Solubility of Thiotriazinone in Ethanol, 1-Propanol, 2-Propanol, 1-Butanol, Acetonitrile, Acetone, Ethyl Acetate, and Water from 293 K to 343 K

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The solubility of thiotriazinone in ethanol, 1-propanol, 2-propanol, 1-butanol, acetonitrile, acetone, ethyl acetate, and water was measured using a laser technique with a temperature range from 293.65 K to 343.70 K. The results of these measurements were correlated with a semiempirical equation. The calculated results of which are proved to show fine representation of experimental data.

Introduction

Thiotriazinone (2,5-dihydro-6-hydroxy-3-mercapto-2-methyl-5-oxo-1,2,4-triazine, $C_4H_5N_3O_2S$ (Figure 1), molar mass 159.13 g·mol^{-1}, CAS Registry No. (supplied by author) 58909-39-0) is a kind of white crystalline powder. As an intermediate of the β-lactam antibiotic, thiotriazinone has been widely used in synthesis of medicament for ceftriaxone and other antibiotics for combination drugs.[1] In the industrial production, the thiotriazinone was synthesis in the solvent. To determine the proper solvent and to design an optimized crystallization process, it is necessary to know its solubility in different solvents. In the present work, the solubility of thiotriazinone was measured in the temperature range from 293.65 K to 343.70 K in various organic solvents and water using a laser monitoring observation technique. The method employed in this work was classed as a synthetic method, which was much faster and more readily available than the analytical method.[2]

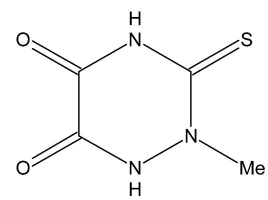

Figure 1. Structural formula of thiotriazinone.

Experimental Section

Materials. A white crystalline powder of thiotriazinone was purchased from ShiJiaZhuang HeJia Health Products Co., Ltd. Its mass fraction purity determined by HPLC was higher than 0.994. Other reagents were analytical research grade reagent from Beijing Chemical Reagent Co. All the solvents used in the experiments had a minimum mass-fraction purity of 0.995.

Apparatus and Procedures. The solubility of thiotriazinone was measured by using an apparatus similar to that described as literature[2–8] and described briefly here. A 500 mL jacketed vessel was used to determined the solubility, the temperature was controlled to be constant (fluctuates with 0.05 K) through a thermostat water bath. A mercury-in-glass thermometer was inserted into the inner chamber of the vessel with an uncertainty of ± 0.05 K. The dissolution of the solute was examined by the laser beam penetrating the vessel. To prevent the evaporation of the solvent, a condenser vessel was introduced. The masses of the samples and solvents were weighted using an analytical balance (Sartorius CP224S) with an uncertainty of ± 0.0001 g. During experiments the fluid in the glass vessel was monitored by a laser beam. Predetermined excess amounts of solvent and thiotriazinone of known mass were placed in the inner chamber of the vessel. The contents of the vessel were stirred continuously at a required temperature. In the early stage of the experiment, the laser beam was blocked by the undissolved particles of thiotriazinone in the solution, so the intensity of laser beam penetrating the vessel was lower. Along with the dissolution of the particles of the solute, the intensity of the laser beam increased gradually. When the solute dissolved completely, the solution was clear, and the laser intensity reached maximum. Then additional solute of known mass {about (1 to 5) mg} was introduced into the vessel. This procedure was repeated until the penetrated laser intensity could not return to maximum or, in other words, the last addition of solute could not dissolve completely. The interval of addition was 120 min. The total amount of the solute consumed was recorded. The same solubility experiment was conducted three times, and the mean values were used to calculate the mole fraction solubility (x_1) based on eq 1

$$x_1 = \frac{m_1/M_1}{m_1/M_1 + m_2/M_2} \tag{1}$$

where m_1 and m_2 represent the mass of the solute and solvent, respectively, and M_1 and M_2 are the molecular weight of the solute and solvent, respectively. The uncertainty of the experimental solubility values is about 0.5 %. The uncertainty in the solubility values can be due to uncertainties in the temperature measurements, weighing procedure and instabilities of the water bath.

Results and Discussion

The solubility of thiotriazinone is listed in Table 1. The relationship between temperature and solubility of the thiotriazinone is correlated with a semiempirical equation: [9]

$$\ln x_1 = a + \frac{b}{T} + c \ln T \tag{2}$$

where T is the absolute temperature and a, b, and c are empirical constants. The difference between experimental and calculated

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Table 1. Mole Fraction Solubility of Thiotriazinone x_1 in Different Solvents between 293 K and 343 K

T/K	10^3x_1	$10^3(x_1 - x_1^{calc})$	T/K	10^3x_1	$10^3(x_1 - x_1^{calc})$
		Ethanol			
293.23	12.52	−0.04	323.41	22.80	0.06
298.35	13.97	0.12	328.23	25.50	0.43
303.33	15.24	−0.01	333.53	27.77	−0.17
308.29	16.87	0.06	338.63	30.74	−0.28
313.47	18.59	−0.03	343.33	34.49	0.31
318.47	20.47	−0.11			
		1-Propanol			
292.99	8.588	0.108	323.23	17.63	0.10
298.33	9.588	−0.046	328.47	19.84	−0.04
303.23	10.78	−0.05	333.07	22.35	0.14
308.23	12.19	−0.03	338.33	25.14	−0.06
313.15	13.91	0.16	343.35	28.56	0.14
318.23	15.70	0.16			
		2-Propanol			
293.11	5.565	−0.022	323.07	14.22	−0.13
298.21	6.626	−0.013	328.13	16.42	−0.15
303.13	7.821	0.018	333.09	18.74	−0.27
308.11	9.149	0.004	337.75	21.66	0.10
312.87	10.69	0.09	342.67	24.75	0.21
317.83	12.45	0.14			
		1-Butanol			
293.11	8.716	0.091	322.89	17.84	0.16
298.23	9.642	−0.122	328.13	19.99	−0.05
302.99	10.94	−0.01	333.39	22.38	−0.34
308.11	12.38	−0.02	338.07	25.49	0.11
313.13	14.08	0.09	343.23	28.84	0.16
318.05	15.89	0.14			
		Acetonitrile			
293.21	2.211	0.002	323.11	4.203	0.055
298.23	2.482	0.041	328.13	4.634	−0.007
303.15	2.683	−0.017	333.23	5.205	−0.006
308.11	2.988	−0.007	338.17	5.849	0.012
313.07	3.333	0.004	342.75	6.538	0.046
317.95	3.749	0.048			
		Acetone			
293.25	14.97	0.03	312.79	17.84	0.19
298.25	15.50	0.02	318.03	18.58	−0.10
303.09	16.04	−0.06	323.07	19.89	0.08
308.05	16.77	−0.07	327.37	20.85	−0.04
		Ethyl Acetate			
293.07	5.739	0.025	323.49	8.603	0.061
298.49	6.172	0.044	328.61	9.180	0.025
303.41	6.429	−0.105	333.53	9.851	0.061
308.49	6.972	−0.015	338.23	10.45	0.01
313.53	7.468	−0.003	343.33	11.11	−0.09
318.67	7.986	−0.018			
		Water			
293.23	1.388	0.010	322.85	3.662	−0.016
298.15	1.582	−0.024	327.77	4.376	−0.003
302.93	1.868	−0.004	332.83	5.216	−0.037
293.23	1.388	0.026	337.35	6.232	0.039
312.93	2.631	0.021	342.47	7.483	0.004
317.65	3.057	−0.011			

Table 2. Parameters of Equation 2 for Thiotriazinone in Different Solvents

solvent	a	b	c	10^3 rmsd
ethanol	−106.20	3082.0	16.073	0.218
1-propanol	−100.82	2471.7	15.425	0.098
2-propanol	−8.4256	−2368.5	1.9925	0.142
1-butanol	−90.965	2013.9	13.967	0.150
acetonitrile	−141.60	4507.8	21.140	0.094
acetone	−159.03	6322.8	23.458	0.096
ethyl acetate	−70.174	1915.2	10.294	0.055
water	−239.98	8030.3	36.263	0.021

results is also presented in Table 1. The values of the three parameters a, b, and c together with the root-mean-square deviations (rmsd) are listed in Table 2. The rmsd is defined as follows:

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

where N is the number of experimental points, $x_{1,j}^{\text{calc}}$ is the solubility calculated from eq 2, and $x_{1,j}$ is the experimental value of solubility.

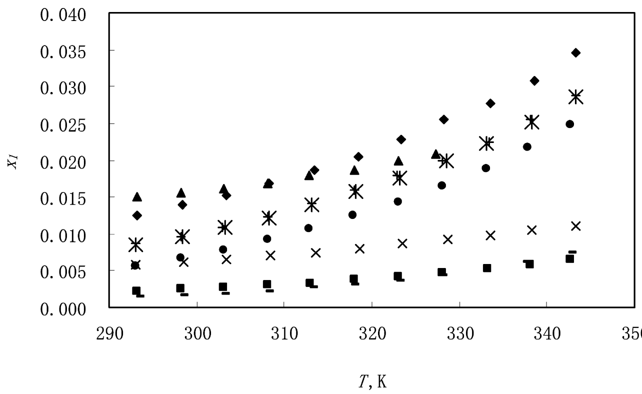

Figure 2. Solubility of thiotriazinone in eight solvents: ◆, ethanol; ■, acetonitrile; ▲, acetone; ×, ethyl acetate; *, 1-propanol; ●, 2-propanol; +, 1-butanol; —, water.

From Table 1, Table 2, and Figure 2, we could elicit the conclusions: (1) The solubility of thiotriazinone in these solvents increased with temperature, but the increment with temperature varied according to different solvents. (2) When the temperature was under 310 K, thiotriazinone dissolved much more in acetone than in other seven solvents. When the temperature was higher than 310 K, the solubility of thiotriazinone was the highest in ethanol. The solubility of thiotriazinone was the lowest in water. (3) All the experimental data could be regressed by eq 2 for these eight solvents. The experimental solubility and correlation equation in this work could be used as essential models in the manufacturing and purifying processes of thiotriazinone in industry.

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