Solubility of Novel CO_2-Soluble Pyridine Derivatives in Supercritical Carbon Dioxide

Fei Chang, Hakwon Kim,* and Yunja Kwon

Department of Chemistry and Advanced Materials, Industrial Liaison Research Institute and Institute of Natural Sciences, Kyung Hee University, Gyeonggi-do 446-701, Republic of Korea

The solubility of newly synthesized amide-group-containing pyridine derivatives, *N*-hexyl-*N*-(4-pyridyl)-pentadecafluorooctanamide, *N*-hexyl-*N*-(4-pyridyl)octanamide, and *N*-(4-pyridyl)pentadecafluorooctanamide in supercritical carbon dioxide (Sc-CO_2) was determined at temperatures ranging from (313 to 343) K and pressures ranging from (8.8 to 24.9) MPa. The solubility of the amide-containing pyridine series was determined primarily by variations in the molecular structure of the solutes, temperature, and pressure. The measured solubility was satisfactorily correlated by a semiempirical model.

Introduction

Supercritical carbon dioxide has become a promising alternative solvent for separation techniques and extraction processes because it is essentially nontoxic, inexpensive, environmentally benign, and has easily available critical constants ($T_C = 304.2$ K, $P_C = 7.38$ MPa).[1] Because of its superior mass transfer properties, easy recycling, and lack of secondary waste formation, Sc-CO_2 has been extensively used as an extraction solvent for metals.[2] Although Sc-CO_2 has been successfully used in the industrial separation of organic compounds,[3] the direct extraction of metal ions using neat Sc-CO_2 was found to be inefficient as a result of charge neutralization requirements and weak solute−solvent interaction.[2] A solution to this problem is to add a CO_2-soluble organic chelating agent, which produces a metal complex that can be easily extracted into Sc-CO_2 from sample matrices.[4−7] Therefore, design and synthesis of highly CO_2-soluble chelates has special significance for efficient extraction.

In general, pyridine and its derivatives are utilized in the synthesis of functional compounds and are suitable ligands for the extraction of d-transition metal ions from organic solvents.[8] To enhance their solubility in Sc-CO_2, Beckman et al. functionalized pyridine compounds with fluorinated alkyl or ether chains and observed high dispersion of modified pyridine compounds in the CO_2 medium.[9,10] We have previously reported the synthesis of new amide-containing pyridine derivatives with fluorinated or nonfluorinated substituents[11] and found these compounds to be suitable for metal extraction in Sc-CO_2. To further our study, we focused on solubility evaluations of selected synthesized compounds *N*-hexyl-*N*-(4-pyridyl)pentadecafluorooctanamide (1), *N*-hexyl-*N*-(4-pyridyl)octanamide (2), and *N*-(4-pyridyl)pentadecafluorooctanamide (3) in Sc-CO_2 at temperatures ranging from (313 to 343) K and pressures ranging from (8.8 to 24.9) MPa in a high-pressure apparatus. The obtained solubility data was correlated with calculated values using a semiempirical model.[12−15] These studies provide useful data regarding the effects of pressure and temperature on the solubility of the amide-containing pyridine derivatives, which is beneficial for predicting the phase behaviors of these compounds at higher pressures and temperatures outside of experimental conditions. Furthermore, the data will serve as a guideline for optimizing operation conditions for metal extraction in Sc-CO_2.

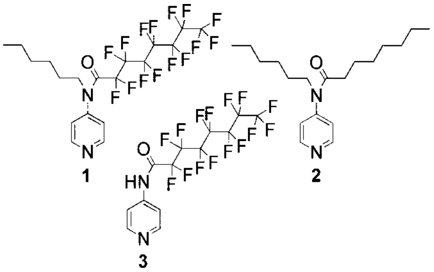

Figure 1. Structures of newly synthesized amide-containing pyridine compounds: (1) *N*-hexyl-*N*-(4-pyridyl)pentadecafluorooctanamide, (2) *N*-hexyl-*N*-(4-pyridyl)octanamide, and (3) *N*-(4-pyridyl)pentadecafluorooctanamide.

Experimental Section

Chemicals. Pure carbon dioxide (99.99 %) was obtained from Air Tech., Korea. All other chemicals were from Aldrich Chemicals and used without further purification. These amide-containing pyridine compounds were prepared from 4-aminopyridine by the previously developed procedure in our group and were pure enough to do our experiment (more than 99 % pure determined by NMR spectroscopy).[11] Their structures are shown in Figure 1.

Equipment and Procedures. A variable-volume cell with two sapphire windows ($V_{min} = 10$ mL, $V_{max} = 20$ mL, 0.2 mL per rotation; Hanwoul Eng., Korea) was utilized to determine the solubility of each compound continuously. An appropriate amount of compound was loaded into the cell using a micropipette or weighing paper, and the cell was tightly sealed. After heating to the desired temperature, CO_2 was continuously charged with a syringe pump (260D, ISCO) until a single phase was clearly observed. The pressure was then slowly decreased until two phases appeared at a fixed temperature. The solubility could be determined visually via sapphire windows placed on both sides. Each reported value is the average of three replicate

---

* Corresponding author. Tel: +82-31-201-2459. Fax: +82-31-202-7337. E-mail: hwkim@khu.ac.kr.

10.1021/je800737d CCC: \$40.75

Table 1. Solubility of *N*-Hexyl-*N*-(4-pyridyl)pentadecafluorooctanamide in Sc-CO_2[a]

T/K	P/MPa	ρ/kg·m^{-3}	10^4x	10^4x_{calcd}	100 ARD
313	9.3	556	18.6	19.9	6.99
	9.1	517	16.1	16.9	4.97
	9.0	493	14.2	15.2	7.04
	8.9	465	12.9	13.4	3.88
	8.8	436	12.1	11.8	2.48
323	10.8	484	21.6	17.7	18.1
	10.5	449	18.8	15.3	18.6
	10.2	411	17.2	13.1	23.6
	10.1	399	15.2	12.5	17.6
	10.0	387	13.7	11.9	12.8
343	14.4	478	21.1	25.5	20.8
	13.7	442	18.4	22.5	22.2
	13.1	409	16.7	20.1	20.4
	12.6	380	15.5	18.2	17.2
	12.4	369	13.9	17.5	25.9
	12.3	363	13.0	17.1	31.3

[a] Temperature: T; pressure: P; Sc-CO_2 density: ρ; mole fraction: x; absolute relative deviation: ARD.

Table 2. Solubility of *N*-Hexyl-*N*-(4-pyridyl)octanamide in Sc-CO_2[a]

T/K	P/MPa	ρ/kg·m^{-3}	10^4x	10^4x_{calcd}	100 ARD
313	9.8	616	15.7	17.6	12.1
	9.6	596	13.1	15.3	16.8
	9.5	584	11.2	14.1	25.8
	9.4	571	9.86	12.8	29.8
	9.3	556	8.86	11.5	29.8
323	12.2	599	16.4	17.8	8.47
	11.7	567	14	14.4	2.86
	11.3	535	12.4	11.5	6.82
	11.1	516	11.1	10.2	8.11
	11.0	506	9.91	9.4	4.84
333	13.4	531	18.2	13.3	30.8
	12.9	501	15.5	10.9	29.7
	12.6	480	13.6	9.43	30.7
	12.3	459	12.3	8.17	33.5
	12.1	444	11.1	7.38	33.5

[a] Temperature: T; pressure: P; Sc-CO_2 density: ρ; mole fraction: x; absolute relative deviation: ARD.

Table 3. Solubility of *N*-(4-Pyridyl)pentadecafluorooctanamide in Sc-CO_2[a]

T/K	P/MPa	ρ/kg·m^{-3}	10^4x	10^4x_{calcd}	100 ARD
313	16.0	796	5.66	5.54	2.12
	13.6	757	4.80	5.02	4.50
	12.1	722	4.22	4.45	5.45
	11.0	686	3.82	3.78	1.05
	10.5	663	3.47	3.45	0.576
	10.2	645	3.19	3.14	1.57
323	20.3	789	5.70	5.51	3.33
	17.0	742	4.88	4.79	1.84
	15.2	706	4.31	4.21	2.32
	14.2	680	3.84	3.78	1.56
	13.5	657	3.49	3.40	2.58
	13.2	646	3.18	3.23	1.57
333	24.9	786	5.72	5.72	0.01
	21.0	740	4.90	4.97	1.43
	19.0	708	4.29	4.43	3.26
	17.4	675	3.87	3.87	0.107
	16.4	650	3.53	3.47	1.7
	16.0	639	3.23	3.30	2.17

[a] Temperature: T; pressure: P; Sc-CO_2 density: ρ; mole fraction: x; absolute relative deviation: ARD.

Table 4. Solubility Constants *a*, *b*, and *c* Obtained from the Data Correlation

compd	a	b/K	c/m^3·kg^{-1}
N-hexyl-*N*-(4-pyridyl)-pentadecafluorooctanamide	11.128	−3795.2	0.00482
N-hexyl-*N*-(4-pyridyl)octanamide	10.674	−3684.0	0.00794
N-(4-pyridyl)pentadecafluorooctanamide	5.9386	−2820.8	0.00674

samples. The mole fractions of the solutes were reproducible to within ± 3 %.

Results and Discussion

In a previous study,[11] we discussed how the molecular structure of the amide-containing pyridine series has influenced phase behaviors in Sc-CO_2. It was apparent that two main interactions should be considered in explaining the miscibility differences among these compounds under identical conditions: self-interaction between chelating agents (solute−solute) and specific intermolecular interaction between the chelating agent and the CO_2 molecule (solute−solvent). Specific intermolecular interaction between solute and solvent in tertiary amides increases their solubility, and the strong self-interaction in secondary amides contrarily decreases their solubility.[11]

To elucidate the effects of temperature and pressure on the miscibility of pyridine derivatives 1, 2, and 3 in Sc-CO_2, solubilities were evaluated under different pressure conditions from (8.8 to 24.9) MPa and at temperatures from (313 to 343) K. Results are listed in Tables 1, 2, and 3. The density of CO_2 under the given conditions and solute mole fractions is also included.[16]

Temperature and pressure are summarized in Figure 2 as functions of solute mole fraction. As previously understood, higher temperature and higher pressure can enhance solute volatility and CO_2 density, respectively.[17] The enhancement of temperature and pressure tends to increase the solubility. As observed, for these three compounds in our study, increased CO_2 pressure led to higher solubility at a constant temperature, and increased temperature resulted in better dispersion within the CO_2 medium at a fixed pressure. The higher miscibility of fluorinated compound 1 than that of its nonfluorinated derivative 2 under the same conditions may be attributed to the presence of fluorinated moieties, which show a higher affinity for solvents than their hydrocarbon counterparts.[9,10] Interestingly, the miscibility of the secondary amide 3 was not as good as that of 2 with the nonfluorinated tertiary amide, suggesting that the strong solute−solute self-interaction and the weak solute−solvent intermolecular interaction existed in the secondary amide, resulting in a low miscibility.[18,19]

The experimental solubility results for these pyridine-containing compounds were subsequently correlated with the following equation proposed by Bartle et al[20]

$$\ln(xP/P_{ref}) = A + c(\rho - \rho_{ref}) \tag{1}$$

where

$$A = a + b/T \tag{2}$$

and

$$\ln(xP/P_{ref}) = a + b/T + c(\rho - \rho_{ref}) \tag{3}$$

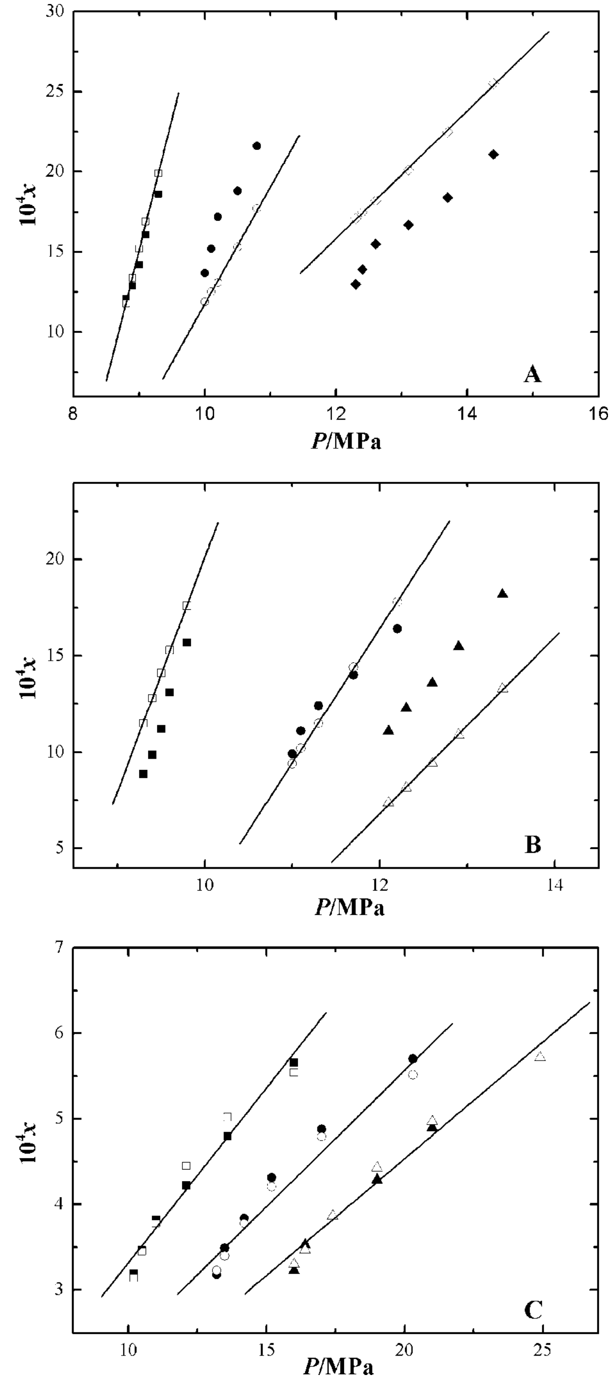

Figure 2. Comparison of experimental and calculated data for those compounds in supercritical CO_2 at: ■,□, 313 K; ●,○, 323 K; ▲,△, 333 K; and ◆,◇, 343 K. (A) *N*-hexyl-*N*-(4-pyridyl)pentadecafluorooctanamide, (B) *N*-hexyl-*N*-(4-pyridyl)octanamide, and (C) *N*-(4-pyridyl)pentadecafluorooctanamide. ■,●,▲,◆, experimental data; □,○,△,◇, calculated data. (See Tables 1, 2, and 3). Lines represent correlation by eq 1.

In the above equation, x is the mole fraction of solute; P is the pressure; P_{ref} is 0.1 MPa; ρ is the density of pure carbon dioxide at fixed temperature and pressure; ρ_{ref} is a reference density of 700 $\text{kg}\cdot\text{m}^{-3}$; and A, a, b, and c are constants. The initial step was to plot $\ln(xP/P_{\text{ref}})$ against each isotherm density, and resulting plots were fitted with a straight line using least-squares regression to estimate A and c, by the intercept and slope in each corresponding plot (Figure 3). Value c was then averaged for each compound and listed in Table 4.

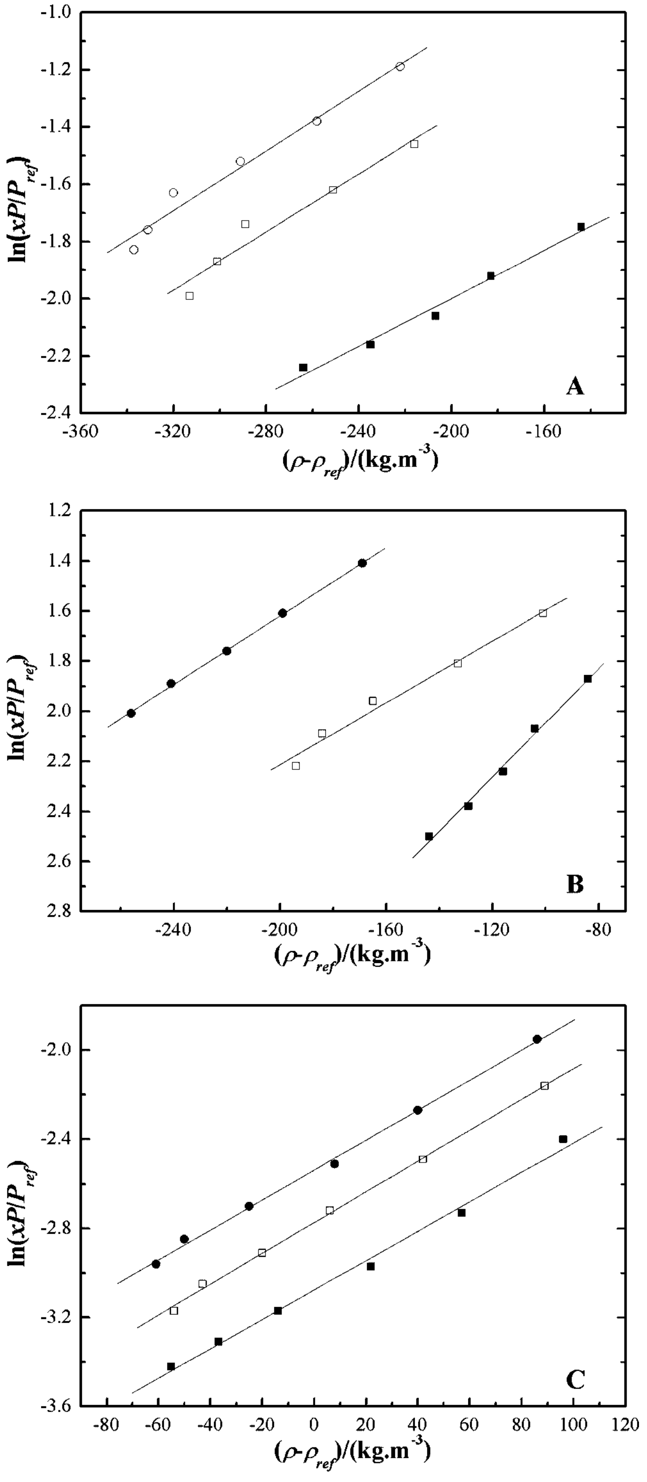

Figure 3. Plots of $\ln(xP/P_{\text{ref}})$ versus $(\rho - \rho_{\text{ref}})/(\text{kg}\cdot\text{m}^{-3})$ for these tested compounds at: ■, 313 K; □, 323 K; ●, 333 K; ○, 343 K. (A) *N*-hexyl-*N*-(4-pyridyl)pentadecafluorooctanamide; (B) *N*-hexyl-*N*-(4-pyridyl)octanamide; and (C) *N*-(4-pyridyl)pentadecafluorooctanamide.

With the average value of c available, the experimental solubility data were then used to calculate the A value for each compound. The variations of A with respect to $1/T$ for each compound resulted in a linear plot (Figure 4). Values of a and b were determined from the equation $A = a + b/T$ and are included in Table 4. Finally, predicted solubility data obtained from the above equation were compared with the experimental data, resulting in the absolute relative deviation (ARD) in Tables 1, 2, and 3. The average absolute relative

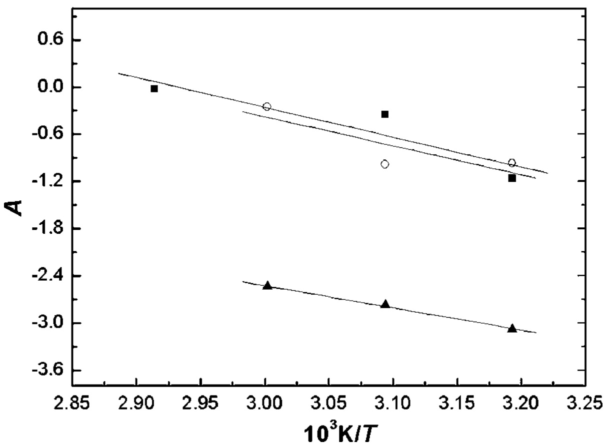

Figure 4. Plots of A versus 10^3 K/T for these tested compounds (■, *N*-hexyl-*N*-(4-pyridyl)pentadecafluorooctanamide; ○, *N*-hexyl-*N*-(4-pyridyl)octanamide; and ▲, *N*-(4-pyridyl)pentadecafluorooctanamide.

deviation (AARD) is generally used to evaluate the correlation outcome. A lower AARD value means better correlation results.

$$\mathrm{AARD} = 1/n \sum |(x_{\mathrm{calcd}} - x_{\mathrm{exptl}})/x_{\mathrm{exptl}}| \qquad (4)$$

AARD values were calculated to be 16 %, 20 %, and 2.1 % for compounds 1, 2, and 3, respectively. It can be concluded that the correlation of 3 is much better than those of 1 and 2. Even though we cannot explain the exact reason for the large discrepancies in AARD values, it might be proposed that better solubility observations and a modification of Bartle's equation should improve the correlation. Further works are needed to explain, and the results will be reported in the near future.

Conclusions

The solubility of amide-bearing pyridine compounds was tested in Sc-CO_2 at temperatures ranging from (313 to 343) K and pressures ranging from (8.8 to 24.9) MPa. The solubility differences in this series resulted from differing molecular structures, temperatures, and pressures within our experiment. Solubility data were correlated with a semiempirical model proposed by Bartle et al. The correlated data were found to be satisfactorily accordant with experimental data. The corresponding AARDs were determined to be 16 %, 20 %, and 2.1 % for compounds 1, 2, and 3, respectively.

Literature Cited

(1) DeSimone, J. M. Practical Approaches to Green Solvents. *Science* **2002**, *297*, 799–803.
(2) Erkey, C. Supercritical Carbon Dioxide Extraction of Metals from Aqueous Solutions: A Review. *J. Supercrit. Fluids* **2000**, *17*, 259–287.
(3) Smart, N. G.; Carleson, T. E.; Elshani, S.; Wang, S. F.; Wai, C. M. Extraction of Toxic Heavy Metals Using Supercritical Fluid Carbon Dioxide Containing Organophosphorus Reagents. *Ind. Eng. Chem. Res.* **1997**, *36*, 1819–1826.
(4) Laintz, K. E.; Wai, C. M.; Yonker, C. R.; Smith, R. D. Solubility of Fluorinated Metal Diethyldithiocarbamates in Supercritical Carbon Dioxide. *J. Supercrit. Fluids* **1991**, *4*, 194–198.
(5) Lin, Y. H.; Brauer, R. D.; Laintz, K. E.; Wai, C. M. Supercritical Fluid Extraction of Lanthanides and Actinides from Solid Materials with a Fluorinated β-Diketone. *Anal. Chem.* **1993**, *65*, 2549–2551.
(6) Wai, C. M.; Lin, Y. H.; Brauer, R. D.; Wang, S. F.; Beckert, W. F. Supercritical Fluid Extraction of Organic and Inorganic Mercury from Solid Materials. *Talanta* **1993**, *40*, 1325–1330.
(7) Lin, Y. H.; Smart, N. G.; Wai, C. M. Supercritical Fluid Extraction and Chromatography of Metal Chelates and Organometallic Compounds. *Trends Anal. Chem.* **1995**, *14*, 123–133.
(8) Ziessel, R. Schiff-Based Bipyridine Ligands. Unusual Coordination Features and Mesomorphic Behavior. *Coord. Chem. Rev.* **2001**, *216–217*, 195–223.
(9) Yazdi, A. V.; Beckman, E. J. Design, Synthesis, and Evaluation of Novel, Highly CO_2-Soluble Chelating Agents for Removal of Metals. *Ind. Eng. Chem. Res.* **1996**, *35*, 3644–3652.
(10) Yazdi, A. V.; Beckman, E. J. Design of Highly CO_2-Soluble Chelating Agents. 2. Effect of Chelate Structure and Process Parameters on Extraction Efficiency. *Ind. Eng. Chem. Res.* **1997**, *36*, 2368–2374.
(11) Chang, F.; Kim, H.; Joo, B.; Park, K.; Kim, H. Novel CO_2-Soluble Pyridine Derivatives and the Extraction of Heavy Metals into Sc-CO_2. *J. Supercrit. Fluids* **2008**, *45*, 43–50.
(12) Sun, Y.; Li, S.; Quan, C. Solubility of Ferulic Acid and Tetramethylpyrazine in Supercritical Carbon Dioxide. *J. Chem. Eng. Data* **2005**, *50*, 1125–1128.
(13) Bao, P.; Dai, J. Relationships between the Solubility of C. I. Disperse Red 60 and Uptake on PET in Supercritical CO_2. *J. Chem. Eng. Data* **2005**, *50*, 838–842.
(14) Su, B.; Lv, X.; Yang, Y.; Ren, Q. Solubilities of Dodecylpolyoxyethylene Polyoxypropylene Ether in Supercritical Carbon Dioxide. *J. Chem. Eng. Data* **2006**, *51*, 542–544.
(15) Liu, J.; Yang, H.; Wang, W.; Li, Z. Solubilities of Amide Compounds in Supercritical Carbon Dioxide. *J. Chem. Eng. Data* **2008**, *53*, 2189–2192.
(16) Lemmon, E. W.; Peskin, A. P.; McLinden, M. O.; Friend, D. G. NIST Thermodynamic and Transport Properties of Pure Fluids (NIST 12), version 5.0; National Institute of Standards and Technology: Gaithersburg, MD, 2000.
(17) Knez, Ž.; Škerget, M.; Senčar-Božič, A. Solubility of Nifedipine and Nitrendipine in Supercritical CO_2. *J. Chem. Eng. Data* **1995**, *40*, 216–220.
(18) Sarbu, T.; Styranec, T.; Beckman, E. J. Non-Fluorous Polymers with Very High Solubility in Supercritical CO_2 down to Low Pressures. *Nature* **2000**, *405*, 165–168.
(19) Beckman, E. J. A Challenge for Green Chemistry: Designing Molecules that Readily Dissolve in Carbon Dioxide. *Chem. Commun.* **2004**, 1885–1888.
(20) Bartle, K. D.; Clifford, A. A.; Jafar, S. A.; Shilstone, G. F. Solubilities of Solids and Liquids of Low Volatility in Supercritical Carbon Dioxide. *J. Phys. Chem. Ref. Data* **1991**, *20*, 713–756.

Received for review October 9, 2008. Accepted February 5, 2009. This work is the outcome of a Manpower Development Program for Energy & Resources supported by the Ministry of Knowledge and Economy (MKE). Y.K. acknowledges the support from a Korea Research Foundation grant (KRF-2005-005-J00802).

JE800737D