Experimental Measurement and Correlation of the Solubilities of 2,4-Dichloro-5-methoxypyrimidine in Ethyl Ethanoate, Methanol, Ethanol, Acetone, Tetrachloromethane, and Heptane at Temperatures between (295 and 320) K

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The solid−liquid equilibrium of 2,4-dichloro-5-methoxypyrimidine was first determined in this article. Using a laser monitoring observation technique, the solubilities of 2,4-dichloro-5-methoxypyrimidine in ethyl ethanoate, methanol, ethanol, acetone, tetrachloromethane, and heptane have been determined experimentally from (295.60 to 316.39, 302.37 to 316.95, 299.44 to 316.61, 297.35 to 311.37, 298.60 to 312.15, and 298.10 to 320.08) K, respectively. The results are correlated with $\lambda-h$ equation and Apelblat equation. The calculated results show that the correlation of the Apelblat model for six measured systems has less deviation than that of the $\lambda-h$ equation.

Introduction

Figure 1 shows the structure of 2,4-dichloro-5-methoxypyrimidine that is a type of white or pale yellow powdery crystal, with a melting temperature of 342.15 K. It is an important raw material widely used as an intermediate in the production of medicine and pesticide as well as other substances.[1−3] For these processes, knowledge of solubility is an important physicochemical property. Indeed, solvating-out crystallization is used to separate and recrystallize 2,4-dichloro-5-methoxypyrimidine, and in this procedure solubility data is essential for engineering design.

However, there is no article found in the archival literature reporting the solubility of 2,4-dichloro-5-methoxypyrimidine, and thus, in this study, the solubility of 2,4-dichloro-5-methoxypyrimidine in ethyl ethanoate, methanol, ethanol, acetone, tetrachloromethane, and heptane has been measured. The experimental data were correlated with the Apelblat equation and the $\lambda-h$ models.

Experimental Section

Materials. 2,4-Dichloro-5-methoxypyrimidine was produced in our laboratory with the procedure reported in ref 4. In this reaction, which was catalyzed by sodium, methyl methoxyacetate and ethyl methanoate were condensed in toluene, and the intermediate product reacted by refluxing with urea in ethanol to form 5-methoxy-1*H*-pyrimidine-2,4-dione that is then reacted in toluene with phosphorus trichloride oxide to form 2,4-dichloro-5-methoxypyrimidine. The product was further purified by recrystallization from ethanol. After filtration and drying, the mass fraction purity of 2,4-dichloro-5-methoxypyrimidine was determined by high-performance liquid chromatography (HPLC; Daojin LC-A) to be 0.998. The solvents were obtained from were obtained from Tianjin Kermel Chemical Reagent Co., Ltd., China, with the following cited purities: ethanol [CAS RN 64-17-5] had a mass fraction purity of 0.997, methanol [CAS RN 67-56-1] a mass fraction purity of 0.995, acetone [CAS RN 67-64-1] a mass fraction purity of 0.995, *n*-heptane [CAS RN 142-82-5] a mass fraction purity of 0.995, tetrachloromethane [CAS RN 56-23-5] a mass fraction purity of 0.995, and ethyl ethanoate [CAS RN 141-78-6] a mass fraction purity of 0.995.

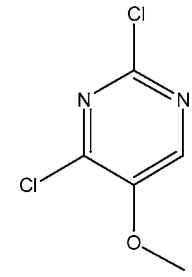

Figure 1. Structure of 2,4-dichloro-5-methoxypyrimidine.

Apparatus and Procedure. The normal melting temperature T_m and melting enthalpy $\Delta_{fus}H$ of 2,4-dichloro-5-methoxypyrimidine were determined by differential scanning calorimetry (DSC, NETZSCH, type STA409PC-luxx) in the presence of nitrogen with a rate of temperature increase with respect to time of 0.05 $K \cdot s^{-1}$. The normal melting temperature of 2,4-dichloro-5-methoxypyrimidine is (342.15 ± 0.5) K, and its enthalpy of fusion is (98.74 ± 0.1) $J \cdot g^{-1}$, that is, (17674 ± 18) $J \cdot mol^{-1}$.

In this work, the solubilities of 2,4-dichloro-5-methoxypyrimidine in each solvent were determined with the dynamic method described elsewhere.[5] The apparatus formed from a glass dissolution flask of nominal volume of 50 cm^3 was fitted with an insulating jacket. The reactor was fitted with a magnetic stirrer, and the flask also accommodated a thermometer, for which the uncertainty, as determined by the Tianjin Metrology Institute (Tianjin, China), was found to be ± 0.01 K.

The mass of about 0.01 g of 2,4-dichloro-5-methoxypyrimidine to be dissolved in a solvent was determined with an electronic balance (type AB204-N, produced by Mettler-Toledo Group) with an uncertainty of ± 0.001 g. The temperature increase was controlled to be less than 0.1 $K \cdot h^{-1}$, especially near the solid−liquid equilibrium temperature. A laser was shone

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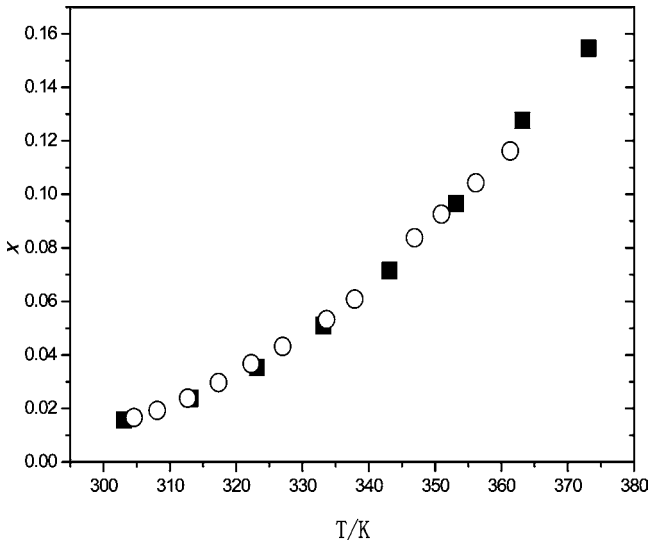

Figure 2. Solubilities of ethane 1,2-dicarboxylic acid in water: ■, experimental data; ○, literature data.[10]

onto the sample and the light detected on the opposite side of the flask where the received light power was converted into electrical signal; this system was fabricated by College of Physical Science and Engineering, Zhengzhou University.[6−9] When 2,4-dichloro-5-methoxypyrimidine was first placed into the solvent, the laser beam was partly blocked by the unsolved particles of 2,4-dichloro-5-methoxypyrimidine in the solution; the intensity of the laser beam penetrating the vessel was lower. The intensity increased with increasing time as the 2,4-dichloro-5-methoxypyrimidine dissolved. The solid was assumed dissolved when the intensity of the received laser light reached the largest value found for the pure solvent. The temperature measured at the greatest light intensity was assumed to be the temperature of the solid + liquid equilibrium. The laser used was a He−Ne with a wavelength of 632.8 nm that gave an approximate particle size detection limit of 1 nm.

Each solubility measurement was performed thrice to determine the reproducibility and standard deviation that was less than 1 %. The uncertainty and reproducibility of the temperature measurements was 0.01 K, which corresponds to a relative deviation in composition less than 1 %. The uncertainty of the measurement was determined with measurements of the solubility of ethane 1,2-dicarboxylic acid in water and the results, shown in Figure 2, compared with values obtained from the literature[10] that differ by less than 1 %, confirming the cited uncertainty.

Results and Discussion

Experimental Results. The solubility of 2,4-dichloro-5-methoxypyrimidine in ethyl ethanoate, methanol, ethanol, acetone, tetrachloromethane, and heptane are listed in Table 1. The comparisons between the calculated solubilities and the experimental data (ln x) are shown in Figure 2.

The $\lambda-h$ model[11,12] given by

$$\ln\left[1 + \frac{\lambda(1 - x)}{x}\right] = \lambda h\left(\frac{\mathrm{K}}{T} - \frac{\mathrm{K}}{T_{\mathrm{m}}}\right) \qquad (1)$$

can be used to correlate the solubilities of 2,4-dichloro-5-methoxypyrimidine in solvents. In eq 1, x is the mole fraction of 2,4-dichloro-5-methoxypyrimidine, and T_{m} is normal melting temperature of 2,4-dichloro-5-methoxypyrimidine. The values of λ and h for each solvent obtained by regression analysis are listed in Table 2. An alternative representation of the measurements can be obtained from the Apelblat equation[13,14] given by

$$\ln x = A + B\left(\frac{\mathrm{K}}{T}\right) + C\ln(T/\mathrm{K}) \qquad (2)$$

where x is the mole fraction solubility of 2,4-dichloro-5-methoxypyrimidine, T is the temperature, and A, B, and C are constants determined by regression analysis with the results listed in Table 3. The measurements and correlation given by eq 2 are compared in Figure 3.

The average absolute deviation defined by:

$$\sigma = \frac{1}{n}\sum_{\mathrm{i}=1}^{n}\left|\frac{x_{\mathrm{ci}} - x_{\mathrm{i}}}{x_{\mathrm{i}}}\right| \qquad (3)$$

can be used as a measure of the performance of the two models, and the values obtained are listed in Table 4. In eq 3 x_{i} is the experimental solubility, $x_{\mathrm{c,i}}$ the calculated value, and n the number of measurements. The average absolute deviations for the $\lambda-h$ model and Apelblat model are less than 3.14 % and 0.59 %, respectively, and on the basis of this comparison the Apelblat model is preferred.

Table 1. Mole Fraction x Solubilities of 2,4-Dichloro-5-methoxypyrimidine in Different Solvents at Temperature T

T/K	$10^2\,x$	T/K	$10^2\,x$	T/K	$10^2\,x$
2,4-Dichloro-5-methoxypyrimidine + Methanol					
302.37	5.977	308.12	8.933	313.55	14.58
303.78	6.585	309.67	10.15	314.81	16.28
305.44	7.338	311.15	11.43	315.80	18.15
306.57	8.030	312.43	12.97	316.95	20.23
2,4-Dichloro-5-methoxypyrimidine + Ethanol					
299.44	4.743	307.06	7.451	314.00	12.54
301.27	5.266	309.05	8.551	315.47	14.11
303.17	5.839	310.73	9.721	316.61	15.77
305.17	6.554	312.58	11.04		
2,4-Dichloro-5-methoxypyrimidine + Acetone					
297.35	34.77	304.54	42.01	310.25	48.10
299.36	36.77	306.18	43.58	311.37	49.23
301.17	38.61	307.53	45.04		
303.13	40.34	308.97	46.59		
2,4-Dichloro-5-methoxypyrimidine + Tetrachloromethane					
298.60	12.28	303.35	17.77	308.20	26.11
299.42	13.01	304.82	19.59	309.57	28.77
300.63	14.34	305.80	21.43	310.90	31.49
301.97	15.91	306.87	23.66	312.15	34.32
2,4-Dichloro-5-methoxypyrimidine + Ethyl Ethanoate					
295.60	28.83	304.15	36.45	313.07	46.75
296.53	29.49	305.62	38.18	314.57	49.04
298.25	31.11	307.47	40.07	316.39	51.28
300.66	33.01	309.19	42.16		
302.28	34.73	311.16	44.35		
2,4-Dichloro-5-methoxypyrimidine + Heptane					
298.10	0.9404	307.55	1.566	317.15	2.679
299.83	1.039	309.57	1.737	318.83	2.960
302.10	1.162	310.97	1.921	320.08	3.241
303.81	1.285	312.89	2.139		
305.72	1.415	315.04	2.391		

Conclusion

As shown in Table 1 and Figure 3, the solubilities of 2,4-dichloro-5-methoxypyrimidine increase with an increase in temperature. It can be observed from Table 1 that the solubilities of 2,4-dichloro-5-methoxypyrimidine in six different organic

Table 2. Parameters in the $\lambda-h$ Equation for Different Solvents

mixture	λ	h	R^2
2,4-dichloro-5-methoxypyrimidine + ethyl ethanoate	0.78653	2991.1	0.99968
2,4-dichloro-5-methoxypyrimidine + methanol	1.4191	5888.5	0.99127
2,4-dichloro-5-methoxypyrimidine + ethanol	0.58262	10665	0.99314
2,4-dichloro-5-methoxypyrimidine + acetone	0.81013	2580.3	0.99946
2,4-dichloro-5-methoxypyrimidine + tetrachloromethane	5.4096	1606.5	0.99868
2,4-dichloro-5-methoxypyrimidine + heptane	0.036720	99323	0.99937

Table 3. Parameters in Apelblat Equation for Different Solvents

mixture	A	B	C	R^2
2,4-dichloro-5-methoxypyrimidine + methanol	−2349.2	101040	352.30	0.99976
2,4-dichloro-5-methoxypyrimidine + ethanol	−1707.4	72404	256.50	0.99982
2,4-dichloro-5-methoxypyrimidine + acetone	104.73	−6733.9	−14.599	0.99975
2,4-dichloro-5-methoxypyrimidine + tetrachloromethane	21.928	−7175.9	0.00009	0.99938
2,4-dichloro-5-methoxypyrimidine + ethyl ethanoate	−104.29	2482.0	16.636	0.99981
2,4-dichloro-5-methoxypyrimidine + heptane	−407.49	13979	62.472	0.99965

solvents follow the order acetone > ethyl ethanoate > tetrachloromethane > methanol > ethanol > heptane, which is inconsistent with the order of solvent polarity for these six solvents.

The experimental results also show that the change in the solubility of ethanol with temperature is more sensitive, and thus, ethanol is preferred for crystallization and purification processes for 2,4-dichloro-5-methoxypyrimidine.

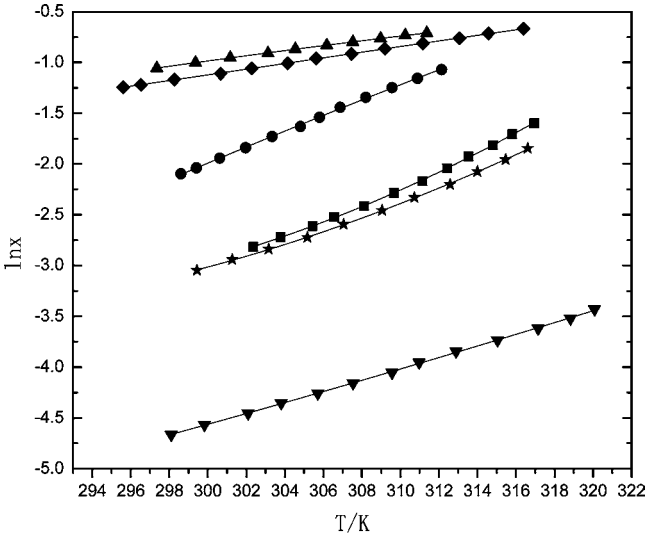

Figure 3. Comparison of experimental solubilities with calculated values by the Apelblat model for 2,4-dichloro-5-methoxypyrimidine in different solvents: ■, methanol; ▲, acetone; ▼, heptane; ◆, ethyl ethanoate; ●, tetrachloromethane; ★, ethanol; solid line, Apelblat model.

Table 4. Comparison of Absolute Average Relative Deviation for Different Models

	100 σ	
mixture	$\lambda-h$	Apelblat
2,4-dichloro-5-methoxypyrimidine + ethyl ethanoate	0.46	0.28
2,4-dichloro-5-methoxypyrimidine + methanol	3.14	0.46
2,4-dichloro-5-methoxypyrimidine + ethanol	2.58	0.40
2,4-dichloro-5-methoxypyrimidine + acetone	0.33	0.12
2,4-dichloro-5-methoxypyrimidine + tetrachloromethane	1.51	0.59
2,4-dichloro-5-methoxypyrimidine + heptane	1.11	0.56
total average deviation	1.52	0.40

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