Solubility of Adenosine 5′-Monophosphate in Different Solvents from (288.15 to 330.15) K

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The solubilities of adenosine 5′-monophosphate (AMP) in water, methanol, ethanol, and acetic acid between (288.15 and 330.15) K were measured using a laser monitoring observation technique. Results of these measurements were correlated with a modified Apelblat equation, which can be used as a useful model in the crystallization process of AMP.

Introduction

Adenosine 5′-monophosphate (AMP, $C_{10}H_{14}N_5O_7P$, molecular weight of 347.2, CAS RN 61-19-8) is a white crystalline powder. In the fields of food, medicine, and fine chemistry industries, it has been widely used.[1−3]

In the purification and crystallization process of AMP, it is necessary to know the solubility data of AMP in different solvents. In this paper, the solubilities of AMP in methanol, ethanol, acetic acid, and water were experimentally determined in the temperature range from (288.15 to 330.15) K at atmospheric pressure, which were helpful to optimize the purification and crystallization process of AMP. The method employed in this work was classed as a synthetic method, which was much faster and more reliable than the analytical method.[4]

Experimental Section

A white crystalline powder of AMP was purchased from the National Engineering Research Center for Biotechnology (NER-CB) of China. Its moisture content was about 4.7 % (wt %, compared with standard sample by high-performance liquid chromatography, HPLC). After being heated up for 24 h at 353 K to remove water, the mass fraction purity of the powder determined by HPLC was 99.16 %. A digital thermometer at a precision of 0.01 K was used to measure the internal temperature of the vessel. The masses of the samples and solvents were weighed using a digital analytical balance (Sartorius BS110S, Germany) at a precision of 0.0001 g.

Solubility was determined by a synthetic method.[5,6] First, predetermined known masses of AMP and solvent were transferred in the glass vessel. Then, the contents of the vessel were stirred. A laser monitoring technique has been used to measure the solubilities of AMP in different solvents at a constant temperature. During the measuring process, the fluid in the glass vessel was monitored by a laser beam. The intensity of the laser beam penetrating the vessel was low at beginning because the laser beam was blocked by the undissolved solids of AMP in the solution. When the last portion of solids disappeared, the intensity of the laser beam penetrating the vessel reached its maximum. An additional solute of known mass (1 to 5 mg) was introduced into the vessel repeatedly until the last addition of solute could not dissolve completely. Then, in methanol and ethanol experiments, an additional solvent of known volume (1 mL) was introduced into the vessel repeatedly until the last addition of solute could dissolve completely. The total amounts of the solute and solvent consumed were obtained. The mean values were used to calculate the mole fraction solubility x_1 based on

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

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 estimated uncertainty of the solubility values based on error analysis and repeated observations was within 1.0 %.

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Table 1. Mole Fraction Solubility of AMP, x_1, in Different Solvents from (288.15 to 330.15) K

T/K	$10^6\ x_1$	$10^6\ x^{calcd}$	T/K	$10^6\ x_1$	$10^6\ x^{calcd}$
	Water			Methanol	
288.20	257.4	261.3	288.15	8.592	8.532
294.20	336.2	331.9	294.15	9.353	9.403
300.20	412.5	416.7	300.15	10.42	10.40
306.20	526.0	517.7	306.15	11.46	11.55
312.20	635.6	636.6	312.15	12.97	12.86
318.20	768.0	775.4	318.15	14.06	14.36
324.20	933.7	936.1	324.15	16.49	16.07
			330.15	17.86	18.03
	Ethanol			Acetic Acid	
288.15	5.297	5.199	288.15	78.48	73.36
294.15	5.609	5.853	294.15	122.4	119.8
300.15	6.748	6.679	300.15	185.6	186.9
306.15	7.729	7.716	306.15	276.0	279.5
312.15	9.235	9.014	312.15	394.6	402.0
318.15	10.62	10.64	318.15	564.2	557.4
324.15	12.42	12.68	324.15	749.6	746.9
330.15	15.36	15.24	330.15	967.0	969.4

Results and Discussion

The solubilities (mole fraction) of AMP in water, methanol, ethanol, and acetic acid from (288.15 to 330.15) K were listed in Table 1 and presented more visually in Figure 1.

The results were correlated with a modified Apelblat equation[7,8] as follows

$$\ln x_1 = A + \frac{B}{T/\mathrm{K}} + C \ln(T/\mathrm{K}) \tag{2}$$

where T is the absolute temperature and A, B, and C are empirical constants.

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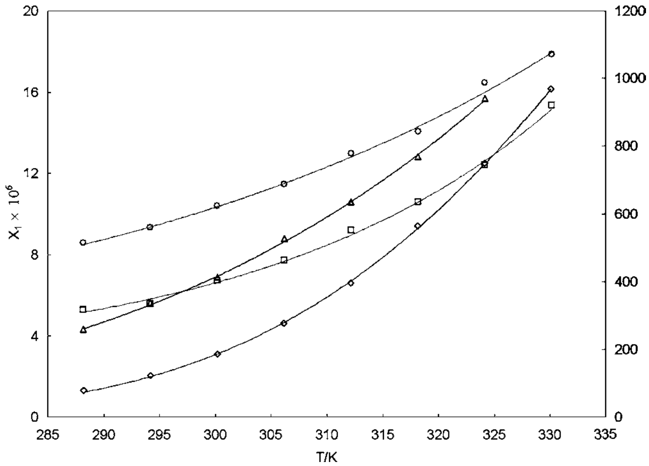

Figure 1. Mole fraction solubility of AMP, x_1, in different solvents: △, water; ◇, acetic acid; ○, methanol; □, ethanol; and calculated data by the Apelblat equation to different solvents in solid lines.

Table 2. Parameters of Equation 1 for AMP in Different Solvents

solvent	*A*	*B*	*C*	10^6 rmsd
water	34.659	−4739.3	−3.2389	5.50
methanol	−130.10	4100.5	13.034	0.21
ethanol	−301.78	11313	30.922	0.17
acetic acid	438.50	−25320	−43.796	4.79

Equation 1 is simplified for eq 3[9]

$$\ln x_1 = \left[\frac{\Delta H_{f,1}}{RT_{f,1}} + \frac{\Delta Cp_{f,1}}{R}(1 + \ln T_{f,1}) - A\right] - \left[B + \left(\frac{\Delta H_{f,1}}{RT_{f,1}} + \frac{\Delta C_{pf,1}}{R}\right)T_{f,1}\right]\frac{1}{T} - \frac{\Delta C_{pf,1}}{R}\ln T \quad (3)$$

where x_1, $\Delta H_{f,1}$, $\Delta C_{pf,1}$, $T_{f,1}$, R, and T stand for the mole fraction of the solute, the enthalpy of fusion, the difference in the solution heat capacity between the solid and liquid at the melting temperature, the melting temperature of the solute, the gas constant, and the equilibrium temperature in the saturated solution, respectively, and A and B stand for empirical constants.

The differences between experimental and calculated results are presented in Table 1. The values of three parameters, A, B, and C, together with the root-mean-square deviations (rmsd's) in eq 4 are listed in Table 2. The rmsd is defined as

$$\text{rmsd} = \sqrt{\frac{\sum_{i=1}^{N}(x_{1,i} - x_{1,i}^{calcd})^2}{N - 1}} \quad (4)$$

where N is the number of experimental points, $x_{1,i}^{calcd}$ is the solubility calculated from the Apelblat model, and $x_{1,i}$ is the experimental value of solubility.

From Table 1 and Figure 1, we could draw the following conclusions: (i) The solubility of AMP increases with temperature in water, methanol, ethanol, and acetic acid. The solubility of AMP is lowest in ethanol and the largest in water. (ii) The experimental solubility and correlation equation in this work can be used as essential data and models in the purification and crystallization process of AMP. The solubility calculated by eq 2 shows good agreement with experimental values.

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