Solubility of D-(*p*-Hydroxy)phenylglycine in Water + 2-Propanol from (293 to 343) K

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The solubility of D-(*p*-hydroxy)phenylglycine in binary 2-propanol + water was measured using a synthetic method with a laser-assisted observation of a solute dissolution in the temperature range from (293 to 343) K and mole fraction (x_2^o) range of 0.0000 to 0.5451. The results were correlated with a semiempirical equation.

Introduction

D-(*p*-Hydroxy)phenylglycine (CAS registry no. 22818-40-2) is a white or almost white crystalline powder and a useful chemical for preparation of semisynthetic penicillins and cephalosporins. To determine the proper solvent and to design an optimized crystallization process, it is necessary to know its solubility in different solvents. From a review of the literature on D-(*p*-hydroxy)phenylglycine, it was found that some experimental solubility data in water + 1-butanol at 298.15 K were available.[1] The solubility in water, methanol, ethanol, carbon tetrachloride, toluene, and *N*,*N*-dimethylformamide between (278 and 323 K) is available.[2] In this article, the solubility of D-(*p*-hydroxy)phenylglycine in water + 2-propanol from (293 to 343) K was determined using a synthetic method with a laser-assisted observation of a solute dissolution at atmospheric pressure. The method employed in this work was classified as a synthetic method, which was much faster and more reliable than the analytical method.[3] For the solubility of D-(*p*-hydroxy)-phenylglycine in water at 318.17 K, there is a 2.5 % difference between data in this article and those in reference 2, which shows that the measurement method is more reliable.

Experimental Section

Materials. A white crystalline powder of D-(*p*-hydroxy)phenylglycine, purchased from Shijiazhuang Pharmaceutical Group (CSPC) was prepared by recrystallization from solution of water three times. Its mass fraction purity determined by HPLC was greater than 0.994. 2-Propanol was an analytical research grade reagent from Beijing Chemical Reagent.

Apparatus and Procedures. The solubility of D-(*p*-hydroxy)phenylglycine was measured using an apparatus that is similar to that described in literature[2,4−9] and is described briefly here. A 500 mL jacked vessel was used to determine the solubility; the temperature was controlled to be constant (fluctuates within 0.05 K) by a thermostat water bath. The dissolution of the solute was examined by the laser beam penetrating the vessel. To prevent evaporation of the solvent, a condenser vessel was introduced. The mass of the samples and solvents was determined using an analytical balance (Sartorius CP224S, Germany) with an uncertainty of ± 0.0001 g. During the experiments, predetermined excess amounts of solvent and D-(*p*-hydroxy)phenylglycine of a known mass were placed in the inner chamber of the vessel. The contents of the vessel were stirred continuously at a constant temperature. In the early stage of the experiment, the laser beam was blocked by the undissolved particles of D-(*p*-hydroxy)phenylglycine in the solution, so the intensity of laser beam penetrating the vessel was lower. As the dissolution of the particles of solute occurred, the intensity of the laser beam gradually increased. When the solute dissolved completely, the solution was clear and the laser intensity reached a maximum. Then, additional solute of a defined mass (about (0.1 to 5) mg) was introduced to the vessel. This procedure was repeated until the penetrated laser intensity could not return to a maximum; in other words, the last addition of solute could not dissolve completely. The interval of addition was 90 min. The total amount of 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) on the basis of eq 1. The composition of solvent mixture (x_2^o) is defined as eq 2

$$x_1 = \frac{m_1/M_1}{m_1/M_1 + m_2/M_2 + m_3/M_3} \tag{1}$$

$$x_2^o = \frac{m_2/M_2}{m_2/M_2 + m_3/M_3} \tag{2}$$

where m_1, m_2, and m_3 represent the mass of the solute, 2-propanol and water, respectively, and M_1, M_2, and M_3 represent the molecular weight of the solute, 2-propanol, and water, respectively.

Results and Discussion

The solubility of D-(*p*-hydroxy)phenylglycine in the mixture of water and isopropanol at different temperatures is shown in Table 1. The relationship between temperature and solubility of the D-(*p*-hydroxy)phenylglycine is correlated with a semiempirical equation[9]

$$\ln x_1 = a + \frac{b}{T/\mathrm{K}} + c \ln(T/\mathrm{K}) \tag{3}$$

where T is the absolute temperature and a, b, and c are empirical constants. The difference between experimental and calculated results is also presented in Table 1. The values of the three parameters a, b, and c together with the root-mean-square

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Table 1. Mole Fraction Solubility of D-(*p*-Hydroxy)phenylglycine (1) in the Mixture of 2-Propanol (2) and Water (3) in the Temperature Range of (293 to 343) K

T/K	$10^3(x_1)$	$10^3(x_1 - x_1^{calcd})$	T/K	$10^3(x_1)$	$10^3(x_1 - x_1^{calcd})$
		$x_2^o = 0.0000$			
293.25	1.960	−0.002	323.15	2.982	0.024
298.13	2.101	0.007	328.11	3.187	0.014
303.15	2.237	−0.003	333.15	3.439	0.028
308.18	2.407	0.007	338.16	3.663	−0.002
313.15	2.548	−0.022	343.15	3.910	−0.030
318.17	2.718	−0.039			
		$x_2^o = 0.0322$			
293.25	1.631	0.005	323.15	2.592	−0.005
298.12	1.753	0.002	328.13	2.831	0.015
303.15	1.899	0.008	333.15	3.076	0.018
308.11	2.043	0.000	338.16	3.330	0.009
313.05	2.216	0.007	343.05	3.601	−0.001
318.19	2.402	0.004			
		$x_2^o = 0.0697$			
293.19	1.343	−0.009	323.12	2.246	−0.036
298.17	1.457	−0.016	328.13	2.493	−0.001
303.15	1.652	0.046	333.07	2.724	0.002
308.14	1.731	−0.022	338.18	2.982	0.001
313.11	1.929	0.017	343.15	3.259	0.003
318.19	2.079	−0.012			
		$x_2^o = 0.1138$			
293.25	1.090	0.015	323.25	2.004	0.004
298.13	1.187	−0.015	328.16	2.192	0.007
303.15	1.339	−0.002	333.07	2.417	0.036
308.16	1.490	0.000	338.16	2.590	−0.003
313.11	1.634	−0.013	343.14	2.786	−0.025
318.12	1.824	0.008			
		$x_2^o = 0.1665$			
293.18	0.862	−0.012	322.85	1.645	−0.007
298.17	0.991	0.005	328.17	1.819	0.001
303.12	1.125	0.020	332.75	1.928	−0.040
308.13	1.236	0.003	338.12	2.152	0.003
312.98	1.361	−0.003	342.85	2.345	0.030
318.18	1.514	0.002			
		$x_2^o = 0.2305$			
293.25	0.667	−0.009	323.15	1.259	−0.026
298.11	0.762	0.005	328.16	1.421	0.007
303.15	0.858	0.010	333.15	1.541	−0.010
308.16	0.952	0.006	338.16	1.699	0.002
313.15	1.047	−0.004	343.15	1.863	0.012
318.12	1.171	0.008			
		$x_2^o = 0.3100$			
293.24	0.506	0.000	323.15	0.940	−0.003
298.17	0.562	−0.003	328.18	1.029	−0.005
303.15	0.640	0.009	333.13	1.152	0.022
308.13	0.695	−0.006	338.13	1.238	0.006
313.25	0.774	−0.004	343.15	1.325	−0.015
318.17	0.854	−0.003			
		$x_2^o = 0.4114$			
293.25	0.340	−0.002	323.14	0.570	−0.010
298.12	0.375	0.002	328.16	0.645	0.011
303.17	0.416	0.008	333.15	0.699	0.008
308.16	0.442	−0.004	338.16	0.760	0.006
313.15	0.488	0.001	343.16	0.812	−0.009
318.12	0.525	−0.006			
		$x_2^o = 0.5451$			
293.25	0.194	0.000	323.14	0.323	0.000
298.17	0.213	0.000	328.12	0.346	−0.001
303.14	0.234	0.000	333.15	0.371	0.000
308.16	0.255	0.000	338.11	0.396	0.000
313.15	0.277	0.000	343.12	0.421	0.000
318.16	0.300	0.000			

Table 2. Parameters of Equation *3* for D-(*p*-Hydroxy)phenylglycine (1) in Binary 2-Propanol (2) + Water (3) Solvent Mixtures in the Temperature Range of (293 to 343) K

x_2^o	a	b	c	10^4(rmsd)
0.0000	−78.976	2228.1	11.467	0.21
0.0322	−91.609	2642.4	13.409	0.09
0.0697	−84.012	2139.9	12.341	0.22
0.1138	16.333	−2714.1	−2.4490	0.16
0.1665	43.122	−4005.1	−6.4257	0.18
0.2305	2.9027	−2185.9	−0.4838	0.11
0.3100	5.1329	−2248.2	−0.8900	0.10
0.4114	−68.656	1360.3	9.8639	0.07
0.5451	36.097	−3405.0	−5.8146	0.00

deviations (rmsd) are listed in Table 2. The rmsd is defined as follows

$$\text{rmsd} = \left[\frac{\sum_{j=1}^{N}\left(x_{1,j} - x_{1,j}^{\text{calcd}}\right)^2}{N-1}\right]^{1/2} \quad (4)$$

where N is the number of experimental points, $x_{1,j}^{\text{calcd}}$ is the solubility calculated from eq 3, and $x_{1,j}$ is the experimental value of solubility.

From Table 1 and Table 2, we can draw the following conclusions: (1) The solubilities of D-(*p*-hydroxy)phenylglycine in mixture of water and 2-propanol increase with the increase in temperature. (2) The solubilities of D-(*p*-hydroxy)phenylglycine decrease with the increase in 2-propanol in the mixture. (3) All of the experimental data can be regressed by eq 3 for each solvent mixture. The experimental solubility and correlation equation in this work can be used for modeling the solubility of D-(*p*-hydroxy)phenylglycine in a production process.

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