Solubilities of Sulfamethazine, Sulfadimethoxine, Sulfamethoxydiazine, Sulfamonomethoxine, Sulfamethoxazole, and Sulfaquinoxaline in 1-Octanol from (298.15 to 333.15) K

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The solubilities of sulfamethazine, sulfadimethoxine, sulfamethoxydiazine, sulfamonomethoxine, sulfamethoxazole, and sulfaquinoxaline in 1-octanol have been determined from (298.15 to 333.15) K. The experimental data were correlated with the modified Apelblat equation.

Introduction

Sulfonamides are a group of synthetic organic drugs derived chiefly from sulfanilamide that are widely used in agriculture to prevent diseases in livestock and treat illness; therefore, soil and groundwater body have been badly contaminated. The 1-octanol solubility plays a prominent role in the prediction of the environmental fate of chemicals and can characterize transportation through membranes and the topical activity of drugs.[1] In determining the transport of sulfonamides in the environment and assessing their risk to terrestrial and aquatic ecosystems, it is necessary to know their solubilities in 1-octanol. However, only a limited amount of solubility data for sulfonamides has been reported from (298.15 to 313.15) K.[2,3] In this study, solubilities of six sulfonamides in 1-octanol have been measured from (298.15 to 333.15) K. The experimental data were correlated with the modified Apelblat equation.[4−6]

Experimental Section

Materials. Sulfonamides: sulfamethazine, sulfadimethoxine, sulfamethoxydiazine, sulfamonomethoxine, sulfamethoxazole, and sulfaquinoxaline obtained from Daming Biotech. were further purified by recrystallization from aqueous solutions. After filtration and drying, their purity was determined by UV spectrometry (type UV-2401PC, Shimadzu) to be 0.996 in mass fraction. 1-Octanol was obtained from Tianjin Kermel Chemical Reagent (China) and used without any further purification.

Apparatus and Procedure. The solubility was measured by a static equilibrium method.[7] Nearly 100 mg of each sulfonamide was added separately to 50 mL of 1-octanol in glass flasks. The mixtures were then stirred in a mechanical shaker for 1 h. Samples were then allowed to stand in water baths (type 501, Shanghai Laboratory Instrument Works) kept at the appropriate temperature (± 0.02 K). The equilibration of other sulfonamides has been reported to be achieved after 30 h.[3] Therefore, in this work, the initial equilibration time of the saturated solution was 72 h; then, it was analyzed once every 5 h until the analyzing results were replicated three consecutive times. After this time, the supernatant solutions were filtered to ensure that they were free of particulate matter before sampling. We determined concentrations by measuring UV absorbances after appropriate dilution and interpolation from previously constructed calibration curves for each sulfonamide. To permit conversion between molarity and mole-fraction concentration scales, the density of the saturated solutions was determined with a digital density meter. All of the solubility experiments were repeated at least three

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Table 1. Mole Fractions Solubilities (x) of Some Sulfonamides in 1-Octanol Compared with Literature Data

system	T/K	$10^5 x_{exptl}$	$10^5 x_{ref}$	100RD
sulfamethazine + 1-octanol	298.15	25.30	25.29[2]	0.040
	303.15	29.60	29.81[2]	−0.70
	308.15	33.76	33.39[2]	1.11
sulfamethoxazole + 1-octanol	298.15	96.45	96.91[3]	−0.47

Table 2. Solubility Data of Six Sulfonamides in 1-Octanol and the Regression Results Obtained Using the Modified Apelblat Equation

T/K	$10^5 x$	100RD	T/K	$10^5 x$	100RD
sulfamethazine + 1-octanol					
298.15	25.30	−0.57	318.15	42.73	−0.51
303.15	29.60	0.82	323.15	47.83	−0.41
308.15	33.76	0.48	328.15	53.87	1.0
313.15	37.96	−0.46	333.15	58.66	−0.32
sulfadimethoxine + 1-octanol					
298.15	16.72	−0.064	318.15	23.48	−0.035
303.15	17.96	0.11	323.15	26.12	−0.15
308.15	19.41	−0.15	328.15	29.36	−0.025
313.15	21.32	0.23	333.15	33.24	0.076
sulfamethoxydiazine + 1-octanol					
298.15	8.803	−0.060	318.15	11.52	0.040
303.15	9.418	0.054	323.15	12.31	−0.11
308.15	10.07	0.065	328.15	13.19	−0.010
313.15	10.76	−0.030	333.15	14.13	0.051
sulfamonomethoxine + 1-octanol					
298.15	7.923	0.35	318.15	11.26	0.23
303.15	8.677	−0.48	323.15	12.02	−0.34
308.15	9.525	−0.32	328.15	12.91	0.31
313.15	10.44	0.42	333.15	13.63	−0.18
sulfamethoxazole + 1-octanol					
298.15	96.45	0.0027	318.15	156.4	0.023
303.15	112.9	0.053	323.15	167.06	0.058
308.15	128.6	−0.11	328.15	174.6	−0.052
313.15	143.5	0.024	333.15	179.5	0.0040
sulfaquinoxaline + 1-octanol					
298.15	9.116	0.018	318.15	15.38	0.010
303.15	10.68	−0.049	323.15	16.78	−0.014
308.15	12.29	0.050	328.15	18.04	0.027
313.15	13.86	−0.028	333.15	19.10	−0.014

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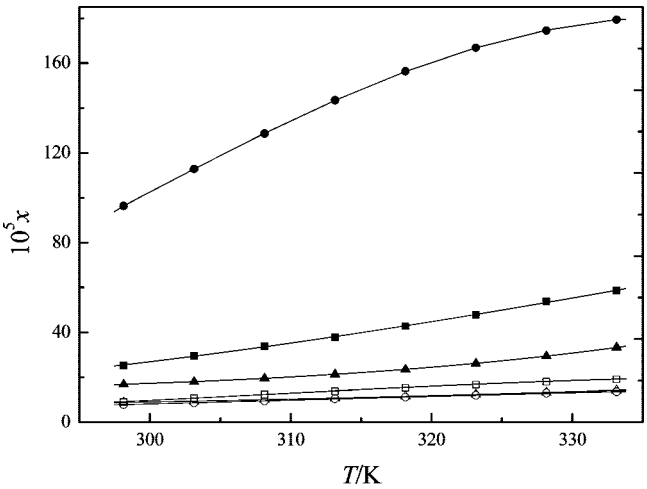


Figure 1. Solubilities of sulfonamides in 1-octanol: ■, sulfamethazine + 1-octanol; ▲, sulfadimethoxine + 1-octanol; △, sulfamethoxydiazine + 1-octanol; ○, sulfamonomethoxine + 1-octanol; ●, sulfamethoxazole + 1-octanol; □, sulfaquinoxaline + 1-octanol; —, calculated from eq 1.

Table 3. Parameters in the Modified Apelblat Equation for Different Systems

system	*A*	*B*	*C*	100ARD
sulfamethazine + 1-octanol	98.779	−7000.2	−14.669	0.026
sulfadimethoxine + 1-octanol	−324.25	13075	47.687	0.0028
sulfamethoxydiazine + 1-octanol	−70.535	1723.9	9.7261	0.00067
sulfamonomethoxine + 1-octanol	108.62	−6818.0	−16.709	0.0035
sulfamethoxazole + 1-octanol	504.30	−25331	−74.819	0.0075
sulfaquinoxaline + 1-octanol	361.79	−19079	−53.900	0.00039

times, and the mean values were considered to be the measured results. The uncertainty of temperature measurements was ± 0.05 K. The reproducibility of temperature measurements was 0.1 K, which corresponds to a relative deviation in composition smaller than 1 %. The results showed that the deviations in the measured solubility from the literature values[2,3] were less than 2 %. Therefore, the reliability of the experimental apparatus was verified.

Results and Discussion

The solubilities of sulfamethazine and sulfamethoxazole in 1-octanol listed in Table 1 are measured, respectively, to complete the data reported in literature.[2,3]

The temperature dependence of sulfonamide solubility in 1-octanol has been described by the modified Apelblat equation[4−6]

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

where x is the mole fraction of sulfonamide, T is the absolute temperature, and A, B, and C are constants determined by least-square analysis. The values of these parameters are listed in Table 3. The relative deviations between the experimental and calculated values are also listed in Table 2. The relative deviations (RD values) are calculated according to

$$\mathrm{RD} = \left(\frac{x - x_c}{x}\right) \tag{2}$$

The average relative deviations for each system in this study are also listed in Table 3. The average relative deviations (ARD values) are calculated according to

$$\mathrm{ARD} = \frac{1}{N}\sum_{i=1}^{N}\left|\frac{x_i - x_{ci}}{x_i}\right| \tag{3}$$

The data in Tables 2 and 3 indicate that the calculated solubilities show good agreement with the experimental data, which demonstrates that the modified Apelblat equation can be used to correlate the solubility data of sulfamethazine, sulfadimethoxine, sulfamethoxydiazine, sulfamonomethoxine, sulfamethoxazole, and sulfaquinoxaline in 1-octanol. The relative deviations among 48 data points for the studied systems do not exceed 1.0 %, and the total average relative deviation is 0.19 %.

By using the data shown in Table 2, we plotted the solubility curves for the studied systems in Figure 1. It is evident that the solubility of each sulfonamide in 1-octanol is low.

According to a pseudochemical reaction process,[8−10] the dissolution process of solid, S, in liquid, W, can be expressed as S + W = SW; the relationship of its dissolution equilibrium constants and activities can be expressed as

$$K_i = \frac{a_i}{a_s a_w} \tag{4}$$

where a_i is the activity of sulfonamide in solution, and a_s and a_w are the activities of pure solid, S, and pure liquid, W, respectively.

Because of the relatively small solubility of each sulfonamide in 1-octanol, it is believed that a_s and a_w almost remain

Table 4. $\Delta_{sol}H$ and $\Delta_{sol}S$ for Different Sulfonamides in 1-Octanol at Different Temperature

T/K		298.15	303.15	308.15	313.15	318.15	323.15	328.15	333.15
sulfamethazine	$\Delta_{sol}H$/kJ·mol^{-1}	21.84	21.23	20.62	20.01	19.40	18.79	18.18	17.57
	$\Delta_{sol}S$/J·mol^{-1}·K^{-1}	73.24	70.02	66.91	63.89	60.97	58.14	55.40	52.74
sulfadimethoxine	$\Delta_{sol}H$/kJ·mol^{-1}	9.502	11.48	13.47	15.45	17.43	19.41	21.40	23.38
	$\Delta_{sol}S$/J·mol^{-1}·K^{-1}	31.87	37.88	43.70	49.33	54.79	60.08	65.20	70.17
sulfamethoxydiazine	$\Delta_{sol}H$/kJ·mol^{-1}	9.777	10.18	10.59	10.99	11.39	11.80	12.20	12.61
	$\Delta_{sol}S$/J·mol^{-1}·K^{-1}	32.79	33.58	34.35	35.09	35.81	36.51	37.19	37.84
sulfamonomethoxine	$\Delta_{sol}H$/kJ·mol^{-1}	15.27	14.57	13.88	13.18	12.49	11.79	11.10	10.40
	$\Delta_{sol}S$/J·mol^{-1}·K^{-1}	51.20	48.07	45.03	42.10	39.25	36.49	33.82	31.23
sulfamethoxazole	$\Delta_{sol}H$/kJ·mol^{-1}	25.14	22.03	18.92	15.81	12.70	9.588	6.478	3.368
	$\Delta_{sol}S$/J·mol^{-1}·K^{-1}	84.32	72.67	61.39	50.48	39.91	29.67	19.74	10.11
sulfaquinoxaline	$\Delta_{sol}H$/kJ·mol^{-1}	25.01	22.77	20.53	18.29	16.05	13.81	11.57	9.330
	$\Delta_{sol}S$/J·mol^{-1}·K^{-1}	83.90	75.12	66.63	58.41	50.45	42.74	35.26	28.01

constant in the experimental range, and each is considered to be a constant.

$$J' = a_s a_w \tag{5}$$

Therefore, eq 4 can be written as

$$K_i = \frac{\gamma_i x_i}{J'} \tag{6}$$

where γ_i is the activity coefficient of sulfonamide, i, in the solution and x_i is the mole fraction of sulfonamide, i, in the solution.

On the basis of the assumption used in the inferential process for the modified Apelblat equation that the activity coefficient is invariable during a certain temperature range,[11] γ_i in eq 6 can be merged into J'. Equation 7 can be obtained from eq 6 by logarithmic treatment

$$\ln K_i = \ln x_i + J \tag{7}$$

where $J = \ln \gamma_i - \ln J'$ is a temperature-independent constant.

On the basis of the Gibbs equation and the modified Van't Hoff method,[12−15] the equation for calculating the molar enthalpies of dissolution $\Delta_{sol}H$ can be obtained

$$\Delta_{sol}H = -R\frac{\mathrm{d} \ln K_i}{\mathrm{d}T^{-1}} \tag{8}$$

Substituting the differential of eq 7 into eq 8 yields

$$\Delta_{sol}H = -R\frac{\mathrm{d} \ln x_i}{\mathrm{d}T^{-1}} \tag{9}$$

Using eq 1 to obtain the derivative and substituting it into eq 9 gives

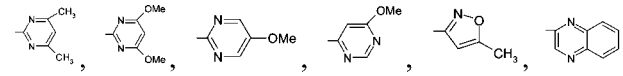
$$\Delta_{sol}H = RT(C - B/(T/\mathrm{K})) \tag{10}$$

According to the fundamental thermodynamic relation,[16] the equation for calculating the molar entropies of dissolution $\Delta_{sol}S$ can be obtained accordingly

$$\Delta_{sol}S = R(C - B/(T/\mathrm{K})) \tag{11}$$

According to parameters of the modified Apelblat equation listed in Table 3, $\Delta_{sol}H$ and $\Delta_{sol}S$ listed in Table 4 can be calculated from eqs 10 and 11, respectively.

From Table 4, it is found that the course of each sulfonamide dissolving in 1-octanol in the experimental temperature range was endothermic, $\Delta_{sol}H > 0$, and $\Delta_{sol}S$ for each sulfonamide dissolving in 1-octanol was relatively large. The positive $\Delta_{sol}H$ and $\Delta_{sol}S$ for each sulfonamide revealed that each sulfonamide being dissolved in 1-octanol was an entropy-driving process. This phenomenon likely resulted from the different molecular structure and space conformation between solute and solvent. 1-Octanol molecules as solvent are strong association complexes with small molecular dimension.[17,18] Owing to the solute sulfonamide molecules containing basic groups such as $-NH_2$, acidic groups such as $-SO_2H$, and complicated groups with different characteristics such as , sulfonamides perhaps involve various forces



such as electrostatic force, hydrogen bond, hydrophobic interaction, and stereoscopic effect in the dissolving process.[16] The reason for the entropy increase during the dissolution process is that sulfonamides disrupted the alignment of 1-octanol molecules and therefore reduced the degree of order of the system while they were dissolved in 1-octanol. The endothermic effect in the dissolving process ($\Delta_{sol}H > 0$) is perhaps because the interactions between sulfonamide molecules and 1-octanol molecules are more powerful than those between the 1-octanol molecules; the newly formed bond energy between sulfonamide molecule and 1-octanol molecule is not powerful enough to compensate the energy needed for breaking the original association bond in 1-octanol.

Conclusions

Using a static equilibrium method, we experimentally determined the solubilities of sulfamethazine, sulfadimethoxine, sulfamethoxydiazine, sulfamonomethoxine, sulfamethoxazole, and sulfaquinoxaline in 1-octanol from (298.15 to 333.15) K. The experimental data were correlated with the modified Apelblat equation. The calculated results show good agreement with the experimental data.

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