solubilities of hemiester or diester. This result is in agreement with the fact that the solubility of the solute in scCO$_2$ depends on the polarity and volatility of solutes and increases when the volatility increases and the polarity decreases. Moreover, the difference in the solubilities of solutes means, in principle, that an eventual extraction process will lead to 2-octanol recovery from a mixture of enzymatic reaction products.

(iii) The solubility of CO$_2$ in ILs is approximately 0.02 mole fraction lower in [omim][N(CN)$_2$] than in [omim][PF$_6$]. This can be observed for systems containing 2-octanol, at 5 MPa and an initial concentration of solute (2-octanol) ≈ 50 mM. Mole fractions of CO$_2$ are 0.6388 and 0.6545 in [omim]-[N(CN)$_2$] and [omim][PF$_6$], respectively.

Results obtained here are in agreement with conclusions shown by Aki et al.,[46] who compare the solubilities of CO$_2$ in [bmim][PF$_6$] and [bmim][N(CN)$_2$] (1-butyl-3-methylimidazolium dicyanamide). They discovered that the solubility of CO$_2$ is higher in ILs with a hexafluorophosphate anion than in those with a dicyanamide one. Brennecke and co-workers interpret this fact as a specific acid/base interaction of CO$_2$ with anions.[46]

(iv) The solubility of 2-octanol in the CO$_2$ phase is higher in the case of [omim][PF$_6$] than in the case of [omim][N(CN)$_2$]. This is an effect of the higher solubility of CO$_2$ in [omim][PF$_6$] than in [omim][N(CN)$_2$]. The higher solubility of CO$_2$ in [omim][PF$_6$] improves the access of CO$_2$ to alcohol remaining in the IL, which enhances the solubility of 2-octanol in high-density CO$_2$.

(v) The composition of the vapor phase varies in a very narrow range for different initial concentrations of solute in IL; however, the solubility of the solute in the vapor phase increases with an increase in the initial concentration of the solute.

(vi) In experiments described in this work, no ILs were detectable in the vapor phase. This is an important conclusion because Han and co-workers[48] discovered that "polar enough" solutes improved the solubility of ILs in scCO$_2$ and, for certain pressures and temperatures, ILs in the vapor phase were observed.[48,49]

VLE experiments were also carried out on five component mixtures containing all three solutes (2-octanol, hemiester, and

Table 2. Experimental VLE Data for CO_2 + IL ([omim][PF_6] or [omim][N(CN)$_2$]) + 2-Octanol + Hemiester + Diester Systems at 35 °C and at 9 and 11 MPa

	$C_{initial}$ (mM)									
p (MPa)	2-octanol	hemiester	diester	$10^4 y_{diester}$	$y_{2-octanol}$	$y_{hemiester}$	$10^4 x_{diester}$	$x_{2-octanol}$	$x_{hemiester}$	x_{IL}
					[omim][PF_6]					
9	194.7	87.3	59.9	0.6	0.0074	0.0003	35.5	0.0114	0.0052	0.0956
11				1.0	0.0115	0.0005	31.6	0.0094	0.0046	0.0801
					[omim][N(CN)$_2$]					
9	197.2	107.1	47.3	0.4	0.0056	0.0002	27.2	0.0112	0.0061	0.1215
11				0.7	0.008	0.0004	25.2	0.0099	0.0057	0.1057

diester). Results are given in Table 2, where the initial concentrations of the solutes in the IL samples, before introduction of CO_2, as well as the measured compositions of the vapor and liquid phases in equilibrium, at 35 °C, for [omim][PF_6] and [omim][N(CN)$_2$] at 9 and 11 MPa, respectively, are given. These results allowed the calculation of separation factors, as described below.
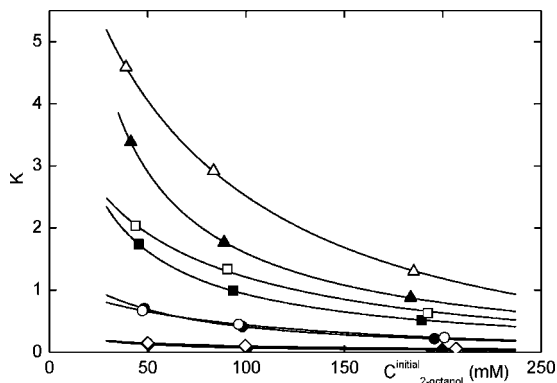
B. Partition Coefficients in Ternary Systems. The partition or distribution coefficient is the ratio of concentrations of a compound in two phases of a mixture of two immiscible solvents at equilibrium. The partition coefficient is commonly used to evaluate the distribution of organic compounds between scCO$_2$ and IL phases.[50,51] It is given by the equation

$$K = \frac{y_{solute1}}{x_{solute1}} \quad (3)$$

where $y_{solute1}$ and $x_{solute1}$ are mole fractions of solute in CO_2- and IL-rich phases. The mole fraction based form of the partition coefficient in compressible or near-critical mixture systems is more valuable than the molar concentration based form, which is used in conventional chemistry, because changes in the temperature or pressure can induce large changes in the density or molar volume.[50]

Figures 3–5 present the partition coefficients in biphasic ternary mixtures as a function of the initial concentrations of the solutes in the mixture with IL. Partition coefficients were calculated according to eq 3, using data from Table 1. Partition coefficients for 2-octanol are 1 order of magnitude higher than partition coefficients for hemiester and 2 orders of magnitude higher than those for diester, for the same range of pressures and initial concentrations of solutes. These observations are a consequence of the higher solubility of 2-octanol than hemiester or diester in dense CO_2.

Additionally, at lower initial concentrations of solutes, partition coefficient values increase dramatically. This is an

effect of diminishing CO_2 solubility with decreasing solute initial concentration.

Partition coefficient data as a function of the initial concentrations of solutes were correlated by regression equations.

C. Separation Factors. Separation factors (α) are usually defined as ratios of partition factors for different solutes, and they measure the ability of a system of immiscible solvents to separate two solutes.

$$\alpha = \frac{K_{solute1}}{K_{solute2}} \quad (4)$$

where $K_{solute1}$ and $K_{solute2}$ are partition coefficients of two solutes, i.e., 2-octanol and hemiester. Because of solute−solute interactions, separation factors measured from real multicomponent mixtures, involving all solutes under study, are often quite
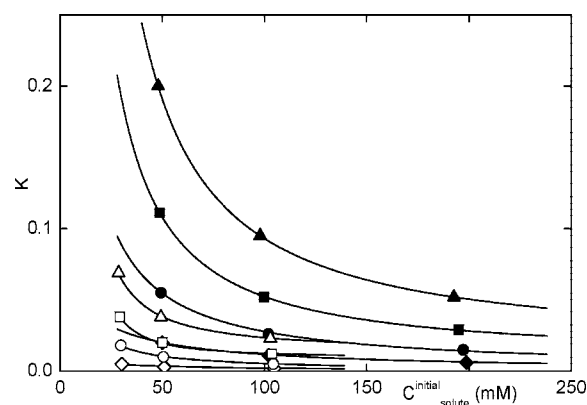
Figure 4. Partition coefficients as a function of the initial concentrations of hemiester (black symbols) and diester (black−white symbols) before adding CO_2 in [omim][PF_6] at ($\diamond$, $\blacklozenge$) 5 MPa, ($\bigcirc$, $\bullet$) 7 MPa, ($\square$, $\blacksquare$) 9 MPa, and ($\triangle$, $\blacktriangle$) 11 MPa.

Figure 3. Partition coefficients as a function of the initial concentrations of 2-octanol (before adding CO_2) in [omim][PF_6] (black−white symbols) and [omim][N(CN)$_2$] (black symbols) at ($\diamond$, $\blacklozenge$) 5 MPa, ($\bigcirc$, $\bullet$) 7 MPa, ($\square$, $\blacksquare$) 9 MPa, and ($\blacktriangle$, $\triangle$) 11 MPa.
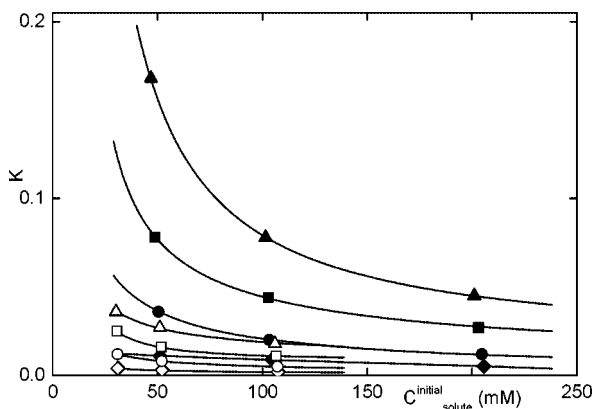
Figure 5. Partition coefficients as a function of the initial concentrations of hemiester (black symbols) and diester (black−white symbols) before adding CO_2 in [omim][N(CN)$_2$] at ($\diamond$, $\blacklozenge$) 5 MPa, ($\bigcirc$, $\bullet$) 7 MPa, ($\square$, $\blacksquare$) 9 MPa, and ($\triangle$, $\blacktriangle$) 11 MPa.
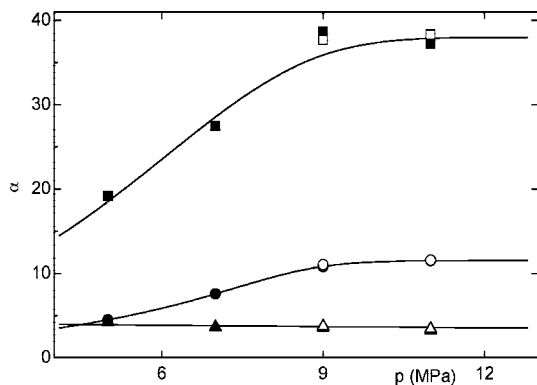
Figure 6. Separation factors for (○, ●) 2-octanol/hemiester, (□, ■) 2-octanol/diester, and (Δ, ▲) hemiester/diester calculated from individual (ternary) experiments (black symbols) and from five-component systems at 9 and 11 MPa (black−white symbols) plotted as a function of the CO_2 pressure in [omim][PF_6].
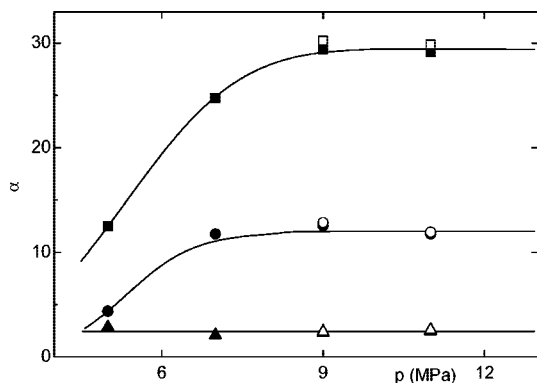
Figure 7. Separation factors for (○, ●) 2-octanol/hemiester, (□, ■) 2-octanol/diester, and (Δ, ▲) hemiester/diester calculated from individual (ternary) experiments (black symbols) and from five-component systems at 9 and 11 MPa (black−white symbols) plotted as a function of the CO_2 pressure in [omim][N(CN)$_2$].

different from estimates based solely on ternary systems.

Figures 6 and 7 present the estimated separation factors between 2-octanol and hemiester, hemiester and diester, and 2-octanol and diester in both ILs, calculated from ternary experiments:

$$\alpha_{solute1/solute2} = \frac{K_{solute1} \text{ calculated from IL} + CO_2 + \text{solute1 ternary system}}{K_{solute2} \text{ calculated from IL} + CO_2 + \text{solute2 ternary system}} \quad (5)$$

As can be seen from Figures 6 and 7, separation factors for 2-octanol/hemiester and 2-octanol/diester are dependent on CO_2 pressures of up to 8 and 10 MPa for [omim][N(CN)$_2$] and [omim][PF_6], respectively, but for higher pressures, they remain close to constant. This means that the higher pressure of CO_2 does not enhance separation, and therefore extraction can be performed with a high yield at 11 MPa of CO_2 pressure. Separation factors for 2-octanol/hemiester in both ILs are very similar and equal to 11.5. However, in [omim][PF_6], the separation factor for 2-octanol/diester is much higher (37.2) than that for [omim][N(CN)$_2$], where $\alpha = 29.1$. It is also worth underlining that separation factors for hemiester/diester systems in both ILs are close to independent of the pressure and equal 3.2 and 2.7 for [omim][PF_6] and [omim][N(CN)$_2$], respectively.

Figures 6 and 7 also include real separation factors calculated from five-component systems (Table 2) at 9 and 11 MPa. It can be concluded that separation factors calculated from individual ternary systems are accurate estimates of the real ones.
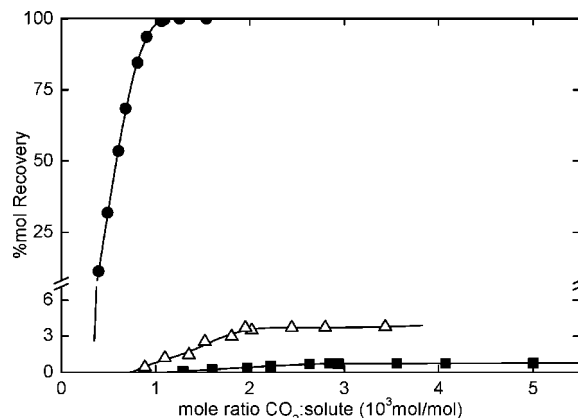
Figure 8. Extraction of reaction products: (●) 2-octanol; (Δ) hemiester; (▲) diester (mol % recovery vs mole ratio CO_2/solute).

This was expected because in this case we dealt with dilute multicomponent systems.

D. Extraction. An extraction study was carried out on a mixture resulting from a lipase-catalyzed reaction carried out in [omim][PF_6]. This sample was selected because of the higher solubility of CO_2 in this IL and the higher ee$_s$ achieved. The initial concentrations of solutes in ILs were as follows: 194.7 mM of 2-octanol, 87.3 mM of hemiester, and 59.9 mM of diester in 3.3324 g of total mass of sample. The initial partial mole fraction of 2-octanol in relation to all solutes (quantity of 2-octanol divided by the sum of solutes' quantities) was 0.569 and in the extract increased to 0.981 while maintaining a high enantiomeric excess (ee$_s$ = 98.42%). To normalize the results for the different compound amounts presented in the extraction vessel, the percent mole recovery as a function of the molar ratio of CO_2 passed through the extractor to organic solutes loaded in the extractor is presented in Figure 8. The extraction performed at 11 MPa and at 35 °C allowed the recovery of > 99.99 mol % of 2-octanol, with low coextraction of other products (3.69 mol % of hemiester and 0.73 mol % of diester). Complete recovery of 2-octanol was achieved for a mole ratio of (CO_2 flow/initial 2-octanol) ≈ 1000. The other two solutes are very difficult to extract, even at 3−5 times higher molar ratios of CO_2/hemiester or CO_2/diester.

4. Conclusions

In this paper, VLE measurement, partition coefficient, and separation factor calculations were presented followed by an extraction study.

The solubility of 2-octanol in CO_2 is more than 1 order of magnitude higher than that of hemiester and diester and additionally is higher in the case of IL with a hexafluorophosphate anion than in the case of dicyanamide IL.

VLE data were used to calculate partition coefficients for examined solutes. Partition coefficients for 2-octanol are 1 order of magnitude higher than those for hemiester and 2 orders of magnitude higher than those for diester in the same range of pressures and initial concentrations of the solutes.

Separation factors estimated from VLE data for ternary systems are in very good agreement with separation factors calculated for the data obtained for a multicomponent sample. Separation factors estimated from partition coefficient data showed that α values for 2-octanol/hemiester in both ILs are very similar and are equal to 11.5. However, in [omim][PF_6], the separation factor for 2-octanol/diester is much higher (37.2) than that for [omim][N(CN)$_2$], where $\alpha = 29.1$.

The extraction study allowed one to recover >99.99 mol % of unreacted (S)-2-octanol with minimal coextraction of other solutes present in the sample and with very high enantiomeric excess equal to 98.42%.

Acknowledgment

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