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Research Article

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Thermodynamic and Viscometric Study of Coumarin Derivatives In 70% Ethanol-Water and Dioxane Water Solvent

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ABSTRACT

Viscosity measurement of coumarin derivatives were carried out in different percentage of binary solvent mixture. The study was implemented for several variation in concentration of solute as well as variation in temperature. The value of coefficient A and β was calculated from Jones Dole equation. The viscometric and thermodynamic parameters enthalpy, entropy and Gibbs' free energy were also evaluated. The data obtained have been used to compute molecular interactions either solute-solute or solute-solvent and structure making/breaking ability of component in binary solvent mixture.

Keywords: Viscosity; Thermodynamic parameter; Coumarin derivative; Molecular interaction

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INTRODUCTION

For decades medicinal chemists explore interesting pharmacological properties of the natural coumarins or synthetic analogs for their applicability as drugs. In pharmacodynamics coumarin and its derivatives represen possess wide spectrum of biological activity [1-3]. Coumarin can be synthesized by pechmann reaction, perkin reaction or by knoevenagel condensation [4]. Coumarines as a family of molecules, exhibit a wide range of fluorescences emission properties. Effect of viscosity and polarity of solvent of fluorescent coumarin derivatives was also studied [5-7]. Coumarin derivatives have been found to have numerous therapeutic applications including photochemotherapy, antitumor, anti-HIV therapy and antibreast cancer potential [8]. Some coumarin based drugs such as anticoagulant and antineurodegenerative agents have been extensively used in clinic. Recently in medicinal chemistry coumarin compounds wre used as anticoagulant, antineurodegenerative, anticancer, antioxidative, antibacterial, antifungal, antiviral, antiparasitic, antiinflammatory and analgesic, antidiabetic, antidepressive and other bioactive agents as well as supramolecular medicinal drugs, diagnostic agents, pathologic probes and biological stains [9].

Viscosity is the measure of the level of resistance to flow of liquid. Viscosity measurement like other transport properties of electrolyte provides useful information about solute-solute and solute -solvent interaction [10-12]. This study has been used to interpret the applicability of synthesized derivative in pharmacodynaics and pharmacokinetics activity.

Many molecules based on the coumarin ring system have been synthesized utilizing innovative synthetic techniques. Beside this applicability very few works have been carried out on viscosity and thermodynamic property of coumarin derivative at different temperature [13,14].

Keeping in view their biological activities, some new coumarin derivatives were synthesized. Present work deals with the study, viscometric and thermodynamic study of coumarin derivative was carried out. From the effect of temperature, the density, relative viscosity and value of thermodynamic parameters like change in free energy (ΔG), enthalpy (ΔH) and entropy (ΔS) was calculated. It gives very important information about change in viscosity with temperature.

EXPERIMENTAL SECTION

The binary mixture of 70% dioxane-water and 70% ethanol-water was prepared gravimetrically in stoppard bottle. The densities of pure liquids and their binary mixtures were measured using single capillary pycnometer. The accuracy of density measurements was within 0.1% kg m^{-3}. Viscosity of pure liquids and their binary mixtures was measured using Ostwalds viscometer calibrated with double distilled water. The thermodynamic measurement was carried out in thermostat. The viscometer containing test liquid was allowed to stand for about 30 min thermostatic bath. From the observation density, relative and specific viscosity can be calculated for all the coumarin derivative in both the solvent. Viscosity data were analyzed in the light of Jones-Dole equation.

$$\eta_{sp} = A + \beta\sqrt{C}$$

Where A and β are the Falkenhagen and the Jones-Dole coefficients.

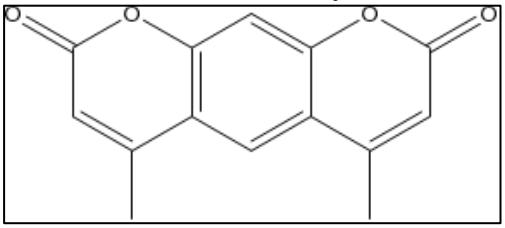
The graph was plotted between verses √ and the value of coefficient 'A' which is the measure of solute– solute interactions and 'β' which is the measure of solute–solvent interactions was calculated.

The present study deals with the viscometric measurement of coumarin derivative 4,6-dimethyl-2H,8H-pyrano[3,2-g]chromene-2,8-dione (L_1) and Ethyl (Z)-2-((4,7-dimethyl-2,9-dioxo-2,9-dihydropyrano[3,2-h]chromen-5-yl)methylene)-3-oxobutanoate (L_2) at 318 K, 328 K and 338 K in binary solvent mixture. Also the value of change in energy (ΔG), enthalpy (ΔH) and entropy (ΔS) were calculated at different temperature.

Synthesis of coumarin derivative

Synthesis of 4,6-dimethyl-2H,8H-pyrano[3,2-g]chromene-2,8-dione (L_1):

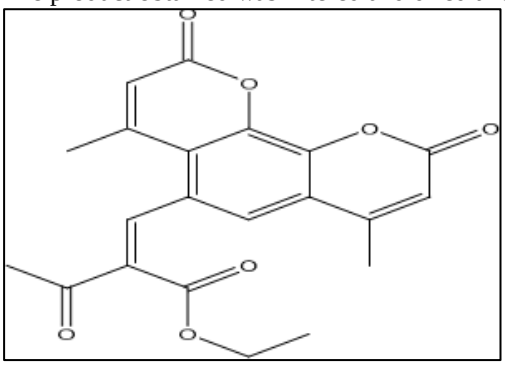
The mixture of 1:2 mole resorcinol and ethylacetoacetate was added in 7 ml of H_2SO_4 which was kept in ice bath (0-5° C) drop by drop with constant stirring. Then the reaction mixture was kept at 0-5°C in a freezer. After 12 hours the reaction, completion of the reaction was monitored by TLC. The reaction mixture was pour into ice cold water. The product obtained was filtered and dried and recrystallized with ethanol.



4,6-dimethyl-2H,8H-pyrano[3,2-g]chromene-2,8-dione

Ethyl (Z)-2-((4,7-dimethyl-2,9-dioxo-2,9-dihydropyrano[3,2-h]chromen-5-yl)methylene) 3-oxobutanoate (L2):

The mixture of 1:3 mole 3,4-dihydroxy benzaldehyde and ethyl acetoacetate was poured in the 7 ml H_2SO_4 which was kept in ice bath (0-5° C) drop by drop with constant stirring. Then the reaction mixture was kept at 0-5°C in a freezer. After 12 hours the reaction mixture was pour into ice cold water. Completion of the reaction was monitored by TLC. The product obtained was filtered and dried and recrystalyzed with ethanol.



Ethyl (Z)-2-((4,7-dimethyl-2,9-dioxo-2,9-dihydropyrano[3,2-h]chromen-5-yl)methylene)-3-oxobutanoate

RESULT AND DISCUSSION

Viscometric study with variation in concentration

Viscometric study of synthesized coumarin derivative L_1 and L_2 at different concentration using 70% dioxane-water system and 70% ethanol-water system as a solvent have been prepared in table 1. The data obtained were used to calculate relative viscosity and density of coumarin derivatives. The relative viscosity decreases in both the solvent shows weak solute-solvent interaction also it decreases with decrease in concentration. The plot between η_{sp} and $\sqrt{C}$ shows a linear graph which shows the validity of Jones-Dole equation for all the tested ligand [15]. The slope of this graph shows the value of β-coefficient and intercept gives the value of coefficient A.

Table 1: Viscometric study with variation in concentration

System	Temp (K)	Conc. (M)	Medium- Dioxane water					Medium-Ethanol-water				
			Density	Relative Viscosity ηr	Specific Viscosity	A	β	Density	Relative Viscosity ηr	Specific Viscosity	A	β
L1	303	0.001	1.025	1.986	31.806			0.9797	1.833	26.87		
		0.0005	1.02	1.823	37.4	57.18	-841.8	0.9662	1.705	32.04	74.58	-1652.97
		0.0001	1.015	1.493	49.3			0.9542	1.605	60.7		
L2	303	0.001	1.012	1.934	30.12			0.9622	1.757	24.41		
		0.0005	1.011	1.785	35.68	60.13	-1009.55	0.9597	1.672	30.54	75.18	-1750.72
		0.0001	1.01	1.51	51			0.9514	1.603	60.3		

It was observed from table 1 that the values of A are positive in both the solvent for L_1 and L_2 shows strong solute–solute interaction. Again the values A are more positive in ethanol-water as compare to dioxane-water medium. On the other hand the value of β-coefficient is negative shows weak solute–solvent interaction which indicates the good drug activity which is in favors of pharmacodynamics and pharmacokinetics activity [16]. The value of β-coefficient is more negative in ethanol-water may be due to strong hydrogen bonding and it is more negative for L_2 shows weak solute-solvent interaction so it gets easily adsorbed. These different results for all the tested ligands may be due to different polarity index of solvent dioxane and ethanol [17].

Viscometric study with variation in temperature

The viscosity was determined at different temperature were used to evaluate thermodynamic parameters like enthalpy change, entropy change and free energy change for coumarin derivative of two different ligands, using 70% dioxane-water system and 70% ethanol-water system as a solvent. The relative viscosity of a liquid generally decreases with rise in temperature in both the solvent (table 2 and table 3). The graph was plotted between log η_r and 1/T which gives the straight line with positive value of slope. The various thermodynamic parameters were calculated by using following expression and the result obtained were computed in table 4.

$\Delta G = -2.303\ R \times slope$

$$log\eta_1 - log\eta_2 = \frac{\Delta H}{2.303}\left[\frac{1}{T_1} - \frac{1}{T_2}\right]$$

$$\Delta S = \frac{\Delta H - \Delta G}{T}$$

Table 2: Viscometric study with variation in temperature (medium – Dioxane-water)

System	Conc. (M)	Temp (K)	1 / T (K^{-1}) × 10^{-3}	Time flow (sec.)	Relative Viscosity ηr	Log (ηr)
L_1	0.001	318	3.15 ×10^{-3}	50	0.8771	-0.057
		328	3.05 × 10^{-3}	47	0.799	-0.097
		338	2.96 × 10^{-3}	44	0.726	-0.137
	0.0005	318	3.15 ×10^{-3}	49	0.86	-0.065
		328	3.05 × 10^{-3}	45	0.766	-0.115
		338	2.96 × 10^{-3}	41	0.676	-0.17
	0.0001	318	3.15 ×10^{-3}	49	0.8343	-0.078
		328	3.05 × 10^{-3}	46	0.7606	-0.118
		338	2.96 × 10^{-3}	37	0.5931	-0.226
L_2	0.001	318	3.15 ×10^{-3}	47	0.798	-0.0979
		328	3.05 × 10^{-3}	46	0.78	-0.108
		338	2.96 × 10^{-3}	40	0.677	-0.169
	0.0005	318	3.15 ×10^{-3}	44	0.773	-0.111
		328	3.05 × 10^{-3}	42	0.706	-0.151
		338	2.96 × 10^{-3}	40	0.652	-0.185
	0.0001	318	3.15 ×10^{-3}	43	0.75	-0.125
		328	3.05 × 10^{-3}	36	0.612	-0.213
		338	2.96 × 10^{-3}	31	0.509	-0.293

Table No 3: Viscometric study with variation in temperature (medium – Ethanol-water)

System	Conc. (M)	Temp (K)	1 / T (K^{-1}) × 10^{-3}	Time flow (sec.)	Relative Viscosity ηr	Log (ηr)
L1	0.001	318	3.15 ×10^{-3}	79	1.301	0.1143
		328	3.05 × 10^{-3}	71	1.153	0.06183
		338	2.96 × 10^{-3}	69	1.107	0.0442
	0.0005	318	3.15 ×10^{-3}	72	1.191	0.0759
		328	3.05 × 10^{-3}	66	1.07	0.0293
		338	2.96 × 10^{-3}	63	1.014	0.00603
	0.0001	318	3.15 ×10^{-3}	66	1.075	0.0314
		328	3.05 × 10^{-3}	64	1.027	0.0116
		338	2.96 × 10^{-3}	62	0.977	-0.0101
L2	0.001	318	3.15 ×10^{-3}	61	0.968	-0.0141
		328	3.05 × 10^{-3}	59	0.952	-0.0213
		338	2.96 × 10^{-3}	58	0.949	-0.0227
	0.0005	318	3.15 ×10^{-3}	61	1.022	0.00945
		328	3.05 × 10^{-3}	60	0.985	-0.0066
		338	2.96 × 10^{-3}	58	0.932	-0.0306
	0.0001	318	3.15 ×10^{-3}	69	1.134	0.05461
		328	3.05 × 10^{-3}	63	1.013	0.00561
		338	2.96 × 10^{-3}	59	0.936	-0.0287

Table 4: Values of thermodynamic parameter

System	70% Dioxane-water			70% Ethanol-water			
	Conc. (M)	ΔG (J $mole^{-1}$)	ΔH (J $mole^{-1}$)	ΔS (J $mole^{-1}K^{-1}$)	ΔG (J $mole^{-1}$)	ΔH (J $mole^{-1}$)	ΔS (J $mole^{-1}K^{-1}$)
L1	0.001M	-8053.23	960.848	29.749	-7118.86	1260.39	27.654
	0.0005M	-10561.49	1404.26	39.4909	-7072.9	1119.34	27.0373
	0.0001M	-14779.57	2757.454	57.877	-4174.05	475.62	15.346
L2	0001M	-7057.584	242.6142	24.093	-8415.11	1177.04	31.657
	0.0005M	-7455.842	868.08	27.4717	-4015.15	384.589	14.521
	0.0001M	-16927.86	2042.558	62.6086	-874.259	173.914	2.0245

The values of thermodynamic parameter Gibbs free energy are negative shows spontaneous reaction between solute and solvent. Again value of ΔG is more negative in 70% dioxane water as compare to 70% ethanol-water solvent indicates strong interaction in dioxane water indicates the more hydrophobic nature of coumarin derivatives. The positive values of change in enthalpy indicate endothermic reaction. We know the entropy measure the randomness in the system. For all the tested ligand the values of entropy is positive shows the randomness of solute molecule in the solvent. In dioxane water the change in Gibbs free energy, enthalpy and change in entropy increases with increase in temperature while in ethanol water value of all thermodynamic parameters goes on decreasing shows the existence of solute solvent interaction.

CONCLUSION

In the present study, the relative viscosity of solution of coumarin derivatives decreases with decrease in concentration of solution. Positive value of A shows strong solute–solute interaction. On the other hand the value of β-coefficient is negative shows weak solute–solvent interaction which is in favors of pharmacodynamics and pharmacokinetics activity. Thermodynamic study shows negative value of Gibbs' free energy. It was observed that the values of ΔG are more negative in 70% dioxane-water indicates the more hydrophobic nature of coumarin derivatives. The positive values of change in enthalpy indicate endothermic reaction. For all the tested ligand the values of entropy is positive shows the randomness of solute molecule in the solvent. The value of thermodynamic parameters increases with increase in temperature in dioxane-water while in ethanol-water it goes on decreasing shows the existence of solute-solvent interaction. These different results for all the tested ligands may be due to different polarity index of solvent dioxane and ethanol

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