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The thermodynamic studies of substituted heterocyclic compound in 1,4 dioxane system in the temperature range 303 to 323K

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Abstract

Densities, viscosities of some substituted heterocyclic drug (Ramipril) in 1, 4 dioxane were measured in the temperature range 303K to 323K. The viscosity was determined by John–Dole equation. The data has been used to calculate Gibb's free energy change (ΔG), entropy change (ΔS), and enthalpy change (ΔH). ΔG and ΔH are negative and ΔS is positive which indicates the spontaneity of reaction according to thermodynamics.

Key word: Viscosity, thermodynamic parameters, substituted heterocyclic compounds.

Introduction

The substituted heterocyclic drug (2S, 3aS, 6aS)-1-[(2S)-2-{[(2S)-1-ethoxy-1-oxo-4-phenylbutan-2-yl] amino} propanoyl]-octahydrocyclopenta[b]pyrrole-2-carboxylicacid (Ramipril). Ramipril is beneficial for cardiovascular events and overt nephropathy in people with diabetes[1]. Ramipril used in kidney diseases[2].

The thermodynamic properties of solution are important in chemistry and biology. Studies of the viscosities of such solutions were among the earliest in the field of solution chemistry Cveto Klofular *et.al.* have been studied the activation Gibb's free energy, entropy and enthalpy change by measuring the viscosity of aqueous solution of tetramethyl, tetraethyl, tetra n-propyl, tetran-butyl and tetran-pentyl ammonium cyclohexa sulfamate in the temperature range 293.15 to 323.15 K[4]. Sondawale have also studied the viscosity at different temperature using 20% dioxane-water and methanol-water mixture[3]. Agrawal *et.al.* have been studied the thermodynamic parameters from viscosity measurements of ligand in 70% dioxane –water mixture at different temperature[4]. Brent Hawrylak *et. al*. have studied the enthalpy of activation, Gibb's free energy of activation and entropy of activation of mixture of isomeric butandiols with water in the temperature range 25°C to 45°C [5]. Kapadi *et.al*. have studied

the thermodynamic interaction of 2,3 butanediol in water in the temperature range 303.15 t 318.15 K[6]. Man chai Change[7] has studied the viscosity and thermodynamic parameters of liquid sulfur in temperature range 430K to 650 K. He also studied the equilibrium between sulfur-halogen systems by equilibrium equation. Syal[8] *et.al*. has been studied the ultrasonic velocity and viscosity of PEG-8000, PEG- study of acoustical properties, viscosity coefficient of substituted heterocyclic compounds under suitable condition.

Therefore the present work is undertaken to make the systematic study of above substituted heterocyclic drug viscometrically at temperature range 303 K. to 323 K. From viscosity measurements we planned to study thermodynamic parameters.

Experimental

The present work is a continuation of our systematic experimental studies on the thermodynamic properties of the substituted heterocyclic drug Ramipril. 1, 4 Dioxane was purified by Vogel's standard method[8]. All reagent and chemicals used in this work from Aldrich sigma (A.R. grade). The double distilled dioxane was used for preparation of drug solution. The density measurements of the pure solvent and the solutions were performed by means of an Anton Paar DMA 5000 automatic density meter with a precision of $\pm 1 \times 10^{-6}$ g cm^{-3}, between 303.00 and 323.00 K. The viscometer put in double wall glass cell. For viscosity measurement Ostwald viscometer (10 ml) was used. The constant temperature was maintained by circulating water through the double wall measuring cell, made up of glass. The flow time was also measured by using digital clock (0.01 Sec).

Theory :

The relationship between coefficient of viscosity of liquid and temperature is mathematically given by equation.

$$\eta_r = A \cdot e^{-\Delta G / RT} \quad (1)$$

The thermodynamic parameters were calculated by using following equations

$$\Delta G = - 2.303 \text{ R x Slope} \quad (2)$$

$$\log \eta_{r2} / \eta_{r1} = [\Delta H / 2.303R] [T_2 - T_1 / T_1 T_2] \quad (3)$$

$$\Delta S = (\Delta H - \Delta G) / T \quad (4)$$

Result and Discussion

The rise of the temperature is accompanied by a decrease of the viscosity of the solution. The rise of the temperature is accompanied by a decrease of the density of the solution. The table 1 shows values of viscosity and density at different temperature. The thermodynamic functions of viscous flow were estimated from the dynamic Viscosity values. Flow process is governed by the ability of molecule to move into the prepared hole and the readiness with which the holes are prepared in the liquid.

The values of Gibb's free energy were calculated from the slope of graph by plotting logη Vs 1/T (Fig. 1). The values of Gibb's free energy were determine by using equation (2) are given in table 2. The values of Gibb's free energy are negative in all systems. The values of enthalpy change in reaction were determined by using equation (3). The values of enthalpy is also negative in all systems. From the values of ΔG and ΔH, the reaction is

Table 1. Viscosity measurements at various temperatures

Temp.	1/T	Density (Kg/m^3)	Time (Sec.)	η_r	$\log\eta_r$
Ramipril + 1,4 dioxane					
303	$3.3003x10^{-3}$	1.0214	150	1.3604	0.1337
308	$3.2468x10^{-3}$	1.0158	135	1.3041	0.1153
313	$3.1949x10^{-3}$	1.0101	127	1.1658	0.0666
318	$3.1447x10^{-3}$	1.0045	119	1.0592	0.0250
323	$3.0960x10^{-3}$	0.9988	112	0.8664	-0.0623

Table 2. Values of thermodynamic parameters

Systems	ΔG (J $mole^{-1}$ K^{-1})	ΔH (J $mole^{-1}$ K^{-1})	ΔS (J K^{-1})
Ramipril + 1,4 dioxane	-17990.80	-12170.48	18.5954

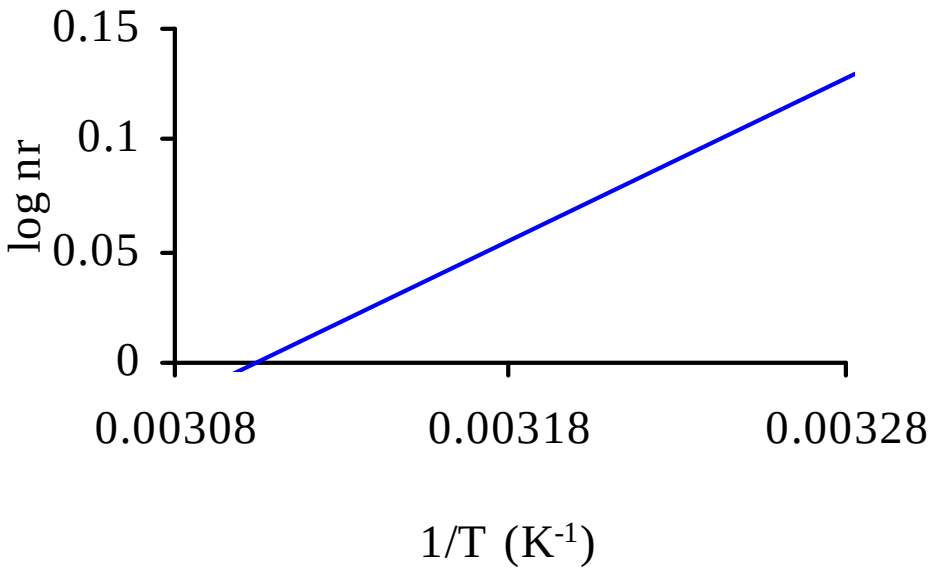

Fig. 1. Plots of log nr Vs 1/T for substituted heterocyclic cmpounds in 1,4 dioxane

spontaneous and exothermic in nature. The values of entropy change were determined from equation (4). The positive value of entropy change indicates the reaction must be spontaneous process of flipping of molecule over each other. ΔS were positive due the destruction of hydrogen bond in compounds.

Conclusion

The viscous flow of these substituted heterocyclic drug in 1, 4 dioxane is thermodynamically spontaneous and exothermic process. Because ΔG and ΔH are negative and ΔS is positive which is indicate the spontaneity of reaction according to thermodynamics.

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