Measurement and Correlation of Solubility of Pimelic Acid in Ether, Tetrahydrofuran, Ethanol, and Methanol

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The solubilities of pimelic acid in ether, tetrahydrofuran, ethanol, and methanol had been determined by the synthetic method. The experimental data were correlated with simplified Apelblat equation. The solubilities correlated by the model showed good agreement with experimental data.

Introduction

1,7-Heptanediol is an important pharmaceutical intermediate and chemical material with wide use and optimum application prospects. We have developed a new technique for the synthesis of 1,7-heptanediol using pimelic acid as the raw material and ether, tetrahydrofuran (THF), ethanol, or methanol as a solvent. This new technique is characterized by a low-boiling solvent and a high product purity and yield. In the synthesis and purification process of 1,7-heptanediol, it is very important to know the solubilities of pimelic acid in solvents, because the solubilities of pimelic acid in solvents have direct effect on the reaction rate and product yield. However, no solubilities of pimelic acid in ether, THF, ethanol, and methanol have been reported so far. In this study, the solubilities of pimelic acid in ether, THF, ethanol, and methanol were determined, respectively. The experimental data of pimelic acid in ether, THF, ethanol, and methanol were correlated with simplified Apelblat equation, and the solubilities correlated by model agreed with the experimental data to within ± 3.6 %.

Experimental Section

Materials. Pimelic acid, ether, THF, ethanol, and methanol were of analytical reagent grade, were obtained from Shanghai Chemical Reagent Co., and had mass fraction purities of 0.995.

Solubility Measurement. The solubilities of pimelic acid in ether, THF, ethanol, and methanol were measured by a synthetic method described previously.[1,2] The laser monitoring observation technique was used to determine the dissolution temperature of the solid−liquid mixture. The uncertainty of the temperature was ± 0.02 K, and the solubility expressed by mole fraction was calculated according to the described previously in ref 2. The uncertainty in the mole fraction solubility x was less than 2 %.

Test of Apparatus. To prove the feasibility and the uncertainty of the measurement, the solubility of NaCl and pimelic acid in water were measured and compared with the values reported in the literature.[3,4] The experimental measurements agreed with the reported values with a mean relative deviation (RD) of 0.25 % and −4.4 %, respectively. The measured values were listed in Table 1.

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Table 1. Solubility of NaCl and Pimelic Acid in Water

NaCl				
T/K	293.15	303.15	313.15	323.15
x	0.0999	0.1004	0.1011	0.1021
x (lit)[5]	0.0996	0.1001	0.1009	0.1019
100 RD	0.25	0.25	0.25	0.24
Pimelic Acid				
T/K	307.15	310.15	313.15	323.15
x	0.01079	0.01263	0.01928	0.08249
x (lit)[6]	0.01127	0.01316	0.01865	0.08064
100 RD	−4.44	−4.19	3.26	2.24

Result and Discussion

The measured solubilities of pimelic acid in solvents at different temperatures were presented in Table 2. The temperature dependence of pimelic acid in solvents was described by the simplified Apelblat equation.[5,6]

$$\ln x = A + B/T \tag{1}$$

where x is the mole fraction solubility of pimelic acid and A and B are the model parameters, respectively. The adjustable parameters can be obtained from simplex optimization.

$$\text{the objective function } F = \min \sum_{i=1}^{N} (x_{ci} - x_i)^2 \tag{2}$$

The solubility curves by eq 1 were shown in Figure 1 and Figure 2.

The root-mean-square deviation (rmsd) is as follows:[2]

$$\text{rmsd} = \left[\frac{1}{N-1}\sum_{i=1}^{N}(x_{ci} - x_i)^2\right]^{1/2} \tag{3}$$

where N is the number of experimental points, x_{ci} represents the solubilities calculated from equations, and x_i represents the experimental solubility values. The model parameters and rmsd are listed in Table 3.

The RDs between the experimental value and the calculated value are also listed in Table 2. RDs were calculated according to:[2]

$$\text{RD} = \frac{x - x_c}{x} \tag{4}$$

The relative average deviations (RADs) by equation are listed in Table 3. The RAD was defined as[2]

10.1021/je900629v
Published on Web 10/22/2009

$$\mathrm{RAD} = \frac{1}{N}\sum_{i=1}^{N}\left|\frac{x_i - x_{ci}}{x_i}\right| \quad (5)$$

For the solid−liquid two-phase system, there was the following equation based on thermodynamic principle when the two-phase equilibrium was reached,[5,6]

$$\ln rx = -\frac{\Delta H_m}{R}\left(\frac{1}{T} - \frac{1}{T_m}\right) \quad (6)$$

where x is the mole fraction solubility of pimelic acid, r represents the activity coefficient, ΔH_m is the melting heat of pimelic acid, and T_m is the melting point of pimelic acid.

Table 2. Solubilities of Pimelic Acid in THF, Ether, Methanol, and Ethanol

T/K	x	100 RD
	THF	
298.95	0.1911	0.62
300.55	0.1978	0.48
302.15	0.2045	0.27
303.65	0.2109	0.09
305.15	0.2185	0.35
307.95	0.2309	−0.12
309.05	0.2347	−0.81
311.75	0.2496	−0.29
313.75	0.2591	−0.67
315.75	0.2710	−0.22
317.75	0.2820	−0.26
320.25	0.2959	−0.39
321.65	0.3061	0.28
323.05	0.3164	0.87
	Ether	
278.95	0.0091	3.60
281.95	0.0102	3.06
284.65	0.0112	0.51
287.05	0.0122	−0.70
290.05	0.0137	−1.86
292.95	0.0152	−3.18
294.75	0.0165	−1.65
296.35	0.0180	0.58
299.15	0.0199	0.07
301.55	0.0222	1.65
	Methanol	
300.75	0.1425	1.42
302.65	0.1521	1.45
304.15	0.1588	0.68
305.95	0.1708	1.95
307.65	0.1798	1.52
310.05	0.1873	−2.23
312.65	0.2048	−1.66
314.85	0.2176	−2.52
317.85	0.2457	0.33
321.35	0.2699	−0.92
323.75	0.2931	0.16
325.55	0.3088	0.08
327.15	0.3239	0.17
328.75	0.3416	0.85
	Ethanol	
298.45	0.1208	−0.04
301.45	0.1309	−1.44
304.25	0.1444	−0.31
305.75	0.1506	−0.64
307.55	0.1581	−1.22
310.25	0.1720	−0.81
312.15	0.1867	1.79
314.85	0.2022	1.98
316.25	0.2065	0.13
317.95	0.2192	1.31
320.95	0.2352	0.04
323.55	0.2485	−1.59
325.65	0.2673	0.06
327.55	0.2805	−0.16
329.25	0.2938	−0.01

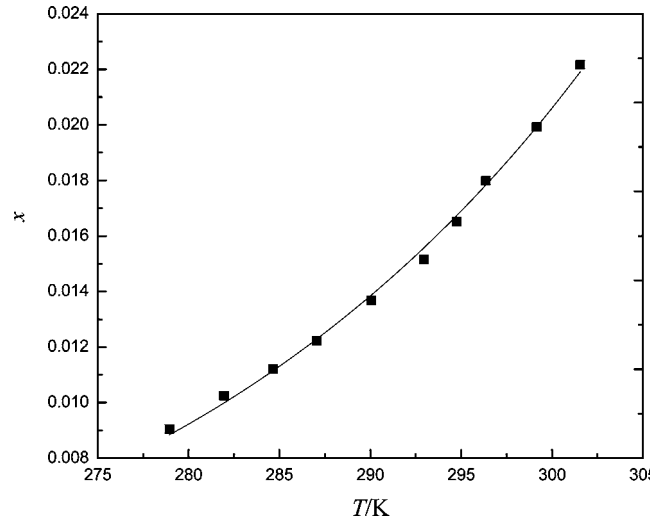

Figure 1. Solubility curves of pimelic acid in ether. ■, experimental data; solid line, calculated values from eq 1.

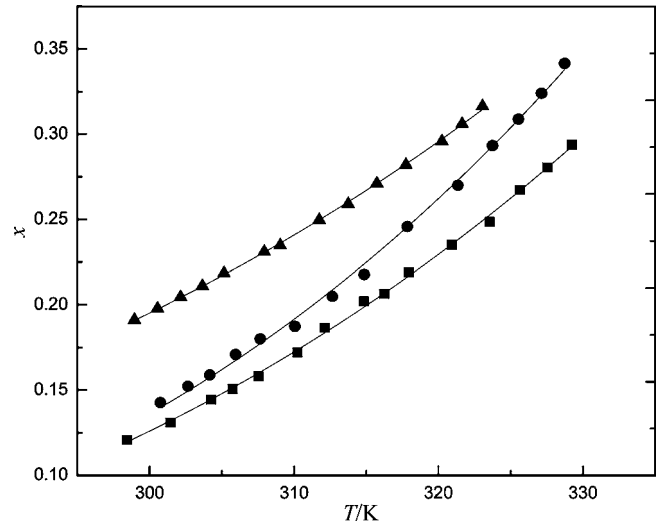

Figure 2. Solubility curves of pimelic acid in THF, ethanol, or methanol. ■, ethanol; ●, methanol;▲, THF; solid line, calculated values from eq 1.

Table 3. Parameters of Pimelic Acid in Ether, THF, Methanol, and Ethanol in eq 1

solvent	A	B	10^3 rmsd	10^2 RAD
ether	7.50	−3413.75	0.29	1.69
THF	5.06	−2010.40	1.27	0.41
methanol	8.37	−3107.20	2.83	1.14
ethanol	7.38	−2834.52	2.10	0.77

Supposing that the activity coefficient r is equal to 1 and the solution as an ideal solution, the eq 6 can be simplified to the simplified Apelblat eq 1. Therefore, the relationships of solubilities with the temperature of pimelic acid in four solvents can be easy to predict with the simplified Apelblat equation.

From Table 3, it can be found that the calculated solubilities show good agreement with the experimental data, and the overall rmsd of 53 data points which are correlated with eq 1 for the pimelic acid in solvents are less than $2.90 \cdot 10^{-3}$. From Table 2, it can be found that the RDs in eq 1 among these values do not exceed 3.6 %, which indicates that the simplified Apelblat equation is suited to correlate the solubility data of pimelic acid in THF, ether, ethanol, and methanol.

As can be seen from the results, the solubility of pimelic acid in four solvents follow the order THF > methanol > ethanol > ether, which agrees with the dielectric constant order of the

investigated solvents: methanol ($\varepsilon = 33.7$) > ethanol ($\varepsilon = 24.50$) > ether ($\varepsilon = 4.33$).[7] However, THF ($\varepsilon = 7.39$) does not agree with the rule. We think that it is may be because of the intermolecular interaction between solvent and solute molecules. Pimelic acid molecules consist two types of groups in its molecular structure, two strongly polar hydrophilic carboxyl groups (−COOH) and a long carbon chain hydrophobic group; in general, pimelic acid should be a medium-polar molecule. THF is also a medium-polar solvent, and it not only has a greater solubility for the hydrophilic groups but also has a strong dissolving capacity for nonpolar hydrophobic groups. Therefore, the solubilities of pimelic acid in THF are the greatest, which agree with the "like dissolves like" rule.

Conclusion

The solubilities of pimelic acid in ether, THF, ethanol, or methanol have been determined by suitable experimental methods and a solubility apparatus.

The simplified Apelblat equation based on solid−liquid phase equilibrium principles is used to correlate the solubility data of pimelic acid in these solvents, and it agrees with the experimental data.

The experimental solubility and correlation equation in this work can be used as essential data and as a model for the synthesis and purification of 1,7-diheptanediol.

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Received for review July 24, 2009. Accepted October 12, 2009.

JE900629V