Density and Viscosity of Clopidogrel Hydrogen Sulfate + Methanol and Clopidogrel Hydrogen Sulfate + Ethanol from (278.15 to 313.15) K

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The densities and viscosities of clopidogrel hydrogen sulfate + methanol and clopidogrel hydrogen sulfate + ethanol have been measured at the temperatures (278.15, 283.15, 288.15, 293.15, 298.15, 303.15, 308.15, and 313.15) K. The experimental data of densities were calculated with the Vogel−Tamman−Fulcher equation, and viscosities were analyzed with linear fit to temperature.

Introduction

With the development of society, human life is becoming more and more abundant, and diseases of cycle obstacles on the mind, brain, and other arteries induced by platelet aggregation are more common.[1−3] Clopidogrel hydrogen sulfate ($C_{16}H_{16}ClNO_2S\cdot H_2SO_4$) is a medicine which can prevent and treat such diseases. It is also a pharmaceutical intermediate, so it has broad applications. Some basic data such as density and viscosity have important significance on the synthesis, separation, and understanding of the properties of clopidogrel hydrogen sulfate[4] and are absent, so densities and viscosities of the systems of clopidogrel hydrogen sulfate + methanol and clopidogrel hydrogen sulfate + ethanol were measured in a temperature range and composition range.

Experimental Section

Materials. Clopidogrel hydrogen sulfate ($C_{16}H_{16}ClNO_2S\cdot H_2SO_4$, CAS RN: 120202-66-6) obtained from Zhengzhou Paini Chemicals Co. was of AR grade, and its mass fraction purity was greater than 99.0. CH_3OH and C_2H_5OH were of AR grade, and their mass fraction purity was greater than 99.5. Water used in the experiments was double-distilled, its conductivity less than 10^{-4} S·m^{-1}.

Density Measurements. The density (ρ) was measured with five Oswald−Sprengel-type pycnometers having a bulb volume of 25 cm^3 and an internal capillary diameter of about 1 mm.[5] The internal volumes of the pycnometers were calibrated with pure water at each of the measured temperatures, and the densities of pure water were taken from Lange's Handbook of Chemistry.[6] The thoroughly cleaned and dried pycnometers were first weighed (mass m_0) on an electronic balance (accuracy is 0.0001 g) and then filled with experimental solutions and immersed in a thermostat (type 501, Shanghai Laboratory Instrument Works Co., Ltd.) controlled to within ± 0.02 K. After thermal equilibrium had been achieved at the required temperature, the pycnometers were removed from the thermostat and properly cleaned, dried, and weighed (m_2). The density was then determined from the mass of the sample and the volume of the pycnometers. The readings from five pycnomenters were averaged to determine the density.

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$$\rho = \frac{m_2 - m_0}{m_1 - m_0}\rho_W \quad (1)$$

where ρ is the density of the measured solution at measured temperature; ρ_W is the density of water at the measured temperature; m_0 is the mass of empty pycnometers; m_1 is the mass of pycnometers filled with water at measured temperature; and m_2 is the mass of pycnometers filled with measured solution at measured temperature.

The uncertainty analysis was based on the International Guide to the Expression of the Uncertainty in Measurement.[7,8] Uncertainties in the density measurement were within ± 0.0002 g·cm^{-3} on the basis of the 95 % confidence level. Uncertainties of temperature and composition are 0.02 K and 0.0001 mol·kg^{-1}, respectively.

Viscosity Measurements. The viscosity was measured using a commercial Ubbelohde capillary viscometer (Shanghai Glass Instruments Factory, China) of 0.4 mm diameter, which was placed inside a thermostat having a constant water circulation for maintaining constant temperature throughout the experiment to an uncertainty of ± 0.02 K. The viscometer was calibrated with redistilled water at (278.15, 283.15, 288.15, 293.15, 298.15, 303.15, and 313.15) K and was thoroughly cleaned and dried, then filled with the experimental solutions. After attained thermal equilibrium, the efflux times of the flow of solutions were recorded with an electronic digital stopwatch correct to ± 0.01 s. At least five repetitions of each datum point obtained were reproducible to ± 0.06 s, and the results were averaged. The standard deviations for the viscosity of parallel measurements were less than 0.002 mPa·s. Because all flow times were greater than 79 s and the capillary diameter (0.4 mm) was far less than its length (90 to 100) mm, the kinetic energy and end corrections, respectively, were found to be negligible. The viscosity was then calculated from the relationship.[9,10]

$$\frac{\eta}{\eta_W} = \frac{\rho t}{\rho_W t_W} \quad (2)$$

where η, ρ, t and η_W, ρ_W, t_W are the viscosity, density, and flow time of the mixture and water, respectively. The densities and viscosities of pure water were taken from Lange's Handbook of Chemistry.[6] The uncertainty in the viscosity measurement is

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Table 1. Experimental Densities ρ for $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + CH_3OH (2) and $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + C_2H_5OH (3) from T = (278.15 to 313.15) K as a Function of Concentration c

c	ρ/g·cm^{-3}							
(mol·kg^{-1})	T/K = 278.15	T/K = 283.15	T/K = 288.15	T/K = 293.15	T/K = 298.15	T/K = 303.15	T/K = 308.15	T/K = 313.15
				$C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + CH_3OH (2)				
0.0000	0.8030	0.7989	0.7952	0.7921	0.7879	0.7837	0.7795	0.7752
0.0010	0.8031	0.7992	0.7954	0.7923	0.7881	0.7840	0.7797	0.7753
0.0030	0.8035	0.7995	0.7958	0.7925	0.7882	0.7841	0.7798	0.7755
0.0050	0.8040	0.8001	0.7962	0.7929	0.7884	0.7843	0.7800	0.7757
0.0070	0.8044	0.8004	0.7964	0.7933	0.7887	0.7845	0.7803	0.7759
0.0090	0.8048	0.8011	0.7971	0.7936	0.7890	0.7850	0.7807	0.7760
0.0110	0.8052	0.8015	0.7975	0.7940	0.7893	0.7853	0.7811	0.7764
0.0130	0.8059	0.8020	0.7982	0.7945	0.7900	0.7858	0.7815	0.7770
0.0150	0.8064	0.8026	0.7990	0.7953	0.7908	0.7866	0.7823	0.7778
				$C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + C_2H_5OH (3)				
0.0000	0.8005	0.7978	0.7939	0.7900	0.7857	0.7809	0.7780	0.7733
0.0010	0.8010	0.798	0.7942	0.7904	0.7861	0.7812	0.7782	0.7737
0.0030	0.8016	0.7984	0.7945	0.7908	0.7866	0.7818	0.7785	0.7739
0.0050	0.8023	0.7989	0.7949	0.7910	0.7869	0.7821	0.7787	0.7742
0.0070	0.8029	0.7993	0.7954	0.7914	0.7872	0.7825	0.7789	0.7745
0.0090	0.8035	0.7998	0.7959	0.7918	0.7877	0.7829	0.7791	0.7748
0.0110	0.8039	0.8001	0.7962	0.7922	0.7880	0.7832	0.7794	0.7752
0.0130	0.8045	0.8006	0.7965	0.7928	0.7884	0.7834	0.7798	0.7757
0.0150	0.8050	0.8009	0.7968	0.7930	0.7887	0.7839	0.7802	0.7760

Table 2. Coefficients of Equation 3, ARD, and SD for the Density of $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + CH_3OH (2) and $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + C_2H_5OH (3) from T = (278.15 to 313.15) K as a Function of Concentration c

A	B	C	D	ARD[a]	SD[b]/(g·cm^{-3})
		$C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + CH_3OH (2)			
1.0507	79.5834	−69.2959	574.2535	0.00033	0.00031
		$C_{16}H_{16}ClNO_2S \cdot H_2SO_4$(1) + C_2H_5OH (3)			
1.2371	196.6197	−109.4974	731.3523	0.00034	0.00036

[a] ARD, average relative deviation. [b] SD, standard deviation.

estimated on the basis of the principle of error propagation to be ± 0.6 % at the 95 % confidence level.

Results and Discussions

Experimental Densities. The experimental densities ρ for $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + CH_3OH (2) and $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + C_2H_5OH (3) from T = (278.15 to 313.15) K as a function of concentration c are listed in Table 1.

The densities increase with increasing c at constant temperature and decrease with the increasing temperature at a fixed c in $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ + CH_3OH and $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ + C_2H_5OH.

Fitting of the Experimental Data for Density. The experimental data were fit by the Vogel−Tamman−Fulcher (VTF) equation[9]

$$\rho/(\mathrm{g \cdot cm^{-3}}) = A \exp\left(\frac{B + C \cdot c/(\mathrm{mol \cdot kg^{-1}})}{T/\mathrm{K} - D}\right) \qquad (3)$$

in which ρ is density; c is mass mole concentration; T is temperature; and A, B, C, and D are equation coefficients. The values of coefficients were listed in Table 2 along with the average relative deviation, ARD, and standard deviation, SD, which were defined by the following

$$\mathrm{SD} = [\sum (Y - Y^{\mathrm{cal}})^2/(p - n)]^{1/2} \qquad (4)$$

$$\mathrm{ARD} = \frac{1}{p}\sum \frac{|Y^{\mathrm{cal}} - Y|}{Y} \qquad (5)$$

where p is the number of data points; n is the number of coefficients; and Y and Y^{cal} refer to the experimental values and the calculated values from the equation, respectively.

Comparing the calculated values with experimental values, the average relative deviation and standard deviations of 72 data points for $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ + CH_3OH are $3.3 \cdot 10^{-4}$ and $3.1 \cdot 10^{-4}$ and for $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ + C_2H_5OH are $3.4 \cdot 10^{-4}$ and $3.6 \cdot 10^{-4}$. It could be seen that the VTF equation could describe the relationship among density, temperature, and concentration of the studied systems very well.

Experimental Viscosities. The experimental viscosities for $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + CH_3OH (2) and $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + C_2H_5OH (3) from T = (278.15 to 313.15) K as a function of concentration c were listed in Table 3.

Fitting of the Experimental Data for Viscosities. The experimental data were analyzed with linear fitting based on eq 6

$$\eta/(\mathrm{mPa \cdot s}) = a + bT/\mathrm{K} \qquad (6)$$

in which a is the intercept, and b is the slope. At a certain concentration, fitting of the experimental viscosity data with temperature and index was listed in Table 4. When R-square values were high, it indicated that, at certain concentrations, viscosities of the studied systems approximately linearly decreased with temperature.

Conclusions

The densities and viscosities of $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + CH_3OH (2) and $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + C_2H_5OH (3) as a function of concentration c at the temperatures (278.15, 283.15, 288.15, 293.15, 298.15, 303.15, 308.15, and 313.15) K were measured. The densities and viscosities decrease with increasing temperature at certain concentrations and increase with the increase of concentration at certain temperatures. The experimental data of densities were fit to the Vogel−Tamman−Fulcher equation, and viscosities were analyzed with linear fitting at

Table 3. Experimental Viscosities η for $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + CH_3OH (2) and $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + C_2H_5OH (3) from T = (278.15 to 313.15) K as a Function of Concentration c

c	η/mPa·s							
(mol·kg^{-1})	T/K = 278.15	T/K = 283.15	T/K = 288.15	T/K = 293.15	T/K = 298.15	T/K = 303.15	T/K = 308.15	T/K = 313.15
				$C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + CH_3OH (2)				
0.0000	0.7418	0.6890	0.6410	0.5990	0.5585	0.5199	0.4857	0.4559
0.0010	0.7441	0.6924	0.6416	0.6006	0.5596	0.5212	0.4870	0.4567
0.0030	0.7470	0.6943	0.6446	0.6022	0.5620	0.5236	0.4898	0.4589
0.0050	0.7487	0.6961	0.6475	0.6042	0.5631	0.5254	0.4901	0.4595
0.0070	0.7505	0.6980	0.6487	0.6049	0.5638	0.5262	0.4906	0.4601
0.0090	0.7525	0.6998	0.6494	0.6060	0.5652	0.5269	0.4919	0.4604
0.0110	0.7529	0.7006	0.6502	0.6077	0.5661	0.5276	0.4936	0.4620
0.0130	0.7577	0.7039	0.6527	0.6096	0.5684	0.5304	0.4943	0.4631
0.0150	0.7582	0.7050	0.6538	0.6111	0.5694	0.5315	0.4967	0.4647
				$C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + C_2H_5OH (3)				
0.0000	1.6292	1.4735	1.3325	1.2097	1.0990	0.9971	0.9083	0.8280
0.0010	1.6324	1.4764	1.3347	1.2106	1.1012	0.9985	0.9134	0.8328
0.0030	1.6377	1.4835	1.3425	1.2137	1.1031	1.0026	0.9149	0.8348
0.0050	1.6455	1.4887	1.3456	1.2234	1.1091	1.0057	0.9166	0.8359
0.0070	1.6650	1.5022	1.3586	1.2347	1.1197	1.0125	0.9224	0.8409
0.0090	1.6712	1.5053	1.3600	1.2365	1.1209	1.0155	0.9236	0.8441
0.0110	1.6736	1.5081	1.3605	1.2375	1.1233	1.0174	0.9256	0.8458
0.0130	1.6800	1.5137	1.3648	1.2428	1.1258	1.0189	0.9280	0.8473
0.0150	1.6868	1.5235	1.3733	1.2502	1.1312	1.0228	0.9307	0.8496

Table 4. Coefficients of Equation 6 for the Viscosity of $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + CH_3OH (2) and $C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + C_2H_5OH (3) from T = (278.15 to 313.15) K as a Function of Mass Mole Concentration c

c				
(mol·kg^{-1})	a	b	residual sum of squares	R-square
		$C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + CH_3OH (2)		
0.0000	3.0037	−0.00818	0.00049	0.9919
0.0010	3.0109	−0.00820	0.00053	0.9914
0.0030	3.0137	−0.00820	0.00053	0.9913
0.0050	3.0286	−0.00824	0.00049	0.9921
0.0070	3.0409	−0.00828	0.00051	0.9918
0.0090	3.0521	−0.00831	0.00052	0.9917
0.0110	3.0460	−0.00826	0.00052	0.9917
0.0130	3.0743	−0.00838	0.00055	0.9913
0.0150	3.0663	−0.00840	0.00055	0.9913
		$C_{16}H_{16}ClNO_2S \cdot H_2SO_4$ (1) + C_2H_5OH (3)		
0.0000	7.9070	−0.02274	0.00065	0.9861
0.0010	7.8960	−0.02269	0.00070	0.9850
0.0030	7.9444	−0.02284	0.00070	0.9853
0.0050	7.9974	−0.02300	0.00066	0.9862
0.0070	8.1205	−0.02338	0.00070	0.9860
0.0090	8.1407	−0.02344	0.00075	0.9850
0.0110	8.1461	−0.02346	0.00077	0.9847
0.0130	8.1920	−0.02360	0.00078	0.9847
0.0150	8.2563	−0.02380	0.00074	0.9857

centain concentrations. Coefficients of the equations were determined, and the equations could describe the relationship very well.

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