Asian Journal of Chemistry; Vol. 23, No. 11 (2011), 4939-4942

ASIAN JOURNAL OF CHEMISTRY

www.asianjournalofchemistry.co.in

Thermodynamic Properties of Matrine in Citric Acid Solution

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(*Received*: 18 November 2010; *Accepted*: 20 July 2011) AJC-10184

The enthalpies of dissolution of matrine in citric acid solution (0.15 mol L^{-1}) were measured using a RD496-2000 Calvet Microcalorimeter at 309.65 K under atmospheric pressure. The differential enthalpy ($\Delta_{dif}H_m$) and molar enthalpy ($\Delta_{sol}H_m$) of dissolution of matrine in citric acid solution (0.15 mol L^{-1}) were determined. The corresponding kinetic equation described the dissolution process was elucidated to be $\frac{d\alpha}{dt} = 10^{-3.96}(1-\alpha)^{0.99}$. Moreover, the half-life, $\Delta_{sol}H_m$, $\Delta_{sol}G_m$ and $\Delta_{sol}S_m$ of the dissolution process were also obtained. This work will provide a potential reference for the clinical application of matrine.

Key Words: Matrine, Thermodynamic, Kinetics, Citric acid solution (0.15 mol L^{-1}).

INTRODUCTION

Matrine, a major quinoilizidine alkaloid with four-loop and molecular formula of $C_{15}H_{24}N_2O$ (Fig. 1), is extracted from sophora alopecuroides L, a Chinese medicinal plant and has been used as a quality control marker in antitumor B mixture. Antitumor B (ATB) is a Chinese traditional medicine and contains a proprietary mixture of six plants including *Sophora tonkinensis*, *Polygonum bistorta*, *Prunella vulgaris, Sonchus brachyotus, Dictamnus dascycarpus* and *Dioscorea bulbifera*. The clinical studies have shown significant chemopreventive efficacy of antitumor B against human esophageal and lung cancers[1,2]. Besides anticancer activity, positive treatment effects of matrine in cardiovascular diseases, like hypertension, ischemia, angiosclerosis and septic shock[3] and inhibition of proinflammatory cytokines in macrophages[4], skin-keratinocytes and fibroblasts[5] and mast cells[6] have been demonstrated.

Since no report is available about the solubility of matrine, now the aims of the present study were in the aspect of dissolution kinetic equation and kinetic parameter. Thus, in this paper, the enthalpy of matrine in citric acid solution was measured by microcalorimetry, which is simple and easy. On the basis of these experimental data and calculated results, the kinetic equation, half-life period, $\Delta_{sol}H_m$, $\Delta_{sol}G_m$ and $\Delta_{sol}S_m$ of the dissolution process were obtained. This work provides a valuable informations for the clinical application of matrine.

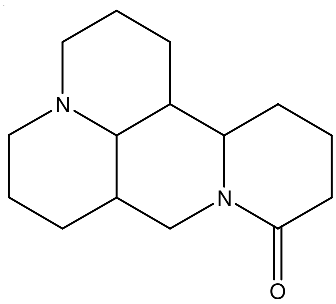

Fig. 1. Structural formula of matrine

EXPERIMENTAL

Matrine (Baoji Fangsheng Biological Development Co., Ltd. Purity: > 99 %) and citric acid (Analytical grade) were used as received.

The experiment was performed using a RD496-2000 Calvet Microcalorimeter (Mianyang CAEP Thermal Analysis Instrument Company, China). The microcalorimeter was calibrated by Joule effect and its sensitivity was 64.22 ± 0.04 $\mu V\ mW^{-1}$ at 309.65 K. The enthalpy of dissolution of KCl (spectrum purity) in distilled water (about 20 mg / 2.00 g) measured at 298.15 K was 17.535 kJ mol^{-1}, which was in an excellent accordance with the literature value[7] 17.545 kJ mol^{-1}, showing that the device of measuring the enthalpy used in this work was reliable.

Experimental methods: The proper amounts of matrine (13.55 mg, 39.97 mg, 45.49 mg, 55.61 mg, 70.84 mg) were dissolved in 2 mL of citric acid solution (0.15 mol L^{-1}) at 309.65 K under the atmospheric pressure. The enthalpy change of the process was detected by the RD496-2000 Calvet Microcalorimeter.

RESULTS AND DISCUSSION

Thermochemical behaviours of the dissolution of matrine in citric acid solution (0.15 mol L^{-1}): The certain mass of matrine was dissolved in citric acid solution (0.15 mol L^{-1}) at 309.65 K. There are five concentration gradients to carry out in this experiment. The curve describing the entire dissolution process of matrine in citric acid solution (0.15 mol L^{-1}) is shown in Fig. 2. The dissolution is an exothermic process. The entire process was repeated three times. The heat flow curves obtained under the same conditions overlap with each other, indicating that the reproducibility of test is satisfactory.

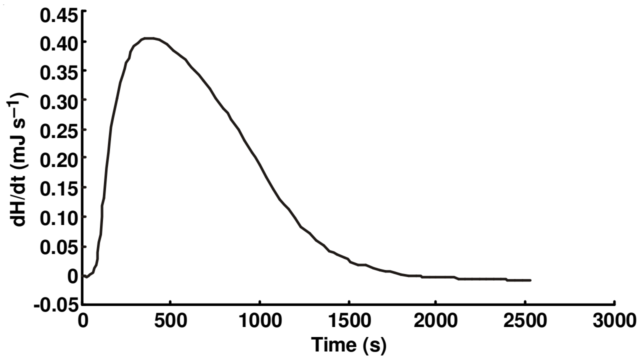

Fig. 2 Heating rate (dH/dt) of the entire dissolution process of matrine in 2 mL citric acid solution (0.15 mol L^{-1})

Table-1 shows the experimental data obtained from the typical thermogram curve of the dissolution with different mass matrine in 2.00 mL citric acid solution (0.15 mol L^{-1}).

TABLE-1
DISSOLUTION ENTHALPHY OF MATRINE IN 2.00 mL CITRIC ACID SOLUTION (0.15 mol L^{-1})

m/mg	10^3 n/mol	Q/J	ΔH/kJ.mol^{-1}
13.55	0.06	1.52	26.74
39.97	0.17	4.81	28.66
45.49	0.19	5.40	28.30
55.61	0.23	6.56	28.10
70.84	0.30	8.28	27.86
Average			27.93

From Table-1, the concentration of the solution almost has little influence on the values of the molar enthalpy($\Delta_{sol}H_m$) at 309.65 K. Thus the average value of $\Delta_{sol}H_m$ can represent the molar enthalpy[8] of the infinite diluted citric acid solution (0.15 mol L^{-1}) at 309.65 K.

The heat effect *vs* the amount of the substance relationships of matrine in 0.15 mol L^{-1} citric acid solution is shown in Fig. 3.

The according linear equation for the citric acid solution (0.15 mol L^{-1}) is as follow:

$$Q = 28121n - 6.7533 \quad r = 0.9996 \tag{1}$$

where, r is correlation coefficient.

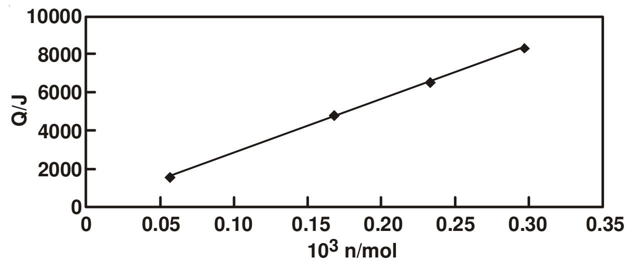

Fig. 3. Linear relationship between the heat effect (*Q*) and the amount of the matrine (*n*)

Differential enthalpy (Δ_{dif}/H_m) of matrine in the citric acid solution (0.15 mol L^{-1}) is about 28.11 kJ mol^{-1}.

Kinetic of dissolution process of matrine in citric acid solution (0.15 mol L^{-1}): The kinetic equation (eqns. 2 and 3) describing the dissolution of matrine in citric acid solution[9]

$$\frac{d\alpha}{dt} = kf(\alpha) \tag{2}$$

$$f(\alpha) = (1-\alpha)^n \tag{3}$$

Combining eqns. 2 and 3, substituting $\alpha = \frac{H_t}{H_0}$ into the equation and then get a logarithmic converter:

$$\ln\left[\frac{1}{H_0}\left(\frac{dH}{dt}\right)_i\right] = \ln k + n\ln\left[1-\left(\frac{H_t}{H_0}\right)_i\right] \quad i = 1, 2, ...,L \tag{4}$$

In these equations, α is the conversion degree; f(α) is the kinetic function; H_t represents the heat at time of t; H_0 is the heat of the whole process; k is the rate of matrine dissolved in the citric acid solution (0.15 mol L^{-1}); *n* is the reaction order and L is the counting number.

The original data is shown in Table-2.

By substituting the data taken from Table- 2, $(dH/dt)_i$, $(H/H_\infty)_i$, H_∞, i = 1, 2, …, L, into the kinetic eqn. 4, the obtained values of n and lnk are listed in Table-3.

Substituting the values of *n* and *k* in Table-3 into eqn. 2 and 3 and then unite them, we can get that the kinetic equation of the dissolution process is $\frac{d\alpha}{dt} = 10^{-3.96}(1-\alpha)^{0.66}$.

The kinetic equation is similar to quasi-first order reaction of the dissolution process. So the half-life period can be calculated with eqn. 5, which was 105.16 min.

$$t_{0.5} = \frac{\ln 2}{k} \tag{5}$$

Thermodynamic of matrine in citric acid solution (0.15 mol L^{-1}): On the basis of these experimental data and calculated results, the kinetic parameters of the dissolution process were obtained through eqn. 6.

$$\ln\frac{k}{T} = \left(\frac{\Delta S_m^\theta}{R} + \ln\frac{k_\theta}{h}\right) - \frac{\Delta H_m^\theta}{RT} \tag{6}$$

eqn. 6 can be changed into the following expression,

$$\ln\frac{kh}{k_B T} = \frac{\Delta_{sol}S_m}{R} - \frac{\Delta_{sol}H_m}{RT} \tag{7}$$

TABLE-2
ORIGINAL DATA OF MATRINE IN 2 mL OF CITRIC ACID SOLUTION (0.15 mol L^{-1})

m/mg	t/s	dH/dt (mJs^{-1})	H t/mJ	Ht/Ho	H/kJ mol^{-1}	m /mg	t/s	dH/d t (mJ s^{-1})	H t/mJ	Ht/Ho	H /kJ mol^{-1}
13.55	0	0.199	176.8	0.116	26.74		400	0.231	4341.8	0.804	
	20	0.206	242.0	0.159			440	0.211	4483.7	0.830	
	40	0.209	308.8	0.203			480	0.190	4612.6	0.854	
	60	0.208	375.7	0.247			520	0.169	4728.1	0.875	
	80	0.204	442.0	0.291			560	0.149	4830.4	0.894	
	100	0.199	506.9	0.333			600	0.130	4920.1	0.911	
	120	0.193	570.0	0.375			640	0.113	4998.2	0.925	
	140	0.186	630.9	0.415			680	0.097	5065.6	0.938	
	160	0.179	689.6	0.454		55.61	720	0.083	5123.5	0.949	28.10
	180	0.171	745.8	0.491			40	0.394	2077.1	0.317	
	200	0.163	799.6	0.526			80	0.382	2326.5	0.355	
	220	0.155	850.7	0.560			120	0.369	2568.0	0.392	
	240	0.147	899.4	0.592			160	0.354	2800.5	0.427	
	260	0.139	945.5	0.622			200	0.339	3023.4	0.461	
	280	0.132	989.0	0.651			240	0.324	3236.5	0.494	
	300	0.124	1030.2	0.678			280	0.308	3439.5	0.525	
	320	0.117	1069.0	0.703			320	0.294	3632.8	0.554	
39.97	0	0.316	2554.3	0.531	28.67		360	0.280	3817.0	0.582	
	40	0.305	2754.2	0.573			400	0.266	3992.5	0.609	
	80	0.293	2946.4	0.613			440	0.254	4159.6	0.635	
	120	0.278	3129.8	0.651			480	0.242	4318.6	0.659	
	160	0.263	3303.6	0.687			520	0.231	4470.3	0.682	
	200	0.246	3467.1	0.721			560	0.220	4615.2	0.704	
	240	0.229	3619.8	0.753			600	0.210	4753.6	0.725	
	280	0.212	3761.7	0.783			640	0.201	4885.6	0.745	
	320	0.195	3892.7	0.810			680	0.192	5011.7	0.765	
	360	0.179	4013.0	0.835			720	0.184	5132.3	0.783	
	400	0.163	4122.8	0.858		70.84	0	0.539	1617.3	0.195	27.87
	440	0.147	4222.2	0.878			40	0.530	1961.3	0.237	
	480	0.130	4311.2	0.897			80	0.516	2297.5	0.277	
	520	0.114	4389.9	0.913			120	0.499	2623.5	0.317	
	560	0.100	4458.6	0.928			160	0.482	2938.4	0.355	
	600	0.087	4518.5	0.940			200	0.465	3242.6	0.392	
	640	0.075	4570.5	0.951			240	0.449	3536.3	0.427	
	680	0.064	4615.0	0.960			280	0.433	3819.5	0.461	
45.49	0	0.384	2319.9	0.429	28.31		320	0.417	4092.4	0.494	
	40	0.373	2563.4	0.475			360	0.401	4355.1	0.526	
	80	0.361	2799.5	0.518			400	0.386	4607.8	0.556	
	120	0.348	3027.4	0.560			440	0.371	4851.0	0.586	
	160	0.333	3246.4	0.601			480	0.358	5085.2	0.614	
	200	0.318	3455.8	0.640			520	0.345	5310.8	0.641	
	240	0.302	3655.1	0.677			560	0.332	5528.1	0.668	
	280	0.285	3843.7	0.712			600	0.319	5737.1	0.693	
	320	0.268	4021.3	0.744			640	0.307	5938.2	0.717	
	360	0.249	4187.5	0.775			680	0.295	6131.2	0.740	

TABLE-3
n AND ln*k* OF MATRINE IN CITRIC ACID SOLUTION (0.15 mol L^{-1}) AT 309.65 K

m/mg	n	ln k (k/s^{-1})	r
13.55	0.68	-8.68	0.9959
39.97	0.68	-9.03	0.9984
45.49	0.74	-8.93	0.9958
55.61	0.61	-9.51	0.9965
70.84	0.60	-9.43	0.9963
Average	0.66	-9.12	

substituting $k = 10^{-3.96}$ s^{-1}, $k_B = 1.38 \times 10^{-23}$ JK^{-1}, $h = 6.626 \times 10^{-34}$ Js^{-1}, $R = 8.314$ *J* mol^{-1} K^{-1}, $\Delta_{sol}H_m = 27.93$ kJ mol^{-1}, T = 309.65 K into eqn. 7, so $\Delta_{sol}S_m = -1016.06$ *J* mol^{-1} K^{-1}.

And then putting $\Delta_{sol}H_m$ and $\Delta_{sol}S_m$ into the following formula:

$$D_{sol}G_m=D_{sol}H_m-T.D_{sol}S_m \quad (8)$$

We obtained $\Delta_{sol}G_m = 342.54$ kJ mol^{-1}.

Conclusion

The molar enthalpy of matrine in the citric acid solution (0.15 mol L^{-1}) was measured with the RD496-2000 type Calvet Microcalorimeter at 309.65 K under the atmospheric pressure. From the results it can be observed that the concentration of matrine have little impact to the enthalpies. Thus, the average value of $\Delta_{sol}H_m$ can represent the molar enthalpy which is 27.93 kJ mol^{-1}.

The kinetic equation of the dissolution process of matrine in the citric acid solution (0.15 mol L^{-1}) at 309.65 K is $\frac{d\alpha}{dt} = 10^{-3.96}(1-\alpha)^{0.66}$. It is a quasi-first order reaction and its half-life is $t_{1/2}$=105.16 min, the rate constant is $k=10^{-3.96}$ s^{-1}.

The dissolution of matrine in citric acid solution (0.15 mol L^{-1}) is an exothermic process. The molar enthalpy ($\Delta_{sol}H_m$) is 27.93 kJ mol^{-1} and $\Delta_{sol}S_m$ is -1016.06 *J* mol^{-1} K^{-1}. The negative value of entropy of activation indicates that the dissolution of matrine in citric acid solution (0.15 mol L^{-1}) get a more ordered system.

ACKNOWLEDGEMENTS

This work was supported by the Phytochemistry Key Laboratory of Shaanxi Province (No. 09JS066) and the Project Foundation of Shaanxi Province (No. 2006k16-G16).

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