Solubility of Dimethyl Fumarate in Methanol, Ethanol, 1-Propanol, 2-Propanol, 1,2-Propanediol, and Water from (289.95 to 347.15) K

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Using the laser monitoring observation technique, the solubilities of dimethyl fumarate in methanol, ethanol, 1-propanol, 2-propanol, 1,2-propanediol, and water have been determined experimentally from (289.95 to 347.15) K. The experimental data were correlated with the modified Apelblat equation. The calculated results showed good agreement with the experimental data.

Introduction

Dimethyl fumarate (Figure 1) is an antifungal preservative with high efficiency, low toxicity, and inexpensiveness. It can be used in acidic or neutral conditions and can inhibit a variety of fungi with extensive development prospects.[1,2] The research works relating to dimethyl fumarate are mainly concerned with synthesis, degradation, and application study. In the synthesis and purification process of dimethyl fumarate, it is necessary to know the solubilities of dimethyl fumarate in methanol, ethanol, 1-propanol, and so on, but the solubilities of dimethyl fumarate have not been reported. In this study, the solubilities of dimethyl fumarate in methanol, ethanol, 1-propanol, 2-propanol, 1,2-propanediol, and water have been measured from (289.95 to 347.15) K at atmospheric pressure. The modified Apelblat equation was applied to correlate the experimental data.[3−5]

Experimental Section

Analytical (AR) grade dimethyl fumarate obtained from Yueyang Kailimuli Co., Ltd. was further purified by recrystallization, and its purity was determined by UV spectrophotometry (type UV-2401PC, Shimadzu Co., Ltd.) to be 0.995 in mass fraction. Methanol, ethanol, 1-propanol, 2-propanol, and 1,2-propanediol were of AR grade; they were obtained from Tianjin Kermel Chemical Reagent Co., Ltd. and had purities of 0.995, 0.995, 0.995, 0.997, and 0.995 in mass fraction, respectively. The water used in the experiments was double-distilled water.

The solubilities of dimethyl fumarate in different solvents were measured by a dynamic method at atmospheric pressure.[6] The laser monitoring technique was used to determine the dissolution temperature of the last crystal. The laser monitoring system consists of a laser generator, a photoelectric transformer, and a recorder. The experiments were carried out in a magnetically stirred, jacketed glass vessel. The contents of the vessel were heated very slowly at rates less than 2 $K \cdot h^{-1}$ with continuous stirring. A condenser was connected with the vessels to prevent the solvents from evaporating. A mercury-in-glass thermometer was inserted into the inner chamber of the vessels for the measurement of the temperature. The uncertainty of the temperature was ± 0.05 K. In the early stage of the experiment, the laser beam was blocked by the turbidity of the solution, so the intensity of the laser beam penetrating the vessel was diminished. The intensity increased gradually along with the increase of the amount of dimethyl fumarate dissolved. When the last portion of dimethyl fumarate disappeared, the intensity of the laser beam penetrating the vessel reached the maximum, and the temperature was recorded as the liquidus temperature.[7] Some of the solubility experiments were conducted two or three times to check the reproducibility. The reproducibility of the temperature measurement was 0.1 K, which corresponds to a relative error in composition less than ± 1 %. In this work, the uncertainty for solubility measurement is estimated based on the principle of the error propagation and found to be within ± 1 % at the 95 % confidence level.

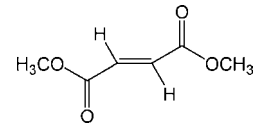

Figure 1. Structure of dimethyl fumarate.

Results and Discussion

The measured mole fraction solubilities (x) of dimethyl fumarate in methanol, ethanol, 1-propanol, 2-propanol, 1,2-propanediol, and water at different temperatures (T) are presented in Table 1. The temperature dependence of dimethyl fumarate solubility at fixed solvent composition is described by the modified Apelblat equation

$$\ln x = A + B/(T/\mathrm{K}) + C \ln(T/\mathrm{K}) \qquad (1)$$

where x is the mole fraction solubility of dimethyl fumarate; T is the absolute temperature; and A, B, and C are the parameters in eq 1. The values of these parameters together with the root-mean-square deviation (rmsd) are listed in Table 2. The rmsd is defined as

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

where N is the number of experimental points and x_{ci} and x_i refer to the solubility values calculated from eq 1 and to the experimental solubility.

By using the data shown in Table 1, the $T-x$ curves are plotted for the dimethyl fumarate + (water, methanol, ethanol,

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Table 1. Mole Fraction Solubilities x of Dimethyl Fumarate in Different Solvents

T/K	$10^2\,x$	$10^2\,x_c$	T/K	$10^2\,x$	$10^2\,x_c$
		Methanol			
297.45	0.7489	0.7558	319.37	2.794	2.774
301.00	0.9483	0.9337	322.28	3.346	3.294
305.55	1.216	1.224	325.93	3.997	4.083
309.17	1.520	1.517	329.15	4.912	4.932
312.85	1.886	1.887	332.30	5.996	5.931
316.45	2.314	2.335	337.65	8.096	8.105
		Ethanol			
289.95	0.3277	0.3317	314.75	1.990	1.992
294.45	0.4650	0.4707	318.65	2.532	2.569
297.55	0.6074	0.5950	322.55	3.261	3.289
303.15	0.9081	0.8966	327.35	4.312	4.419
307.30	1.218	1.202	331.85	5.805	5.779
311.10	1.566	1.561	336.05	7.513	7.370
		1-Propanol			
295.20	0.5038	0.4937	323.65	3.692	3.597
299.95	0.6683	0.6764	328.95	5.351	5.324
304.35	0.9057	0.9115	332.50	6.857	6.945
307.85	1.136	1.161	335.65	8.701	8.809
310.70	1.381	1.417	338.15	10.64	10.65
313.20	1.736	1.690	341.30	13.61	13.55
318.70	2.531	2.507			
		2-Propanol			
295.80	0.5329	0.5202	320.00	3.184	3.135
300.95	0.7476	0.7655	322.80	3.960	3.847
304.35	0.9701	0.9868	326.25	4.860	4.944
306.70	1.170	1.175	329.75	6.287	6.372
309.85	1.481	1.485	332.85	7.853	7.969
312.55	1.827	1.813	335.80	9.971	9.851
316.85	2.502	2.489			
		1,2-Propanediol			
302.75	0.03784	0.03710	323.25	0.8861	0.8649
307.05	0.07970	0.08090	327.95	1.490	1.477
310.55	0.1431	0.1453	332.15	2.296	2.262
314.25	0.2547	0.2578	337.25	3.493	3.561
316.75	0.3661	0.3701	342.35	5.104	5.251
320.05	0.5857	0.5788	347.15	7.300	7.152
		Water			
300.55	0.009273	0.009415	328.05	0.07808	0.07876
302.60	0.01164	0.01167	333.25	0.09888	0.1001
309.85	0.02361	0.02303	337.05	0.1131	0.1160
315.45	0.03649	0.03603	340.65	0.1318	0.1307
322.40	0.05749	0.05753	344.45	0.1478	0.1450

Table 2. Parameters of Correlation for the Solubility Equation for Various Systems

solvent	A	B	C	10^4 (rmsd)
methanol	−215.21	4859.8	34.061	3.6
ethanol	46.518	−7923.7	−4.3916	5.4
1-propanol	−453.70	14941	69.937	5.3
2-propanol	−235.11	4565.9	37.686	6.7
1,2-propanediol	1600.6	−87310	−231.08	6.5
water	1051.5	−55766	−153.40	0.14

1-propanol, 2-propanol, and 1,2-propanediol, respectively) systems in Figure 2.

From Tables 1 and 2, it can be found that the calculated solubilities show good agreement with the experimental data, which indicates that the modified Apelblat equation can be used to correlate the solubility data of dimethyl fumarate in methanol, ethanol, 1-propanol, 2-propanol 1,2-propanediol, and water. The overall rmsd of 72 data points for the methanol, ethanol, 1-propanol, 2-propanol, 1,2-propanediol, and water systems is $5.2 \cdot 10^{-4}$. From Figure 2 we see that the difference of the carbon atom numbers makes the difference of the solubility, but the effect is not significant. The solubility of dimethyl fumarate in 1-propanol is higher than that in 1,2-propanediol. The difference of the structural effects of 1-propanol and 2-propanol is one of

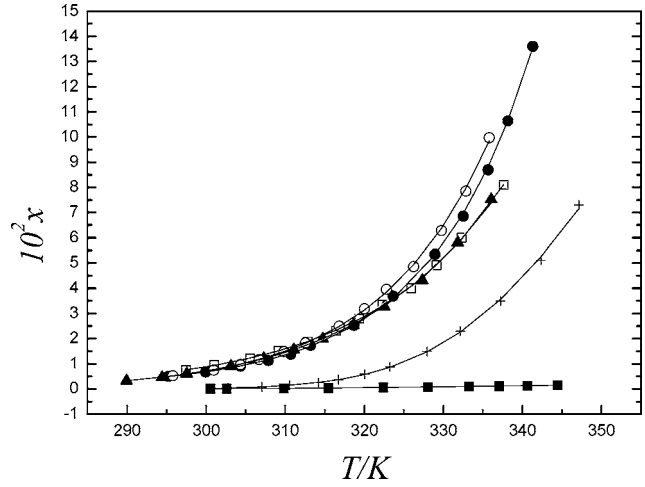

Figure 2. Solubilities of dimethyl fumarate in different solvents. ■, water; □, methanol; ▲, ethanol; ●, 1-propanol; ○, 2-propanol; +, 1,2-propanediol; —, calculated from eq 1.

the factors of the difference of the solubility.[8] According to Scatchard−Hildebrand's theory,[9,10] the solubility of the solute in the solvent is the largest when the solubility parameters of the solute and the solvent are the same. The values of the solubility parameter of dimethyl fumarate in methanol, ethanol, 1-propanol, 2-propanol, 1,2-propanediol, and water are 17.7 (calculated by the Fedors group contribution method[11,12]), 29.7, 26.5, 24.6, 23.6, 30.27, and 47.9, respectively. So, the solubility of dimethyl fumarate may be the minimum in the solvent of water. The experimental solubility and correlation equations in this work are essential to serve for a synthesis and purification process of dimethyl fumarate.

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