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Solubility, Density, and Metastable Zone Width of the (1,4-Dioxan-2-one + Ethyl Acetate) System

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The solubility of 1,4-dioxan-2-one (1) in ethyl acetate (2) was measured over the temperature range from 263.55 K to 295.95 K. The results were correlated by an exponential equation. Densities of their binary mixtures have been measured at temperatures from 263.05 K to 298.55 K and at mole fraction x_1 of 0.2010 to 0.7099. The metastable zone width was measured for the evaluation of the nucleation rate and nucleation temperature. Results for the density and the metastable zone width were correlated by empirical equations.

Introduction

The compound 1,4-dioxan-2-one (*p*-dioxanone) is used as a monomer in the production of poly(*p*-dioxanone), which has been applied to make biodegradable products, especially surgical devices such as surgical suture, anchors, staples, tacks, clips, plates, screws, and bone fixation devices.[1−3] .

A simple method was developed for preparing 1,4-dioxan-2-one by oxidative dehydrogenation of diethylene glycol over metallic catalyst-supported silica particles. Since the resource, diethylene glycol, was readily available at moderate cost, this one-step reaction sharply decreased the cost of 1,4-dioxan-2-one. [1]

Purification of 1,4-dioxan-2-oneis also an important step in order to achieve high molecular weight poly(*p*-dioxanone). This methods includes dissolving a crude reaction product containing 1,4-dioxan-2-one in an aliphatic ester solvent, forming crystals of 1,4-dioxan-2-one, and filtering the mixture to recover solids containing crystalline 1,4-dioxan-2-one, which is relatively pure as compared to the crude reaction product. To achieve an appropriate crystallization rate and the highest purity product, seeding and sweating processes are generally required in the crystallization.[3−5] In addition, separation capacity depends mainly on the type of solvent, which affects the kinetics of crystallization such as nucleation and crystal growth. Therefore, selecting a suitable proper solvent is important for effective crystallization to take place. Although ethyl acetate has been commonly chosen as the recrystallizing solvent, there is a scarce amount of 1,4-dioxan-2-one solubility data available in the literature.

In this work, the solubility and density of 1,4-dioxan-2-one (1) in ethyl acetate (2) was measured over the temperature range of 263.55 K to 295.95 K. The density of 1,4-dioxan-2-one in ethyl acetate was measured over the temperature range from 263.05 K to 298.55 K for the corresponding mole fractions (x_1) of 0.2010 to 0.7099. The metastable zone width ($\Delta T_{\max}$) that was measured over cooling rate ranges from 0.01 K/min to 1.0 K/min.

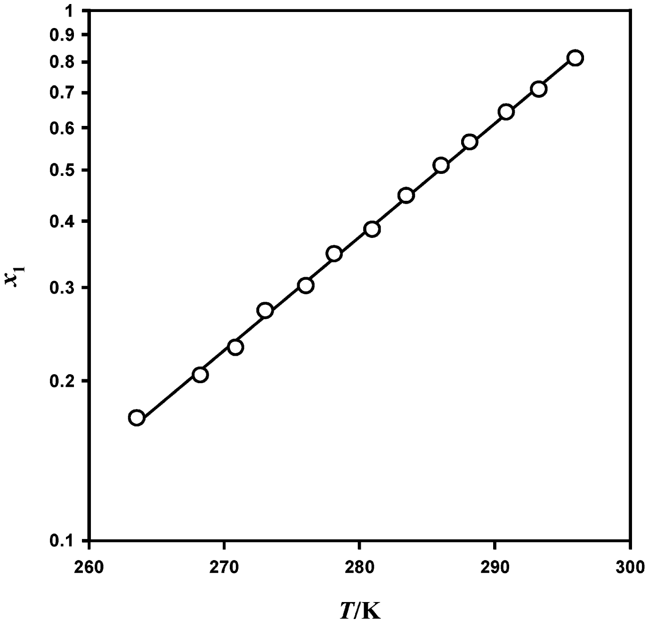

Figure 1. Mole fraction solubility of 1,4-dioxan-2-onein ethyl acetate.

Experimental Section

Materials. 1,4-Dioxan-2-one (CAS Registry No. 3041-16-5, *p*-dioxanone) was prepared and purified in our pilot plant according to the procedures in refs 1 and 2. Its purity, established by a flame-ionization detection gas chromatography (FID DONAM GC 6200) equipped with capillary columns (BP20 1.0 UM, SGC), was found to be greater than 99.95 mass %; the water content, after drying on molecular sieves, was < 0.0005 %. The fusion enthalpy and melting temperature of the pure 1,4-dioxan-2-one were 16.14 kJ/mol and 301.7 K, respectively. The values were determined by differential scanning calorimetry (DSC; TA Instruments, USA) with an uncertainty of ± 0.05 kJ/mol. Reagent-grade ethyl acetate (Aldrich Chemical Co., purity > 99.5 %) was used.

Measurement of Solubility. The mixtures were prepared by mass using a Mettler AG 204 balance with an

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uncertainty of ± 0.0001 g. The estimated uncertainty in the mole fraction is less than $\pm 2 \times 10^{-4}$. The solubility of 1,4-dioxan-2-one in the ethyl acetate was measured using a polythermal method described previously in detail.[6,7]

The glass apparatus used consists of a three jacket vessel into which the equilibrium cell, a cylindrical glass vessel (50 mm i.d., 120 mm long), is inserted by ground-glass joint. The outer jacket was evacuated, and either heated or cooled medium from a thermostated bath could be circulated through the middle jacket and transfers the heat to the equilibrium cell via the contact medium between the equilibrium cell and the middle jacket. An (ethylene glycol + water) solution was thermostated and controlled by a thermoelectric Eurotherm 808 PID controller with ± 0.1 K uncertainty. The cell had a perforated rubber stopper, through which a copper−constantan thermocouple was inserted. The contents were stirred with a magnetic spin bar in the inner jacket. The cell was tightly sealed to protect the system from dust and moisture condensation.

Mixtures of solute and solvent were cooled in bath until an abundant amount of crystal was formed and then heated very slowly at less than $0.001\ \mathrm{K \cdot min^{-1}}$ near the equilibrium temperature. The crystal disappearance temperature, detected visually, was measured with a calibrated thermocouple connected to a recorder (Yokogawa, 180 micro R). The thermocouples were calibrated with a calibrated thermometer from Fisher Scientific (No. 15-078-7), with an uncertainty of ± 0.05 K. The accuracy of the thermocouple measurements is believed to be ± 0.1 K. Some of the experiments were conducted in triplicate to check the uncertainty. The saturation temperature for a given mixture was reproducible to within ± 0.1 K.

Measurement of Density. The density of solutions of 1,4-dioxan-2-one and ethyl acetate was determined using a digital densimeter (Mettler Toledo, AG), with density measurement packages (No. 210260 and No. 238491), which uses the Archimedes' principle. The density of the solution was determined using a sinker of known volume (10 mL). The sinker was weighed in air and then in the solution. The method was described in detail in our previous works.[6,7] Before measurement, the densimeter was calibrated with distilled water at the experimental temperatures. Some of the experiments were conducted to check the uncertainty at the end of measurement. The densimeter in the above configuration appeared to have an uncertainty of ± 0.0002 g/cm^3. The bath temperature was measured with a calibrated thermocouple and maintained constant to ± 0.1 K at the desired temperature.

Measurement of Metastable Zone Width. The metastable zone width was measured by the polythermal method.[9] The equipment used was similar to that in measurement of solubility with minor modifications. A solution with known composition was placed into a thermostated nucleation cell in a 300 mL cylindrical glass vessel (90 mm i.d., 120 mm long) fitted with a triple jacket and agitated by a magnetic bar. The solution temperature was gradually lowered to a constant cooling rate until the first crystals appeared, and then it was increased to a rate of 0.001 K/min until the crystals dissolved. The difference between the two temperatures is called the metastable zone width. The consistency of the crystal disappearance temperature was checked by comparison of the saturation temperature obtained in solubility measurements with mixtures of exactly known composition. The experimental data were in satisfactory agreement with the results from solubility measurements with ± 0.2 K uncertainty.

Table 1. Experimental Solubility Data for the System 1,4-Dioxan-2-one (1) in Ethyl Acetate (2)

x_1	T/K	x_1	T/K
0.1701	263.55	0.4471	283.45
0.2049	268.25	0.5090	286.05
0.2311	270.85	0.5637	288.15
0.2713	273.05	0.6425	290.85
0.3020	276.05	0.7098	293.25
0.3469	278.15	0.8127	295.95

Results and Discussion

Solubility. The solubility of 1,4-dioxan-2-one (1) in ethyl acetate (2) was measured over the temperature range from 263.55 K to 295.95 K, and the values are listed in Table 1 and plotted in Figure 1. It was found that exponential temperature dependence, as shown in Figure 1, permitted a linear interpolation. Thus, the mole fraction solubility (x_1) of 1,4-dioxan-2-one was analyzed using the following equation:[6]

$$x_1 = \alpha \cdot e^{\beta}(T/\mathrm{K}) \tag{1}$$

where T is the absolute temperature and α and β are parameters. The values of α and β obtained by regression procedure in SigmaPlot 8.0 are 3.83×10^{-7} and 4.92×10^{-2} K^{-1}, respectively. The relative standard deviation (RSD) and the absolute average deviation (AAD) between the measured solubility data and the data calculated from eq 1 was 0.0171 and 0.0057, respectively. The RSD is defined by

$$\mathrm{RSD} = \left[\frac{1}{\mathrm{N}}\sum_{i=1}^{N}\left(\frac{x_{1,i}(\mathrm{calc}) - x_{1,i}}{x_{1,i}}\right)^2\right]^{1/2} \tag{2}$$

, and the AAD is defined by

$$\mathrm{AAD} = \frac{1}{\mathrm{N}}\sum_{i=1}^{N}|(x_{1,i}(\mathrm{calc}) - x_{1,i})| \tag{3}$$

where N is the number of data points.

Data of solubility can be used to estimate the activity coefficient through the equilibrium relationship. If no solid−solid transition occurs in the considered temperature range, the following fundamental equation is used to calculate the solid−liquid-phase equilibria:[10,11]

$$\ln x_1^{\mathrm{L}}\gamma_1^{\mathrm{L}} = -\frac{\Delta_{\mathrm{fus}}H_1}{R}\left(\frac{1}{T} - \frac{1}{T_{\mathrm{fus},1}}\right) \tag{4}$$

where x_1^{L} is the mole fraction of component 1 (1,4-dioxan-2-one) in the liquid phase, γ_1^{L} is the activity coefficient of component 1 in the liquid phase, $\Delta_{\mathrm{fus}}\mathrm{H}_1$ is the molar enthalpy of fusion, $T_{\mathrm{fus},1}$ is the melting temperature, T is the absolute temperature of the mixture, and R is the universal gas constant. The activity coefficients (γ_1^{L}) can be calculated using eq 4 from experimentally determined solution composition (x_1^{L}) and temperature (T).

Table 2 gives activity coefficients as a function of mole fractions and equilibrium temperatures. As can be seen Table 2, in nearly all the cases, positive deviation from ideal solution ($\gamma_1 > 1$) are encountered for the system investigated in this work. Such deviation is attributed to the interaction of a chemical nature between the 1,4-dioxan-2-one and ethyl acetate.

Density of Solution of 1,4-Dioxan-2-One and Ethyl Acetate. The densities for the 1,4-dioxan-2-one (1) + ethyl

Table 2. Activity Coefficient for the System 1,4-Dioxan-2-one (1) in Ethyl Acetate (2)

x_1^L	T/K	γ_1^L	x_1^L	T/K	γ_1^L
0.1662	263.55	2.371	0.4428	283.45	1.493
0.2094	268.25	2.140	0.5032	286.05	1.398
0.2381	270.85	2.019	0.5581	288.15	1.324
0.2653	273.05	1.919	0.6374	290.85	1.234
0.3075	276.05	1.788	0.7174	293.25	1.158
0.3010	278.15	1.701	0.8194	295.95	1.077

Table 3. Experimental Density Data for the System 1,4-Dioxan-2-one (1) + Ethyl Acetate (2)

x_1	T/K	ρ/(kg·m^{-3})	x_1	T/K	ρ/(kg·m^{-3})
0.2010	263.05	1003	0.3013	298.05	1001
0.2010	268.05	998	0.4471	278.05	1090
0.2010	273.05	992	0.4471	283.05	1083
0.2010	278.05	986	0.4471	288.05	1078
0.2010	283.05	981	0.4471	293.05	1072
0.2010	288.05	976	0.4471	298.55	1065
0.2010	293.05	969	0.5638	283.05	1115
0.2010	298.05	964	0.5638	288.05	1110
0.3013	268.05	1035	0.5638	293.05	1104
0.3013	273.05	1029	0.5638	298.55	1098
0.3013	278.05	1024	0.7099	288.05	1164
0.3013	283.05	1018	0.7099	293.05	1158
0.3013	288.05	1012	0.7099	298.55	1151
0.3013	293.05	1007			

acetate (2) system were measured in the range of from 263.05 K to 298.55 K for corresponding mole fraction value (x_1) from 0.2010 to 0.7099. Only the average values of the densities from three independent measurements for five concentrations are listed in Table 3. The experimental data were fitted to eq 5 below as a function of absolute temperature (T) and mole fraction (x_1):

$$\rho/(\text{kg·m}^{-3}) = k_1 + k_2x_1 + k_3(T/\text{K}) + k_4x_1(T/\text{K}) \qquad (5)$$

The values of coefficients k_1, k_2, k_3, and k_4 of eq 5, describing densities are 1218.53, 399.416, −1.1017, and −0.10318, respectively. The RSD and the AAD between the measured density data and calculated data were 0.0004 and 0.39 kg/m^3, respectively.

Metastable Zone Width. The most readily available method that is used for determining the degree of nucleation is the measurement of the metastable zone width at different cooling rates.[9−13] The principle of the method is based on the fact that the rate of saturation on reaching the metastable zone is equal to the rate of nucleation. The metastable zone width is regarded as one of nucleaction characteristics revealed macroscopically.

For nucleation from solution cooled at a constant rate, the maximum allowable undercooling (i.e., metastable zone width), $\Delta T_{\max}$ according to cooling rate (b) was measured over the cooling rate range from 0.01 K/min to 1 K/min as follows:

$$\log b/(\text{K·min}^{-1}) = \log \text{k}_n + n \log(\Delta T_{\max}/\text{K}) \qquad (6)$$

where k_n is a constant related to the nucleation rate and n is the nucleation order.

The metastable zone width was taken as the difference between the saturation temperature (T_s) and the temperature at which nuclei were detected for each particular cooling rate. The saturation temperature (T_s) was obtained from the experimentally determined solubility curve. The experimental metastable zone width ($T_{\max}$) as function of the cooling rate (b) at three different saturation temperatures (T_s) are listed in Table 4 and plotted in Figure 2. These results in Figure 2 show that the metastable zone width of the 1,4-dioxan-2-one (1) + ethyl acetate (2) solutions increases with increasing cooling rates and the saturation temperature. The parameter values of eq 6 (k_n and n) were evaluated by regression analysis applied to the slopes and intercepts of curves found in Figure 2. These are shown in Table 5 with the RSD and AAD.

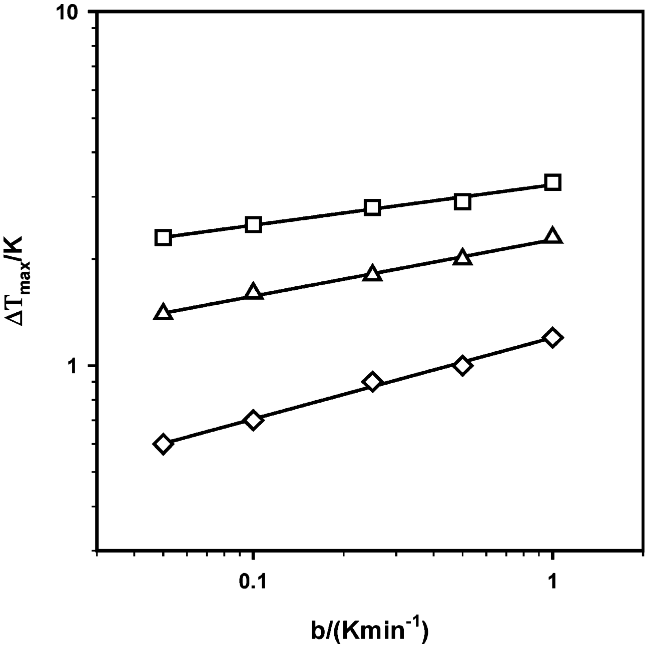

Figure 2. Plots of $T_{\max}$ vs b in 1,4-dioxan-2-one (1) + ethyl acetate (2) system: □, T_s = 293.25 K; △, T_s = 288.15 K; ◇, T_s = 283.45 K.

Table 4. Experimental Metastable Zone Width ($\Delta T_{\max}$) as Function of the Cooling Rate (b) at Three Different Saturation Temperatures (T_s)

	$\Delta T_{\max}$/K		
b/(K·min^{-1})	T_s = 293.25 K	T_s = 288.15 K	T_s = 283.45 K
0.01	1.7	1	0.4
0.05	2.3	1.4	0.6
0.1	2.5	1.6	0.7
0.25	2.8	1.8	0.9
1	3.3	2.3	1.2

Table 5. Parameters, k_n, n on T_s of Equation 6

T_s	k_n	n	RSD	AAD
293.25	4.0654×10^{-5}	8.5706	0.131	0.240
288.15	5.9952×10^{-3}	6.2342	0.013	0.023
283.45	4.5332×10^{-1}	4.3287	0.018	0.012

In Figure 2 and Table 5, the nucleation rate of 1,4-dioxan-2-one in 1,4-dioxan-2-one + ethyl acetate solutions was vary fast despite being the small range of the metastable zone width $T_{\max}$. It means that the purification process of 1,4-dioxan-2-one by the crystallization method is needed in the crystallization process using seed, which is an effective method for controlling nucleation rate and metastable zone width.

Conclusion

Data have been obtained on the solubility, density, and metastable zone width for the 1,4-dioxan-2-one (1) + ethyl acetate (2) system at the temperatures from 263.55 K to 295.95 K and at a mole fraction (x_1) of 0.2010 to 0.7099. These data are well-correlated by the empirical relations described in this study. The solubility of 1,4-dioxan-2-one in ethyl acetate shows a high dependence on temperature due to a large solvent−solute interaction. These results indicate that ethyl acetate can be used as solvent for the recrystallization of 1,4-dioxan-2-one crystals by cooling crystallization.

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