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RAPID COMMUNICATION

Solubility of 5-mercapto-1-methyltetrazole in pure solvents from (283 to 329) K

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Abstract–The solubility of 5-mercapto-1-methyltetrazole in pure solvents from (283 to 329) K was measured using a laser monitoring observation technique at atmospheric pressure. The solubility data were accurately correlated by a modified Apelblat equation. The calculated results of which are proved to show fine representation of experimental data.

Key words: 5-Mercapto-1-methyltetrazole, Solubility, Measurement, Modified Apelblat Equation

INTRODUCTION

Tetrazoles have received much attention due to their important industrial and biological practical applications [1]. In particular, 5-mercapto-1-methyltetrazole (formula: $C_2H_4N_4S$, abbreviated as MTT, molar mass 116.14, CAS Registry No. 13183-79-4) is a kind of white crystalline powder which has been used in the synthesis of pharmacologically active cephalosporins and, as cesium salts, as part of the thiolate/disulfide redox couple [2]. In industrial production, MTT has been an important pharmaceutical intermediate to synthesize the cefoperazone, cefmenoxime, cephalo-sporin nitrogen fluoride and so on. Considering MMT was synthesized in the solvents, it is necessary to know its solubility in different solvents to determine the proper solvent and to design an optimized crystallization process. In this study, the solubility of MTT in glycol, ethanol, 2-propanol, 1-propanol, 1-butanol, isobutyl alcohol, isopentyl alcohol, ethyl acetate, 1-butyl acetate, ethyl formate, 1,2-dichloroethane was measured in the temperature range from (283 to 329) K using a laser monitoring observation technique at atmospheric pressure. That employed in this work was classified as a synthetic method, which was much faster and more reliable than analytical method.

EXPERIMENTAL SECTION

1. Materials

MTT was purchased from Dongyang Tianyu Chemical Co., Ltd. Its mass fraction purity determined by high-performance liquid chromatography (HPLC) was higher than 0.99. The chemical structure of MTT is shown in Fig. 1. Other reagents were analytical research (AR) grade reagent from Tianjin Damao Chemical Reagent Factory and Tianjin Guangfu Technology Development Co., Ltd. All the solvents in the experiments had a minimum mass fraction purity of 99.5% and were used without further purification.

2. Apparatus and Procedure

The apparatus for solubility of MTT measurement was similar to that described in the literature [3-6] and here described briefly.

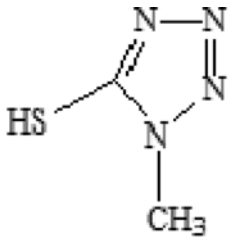

Fig. 1. Chemical structure of MTT.

The dissolution of the solute was carried out in a magnetically stirred jacketed glass vessel (100 mL), which was maintained at a constant temperature by continuous forced water circulation from a super thermostat bath (temperature uncertainty of ±0.05 K) at the required temperature. A mercury in-glass thermometer (fluctuates with ±0.05 K) was inserted into the inner chamber of the vessel to measure the temperature. A condenser was connected to the vessel to prevent the water from evaporating. A laser beam penetrating the vessel was used to monitor the dissolution process. The masses of the samples and solvents were weighted using an analytical balance (Sartorius CP224S, Germany) with an uncertainty of ±0.1 mg. During experiments the dissolution process in the glass vessel was monitored through the laser set. The laser set included a laser generator, a photoelectric transformer, and computer monitoring system which was more accurate and reliable. An electric magnetic stirrer (type 85-2, Shanghai Gouhua Co. Ltd., China) achieved continuous stirring for mixing solution. Excessive solvent and solute of known mass (determined by a preliminary experiment) were loaded into the jacketed vessel. During experiments, the fluid in the glass vessel was monitored by a laser beam penetrating the vessel. In the early stages, the intensity of the laser beam increased gradually with the dissolving of the sample particles in the solution. When the solute dissolved completely, the solution was clear, as well as the laser intensity reached maximum. Then, a little additional solute of known mass was introduced into the vessel. This procedure was repeated until the penetrated laser intensity could not return to a maximum or, in other words, the last addition no longer dissolved completely in the solvent. The interval of addition depended on the speed of

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dissolving at that temperature, and it should last more than 60 min. The total amount of the solute consumed was recorded. The same work was done three times. In this work, the uncertainty of the experimental solubility values, which comes from temperature measurements, weighing procedure, instabilities of the water bath and the interval of addition, was established to be within 2%.

RESULT AND DISCUSSION

The solubility of MTT in above mentioned pure solvents at different temperatures is presented in Table 1 and graphically plotted

Table 1. Solubility of MTT in pure solvents

T/K	x_1	$\frac{10^2(x_1-x_1^{cal})}{x_1}$	T/K	x_1	$\frac{10^2(x_1-x_1^{cal})}{x_1}$
		Glycol			
283.24	0.2856	−0.32	308.14	0.3985	−0.20
288.40	0.3103	0.16	313.16	0.4210	−0.17
293.16	0.3335	0.66	318.17	0.4434	−0.07
298.16	0.3551	0.28	323.19	0.4665	0.24
303.16	0.3762	−0.16	328.16	0.4896	0.16
		Ethanol			
283.26	0.2283	−0.22	308.15	0.3146	−0.06
288.24	0.2465	0.16	313.16	0.3319	0.09
293.16	0.2641	0.34	318.16	0.3476	−0.14
298.33	0.2809	−0.07	323.17	0.3639	−0.05
303.18	0.2975	−0.13	328.94	0.3816	0.26
		2-Propanol			
283.63	0.2514	−0.16	308.13	0.3279	0.09
288.21	0.2660	0.04	313.18	0.3429	−0.09
293.30	0.2817	0.04	318.13	0.3575	−0.25
298.12	0.2967	0.07	323.15	0.3735	−0.05
303.32	0.3124	−0.10	328.10	0.3892	0.13
		1-Propanol			
283.63	0.2180	0.09	308.13	0.3033	0.26
288.21	0.2328	−0.04	313.18	0.3213	0.09
293.30	0.2498	−0.12	318.13	0.3390	−0.12
298.12	0.2667	−0.04	323.15	0.3583	−0.03
303.32	0.2847	−0.14	328.10	0.3772	0.00
		1-Butanol			
283.26	0.2168	−0.14	308.16	0.3068	0.23
289.10	0.2369	−0.04	313.14	0.3251	−0.03
293.14	0.2525	0.55	318.16	0.3432	−0.44
298.16	0.2673	−0.64	323.17	0.3645	0.00
303.22	0.2882	0.21	328.16	0.3850	0.16
		Isobutyl alcohol			
283.26	0.1944	−0.10	307.99	0.2853	0.04
288.11	0.2118	0.00	312.98	0.3035	−0.10
293.46	0.2310	−0.09	318.16	0.3221	−0.31
298.07	0.2489	0.28	323.23	0.3411	−0.21
303.17	0.2673	0.04	328.13	0.3606	0.28
		Isopentyl alcohol			
283.44	0.1903	−0.32	308.24	0.2791	0.04
288.41	0.2079	0.05	313.28	0.2960	−0.54
293.26	0.2255	0.31	318.15	0.3152	−0.13
298.37	0.2432	0.08	323.05	0.3342	0.12
303.57	0.2614	−0.19	328.35	0.3534	0.03

Table 1. Continued

T/K	x_1	$\frac{10^2(x_1-x_1^{cal})}{x_1}$	T/K	x_1	$\frac{10^2(x_1-x_1^{cal})}{x_1}$
		Ethyl acetate			
283.23	0.1879	−0.21	308.15	0.2528	−0.08
288.19	0.2003	0.30	313.25	0.2679	−0.34
293.22	0.2116	−0.14	318.26	0.2849	−0.14
298.22	0.2253	0.22	323.05	0.3024	0.10
303.12	0.2390	0.29	328.17	0.3216	0.16
		1-Butyl acetate			
283.23	0.1675	−0.18	308.14	0.2285	−0.09
288.4	0.1784	−0.17	313.16	0.2432	−0.29
293.84	0.1909	−0.05	318.17	0.2596	−0.27
298.13	0.2016	0.05	323.19	0.2781	0.07
303.16	0.2143	−0.19	328.75	0.2985	−0.13
		Ethyl formate			
283.25	0.1148	0.52	308.16	0.1684	0.42
289.05	0.1241	−1.05	313.15	0.1798	−0.17
293.14	0.1331	−0.53	318.16	0.1913	−0.99
298.16	0.1450	0.34	323.17	0.2061	−0.39
303.22	0.1574	0.95	328.15	0.2225	0.58
		1,2-Dichloroethane			
283.26	0.02385	−0.42	308.26	0.05908	−1.30
288.24	0.02868	0.28	313.25	0.07216	−0.22
293.24	0.03365	−1.84	318.35	0.08858	0.79
298.25	0.04108	−0.24	323.55	0.1066	−0.75
303.29	0.04956	−0.20	328.30	0.1278	−0.94

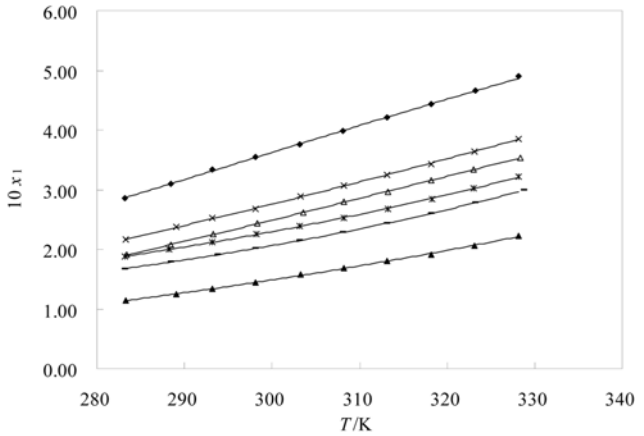

Fig. 2. Solubility of MTT (x_1) in different solvents: ◆, glycol; ×, 1-butanol; △, isopentyl alcohol; ✳, ethyl acetate; –, 1-butyl acetate; ▲, ethyl formate; and calculated data by the Eq. (2) to different solvents in solid lines.

in Figs. 2 and 3 together with their calculated solubility. The mean values were used to calculate the solubility (x_1) of MMT based on Eq. (1).

$$x_1 = \frac{m_1/M_1}{m_1/M_1 + m_2/M_2} \quad (1)$$

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.

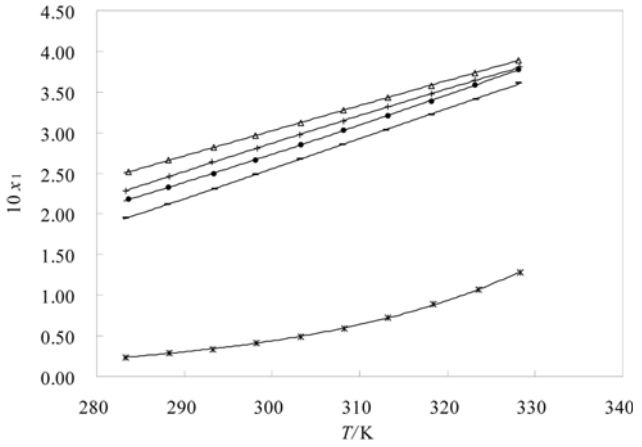

Fig. 3. Solubility of MTT (x_1) in different solvents: △, 2-propanol; +, ethanol; ◆, 1-propanol; –, isobutyl alcohol; ✳, 1,2-Dichloroethane; and calculated data by the Eq. (2) to different solvents in solid lines.

Table 2. Parameters of Eq. (2) for the solubility of MTT in pure solvents

Solvent	a	b	c	10^3RMSD
Glycol	52.193	−3341.2	−7.3759	1.07
Ethanol	53.498	−3371.6	−7.6279	0.56
2-Propanol	23.775	−1903.8	−3.2654	0.42
1-Propanol	18.636	−1879.7	−2.3962	0.37
1-Butanol	18.052	−1880.5	−2.2918	0.97
Isobutyl alcohol	58.019	−3771.6	−8.2072	0.59
Isopentyl alcohol	46.753	−3266.5	−6.5317	0.67
Ethyl acetate	−48.299	1186.4	7.5166	0.55
1-Butyl acetate	−65.326	1889.7	10.072	0.42
Ethyl formate	−13.476	−637.74	2.4011	1.13
1,2-Dichloroethane	−193.16	5664.5	30.007	0.63

The temperature dependence of MTT in different pure solvents is described by the modified Apelblat equation [7].

$$\ln x_1 = a + \frac{b}{T/K} + c\ln(T/K) \quad (2)$$

Where x_1 is the solubility of MTT in mole fraction, T is the absolute temperature, and a, b, c are model parameters. The calculated solubility results of MTT are given in Table 1. The values of a, b, c and the root-mean-square deviations (RMSDs) are listed in Table 2. The RMSD is defined as follows:

$$RMSD = \left[\frac{\sum_{i=1}^{N}(x_{1,i} - x_{1,i}^{cal})^2}{N-1}\right]^{1/2} \quad (3)$$

Where $x_{1,i}$ is the experimental value of solubility, $x_{1,i}^{cal}$ is the solubility calculated from Eq. (2), and N is the number of experimental points.

CONCLUSIONS

From Tables 1 and 2 and Figs. 2 and 3, we can draw the following conclusions: (1) The solubility of MTT in these pure solvents increased with temperature, but the increment varied with different solvents. (2) The solubility of MTT in strong-polar alcohols is higher than that in the weak and moderate-polar solvents. As the solvent polarity increases, the solubility of MTT increases. It shows that the polarity of solvents has a great effect on the solubility of MTT in the solvents selected. For the strong-polar alcohols studied, the solubility of MMT is ranked as glycol>2-propanol>ethanol>1-propanol>1-butanol>isopentyl alcohol, which may result from the difference in their polarity, molecular mass, van der Waals force, and the hydrogen bond and so on. The primary reason is still unclear and needs further study. (3) All the experimental data could be regressed by Eq. (2) for these pure solvents. The calculation solubility shows good agreement with the experimental values. The experimental solubility and correlation equation in this work could be used as essential data and models in the practical process of manufacturing and purifying of MTT in industry.

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NOMENCLATURE

x_1 : mole fraction solubility of solute
$x_{1,i}$: experimental value of solubility
$x_{1,i}^{cal}$: calculated value of solubility
T : absolute temperature
a, b, c : empirical constants
m_i : mass of the i [g]
M_i : molecular weight of i [g/mol]
RMSD : root-mean-square deviation

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