Solubility of Isonicotinic Acid in 4-Methylpyridine + Water from (287.65 to 361.15) K

Liu-Cheng Wang,* Hui Ding, Jian-Hong Zhao, Cheng-Ying Song, and Jian-She Wang

College of Chemical Engineering, Zhengzhou University, Zhengzhou, Henan 450001, People's Republic of China

To provide thermodynamic data for isonicotinic acid production, the solubilities of isonicotinic acid in water and 4-methylpyridine binary solvent mixture were determined from (287.65 to 361.15) K with the solvent mole fraction composition ranging from 0.00 to 1.00. The experimental data were correlated with the modified Apelblat equation. The calculated results show good agreement with the experimental data.

Introduction

Isonicotinic acid is an important intermediate in the synthesis of anti-TB drugs and can also be used as an anticorrosion reagent, plating additive, and photosensitive resin stabilizer.[1] It is manufactured through several chemical methods including potassium permanganate oxidation, air oxidation, and ozone oxidation.[2] An alternative method is the electrolytic method using 4-methylpyridine as the raw material and aqueous sulfuric acid solution as the supporting electrolytes. The reaction conditions are mild, giving high product purity, reducing waste, and nonpolluting.[3] In the synthesis and purification process of isonicotinic acid, it is necessary to know the solubility of the acid in the related solvents, but the solubility data which have been reported are only in water.[4] In this study, the solubilities of isonicotinic acid in water and 4-methylpyridine binary solvent have been measured from (287.65 to 361.15) K at atmospheric pressure.

Experimental Section

Materials. Analytical grade isonicotinic acid obtained from the Shanghai Huixing Biochemical Reagents Co. Ltd. was further purified by recrystallization, and its purity was determined by UV spectrophotometry (type UV-2401PC, Shimadzu Co. Ltd.) to be 0.99 in mass fraction. 4-Methylpyridine from the Shanghai Chemical Reagent Co. was purified by distillation, and the mass fraction was determined by gas chromatography (type GC2010 Shimadzu Co. Ltd., DB-1 capillary column with a FIDdetector) to be 0.995. The water used in the experiments was double-distilled water.

Apparatus and Procedure. The solubilities were measured by a dynamic method at atmospheric pressure.[5−7] The experiment was carried out in a magnetically stirred, jacketed glass vessel (60 cm^3). A constant temperature (± 0.02 K) was maintained by circulating water through the outer jacket from a thermostatically controlled water bath (Shanghai Laboratory Instrument Works Co. Ltd.) at the required temperature. A condenser was upright 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. Solvents for the solubility measurement were prepared by mass using an analytical balance (type AW120, Shimadzu Co.). The balance has a range of measurement up to 120 g, with an uncertainty of ± 0.0001 g. Predetermined amounts of isonicotine acid were weighed and transferred into the vessel. The contents of the vessel were heated very slowly at rates less than 2 $K \cdot h^{-1}$ with continuous stirring. In the early stage of the experiment, there were a lot of undissolved particles in the mixture, so the solution was turbid, and with increasing temperature, the color of the solution gradually shallowed. At the end of dissolution, the temperature was recorded as the liquidus temperature. In the process of solubility measurement, some of the solubility experiments were conducted two or three times to check the reproducibility. The reproducibility of the measurements was 0.1 K, which corresponds to a relative error in composition smaller than ± 1 %. To verify the reliability of the measurement, the solubilities of isonicotinic acid in water were measured, and the results are shown in Figure 1. In Figure 1, T is the absolute temperature and x is the experimental solubility in mole fraction. It is clear from Figure 1 that our experimental results show good agreement with literature data.[4] Compared with the literature data, the deviations of the solubility are less than 2.0 %.

* Corresponding author. E-mail: wanglc@zzu.edu.cn.

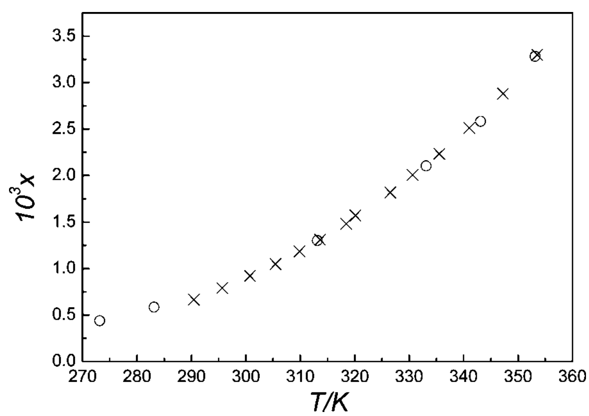

Figure 1. Solubility of isonicotinic acid in water: ○, literature data; ×, experimental data.

Results and Discussion

The measured mole fraction solubilities (x) of isonicotinic acid in 4-methylpyridine + water at different temperatures (T) are presented in Table 1. The mass fraction (w) of 4-methylpyridine in the solvents is 0, 0.10, 0.20, 0.40, 0.60, 0.80, and 1.00,

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Table 1. Mole Fraction Solubilities (x) of Isonicotinic Acid in (w) 4-Methylpyridine + (1 − w) Water, Where w is the Mass Fraction

T/K	10^2x	10^2x_c	T/K	10^2x	10^2x_c
		$w = 0.00$			
290.45	0.06648	0.03393	320.15	0.1572	0.1554
295.65	0.07914	0.07872	326.55	0.1820	0.1820
300.75	0.09214	0.09171	330.65	0.2006	0.2005
305.45	0.1049	0.1050	335.55	0.2234	0.2243
309.85	0.1185	0.1186	341.05	0.2512	0.2532
313.65	0.1311	0.1314	347.25	0.2881	0.2886
318.45	0.1482	0.1489	353.55	0.3300	0.3277
		$w = 0.10$			
287.95	1.414	1.432	333.45	1.724	1.732
295.25	1.491	1.475	338.55	1.760	1.769
305.75	1.551	1.541	343.05	1.795	1.804
311.45	1.584	1.578	348.45	1.840	1.845
317.05	1.618	1.616	353.55	1.887	1.886
322.35	1.653	1.652	361.55	1.967	1.951
327.75	1.687	1.690			
		$w = 0.20$			
292.85	2.491	2.497	332.55	2.825	2.828
302.95	2.573	2.568	338.85	2.886	2.893
309.15	2.620	2.616	344.45	2.947	2.954
314.25	2.659	2.658	350.05	3.018	3.017
318.65	2.698	2.696	356.05	3.091	3.088
324.85	2.757	2.753	361.35	3.158	3.153
		$w = 0.40$			
292.65	3.705	3.716	329.75	4.179	4.187
299.15	3.786	3.777	335.85	4.283	4.291
306.25	3.859	3.855	341.75	4.390	4.398
311.55	3.921	3.920	347.25	4.501	4.505
316.95	3.999	3.992	352.95	4.625	4.622
323.05	4.087	4.081	357.85	4.736	4.727
		$w = 0.60$			
287.65	3.419	3.454	325.65	4.620	4.276
290.55	3.497	3.502	330.75	4.399	4.420
296.35	3.638	3.606	336.05	4.554	4.577
302.55	3.767	3.727	341.15	4.726	4.738
310.15	3.891	3.890	346.05	4.897	4.900
314.25	3.996	3.985	350.95	5.083	5.071
320.25	4.124	4.134	355.35	5.260	5.232
		$w = 0.80$			
294.05	2.468	2.484	328.25	3.838	3.846
297.35	2.603	2.589	334.35	4.159	4.160
302.15	2.752	2.752	340.45	4.483	4.501
306.75	2.920	2.918	346.05	4.845	4.838
311.55	3.116	3.1031	352.35	5.254	5.248
317.75	3.365	3.359	358.55	5.689	5.684
322.15	3.545	3.555			
		$w = 1.00$			
299.65	2.326	2.312	333.45	4.410	4.436
303.55	2.479	2.509	338.25	4.820	4.820
306.65	2.682	2.674	343.85	5.286	5.295
311.65	2.955	2.957	349.35	5.782	5.793
316.25	3.248	3.235	354.65	6.305	6.302
322.25	3.627	3.624	359.35	6.791	6.777
327.45	4.010	3.987			

respectively. The temperature dependence of isonicotinic acid solubility at fixed solvent composition is described by the modified Apelblat equation[8−10]

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

where x is the mole fraction solubility of isonicotinic acid; 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 deviations (rmsd's) are listed in Table 2. The rmsd is defined as

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

where N is the number of experimental points and x_c is the solubility calculated by eq 1. 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 isonicotinic acid in 4-methylpyridine + water. The overall rmsd of 91 data points for the 4-methylpyridine + water system at various contents of isonicotinic acid in the mixed solvent is $1.12 \cdot 10^{-4}$. The experimental solubility and correlation equation in this work can be used as essential data and models to serve the synthesis and purification process of isonicotinic acid.

By using the data shown in Table 1, the dependence of the solubilities x calculated from eq 1 and values of A, B, and C on the mass fraction w of 4-methylpyridine in solvent for the isonicotinic acid + 4-methylpyridine + water system are given in Figure 2. It showed the relations between the solubility and the composition of the mixed solvent at fixed temperatures, and from the results shown in Table 1 and Figure 2, it can be seen that the solubility of isonicotinic acid in 4-methylpyridine + water is higher than that in water and 4-methylpyridine. It also can be seen from Figure 2 that with a temperature increase from (295 to 345) K, the maximum of every curve increases from 40 % to 60 %. According to Scatchard−Hildebrand's theory,[11,12] the solubility of the solute in the solvent is the largest when the solubility parameters of the solute and the solvent are the same. For the binary solvent of A and B, it is possible that the solubility is the maximum when the parameter meets the following relationship, $\delta_A < \delta_1 < \delta_B$. The values of the solubility parameter of isonicotinic, 4-methylpyridine, and water are 24.4 (calculated by the Fedors group contribution method[13,14]), 20.9, and 47.9, respectively, so the solubility of isonicotinic acid may be the maximum in the binary solvent of 4-methylpyridine and water. It shows good agreement with the results of the experiment.

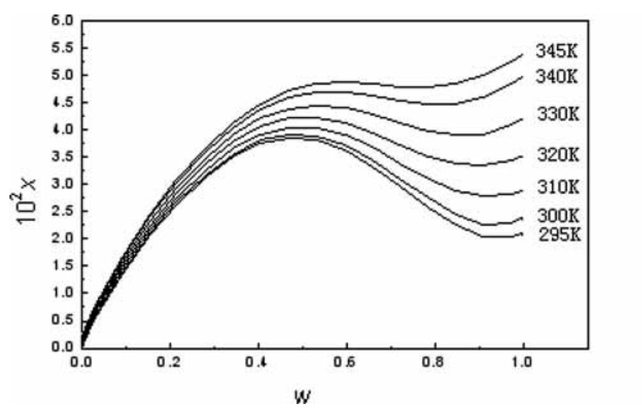

Figure 2. Dependence of the solubilities x calculated from eq 1 and values of A, B, and C at (295 to 345) K on the mass fraction (w) of 4-methylpyridine in solvent for 4-methylpyridine + water.

Table 2. Parameters of Equation 1 for the Isonicotinic Acid + 4-Methylpyridine + Water System at Various Contents of 4-Methylpyridine (w) in the Mixed Solvent

w	A	B	C	10^4(rmsd)
0.0	25.3437	−3706.99	−3.50757	0.10
0.1	−22.6218	506.981	2.93404	0.97
0.2	−31.4529	1026.39	4.27102	0.45
0.4	−42.9838	1566.65	6.04647	0.69
0.6	−52.4856	1790.80	7.57617	2.1
0.8	−58.5235	1485.75	8.75750	0.98
1.0	−5.09073	−1563.78	1.14726	1.5

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