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EFFECT OF TEMPERATURE ON THERMODYNAMIC PARAMETER OF S-TRIAZINOTHIOCARBAMIDES IN 60% DIOXANE-WATER MIXTURE

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ABSTRACT

The drug absorption, transmission, activity and effect of drugs, structure making and breaking properties of ligands, solute-solute and solute-solvent interaction can be explain from thermodynamic parameters of drug. Taking all these things into consideration this research work was carried out. Thermodynamic study of recently synthesized drugs viz. 1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide (L_1), 1-(4-hydroxy-6-methyl)-S-triazino–3-ethylcarbamide (L_2), 1-(4-hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide (L_3), were carried out at 60% dioxane-water mixture at different temperature to investigate effect of structure, group on triazinothiocarbamides.

Key words: 60% Dioxane-water, 1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide, 1-(4-hydroxy-6-methyl)-S-triazino-3-ethylcarbamide,1-(4-hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide, Thermodynamic study.

INTRODUCTION

Viscosity is one of the physical properties of liquid, which measures viscous drug force between adjacent layers in the liquid. Viscosity is directly related to the absorption of drug and metabolic and physiological activity in the body. The structure making and breaking properties of liquids have been considered as a measure of solute-solute and solute-solvent interactions[1-3]. In the twentieth century, many researchers have find out the significance of triazino drugs. The heterocyclic compounds play an immense role in medicinal, pharmaceutical, industrial and biochemical field[4-6]. The drugs having S-triazino nucleus possess anti-tumor[7], anti-cancer[8,9], anti-bacterial[10-12], anti-inflammatory[13] properties. The viscosity is directly related to the thermodynamic parameters ΔG, ΔH and ΔS. The liquid possesses viscosity, which implies resistance to flow. Hence for studying the potency of recently synthesized drugs in this laboratory, the thermodynamic measurements of 1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide (L_1), 1-(4-hydroxy-6-methyl)-S-triazino-3-ethylthiocarbamide(L_2), 1-(4-hydroxy-6-methyl)-S-triazino-3-methylthio carbamides (L_3), were studied in 60% percentage dioxane-water composition at different temperature. This study becomes milestone in the drug medicinal, pharmaceutical of triazinothiocarbamides.

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EXPERIMENTAL

All the chemicals used of A.R grade and doubly distilled water was used. Weighing was made on Mechaniki Zaktady Precyzyjnej Gdansk balance made in Poland (± 0.001 g). Densities of solutions were determined by a bicapillary pyknometer (± 0.2%) having a bulb volume of about 10 cm^3 and capillary having an internal diameter of 1 mm and calibrated with deionised doubly distilled water. The accuracy of density measurements were within ± 0.1 Kg^{-3}. The viscosities were measured by means of Ostwald's viscometer thoroughly cleaned and dried. The viscometer was kept in Elite thermostatic water bath and temperature variation was maintained. For each measurement, sufficient time was allowed to attain thermal equilibrium between viscometer and water bath. The 0.1 M solution of ligand L_1, L_2 and L_3 were prepared in 60% dioxane-water mixture. The densities and viscosities of each ligand solution were at 20°C, 30°C, 40°C. The constant temperature was maintained with the help of elite thermostatic water bath (± 0.1°C). For each measurement, sufficient time was allowed to attain the thermal equilibrium.

RESULTS AND DISCUSSION

The present study deals with the viscosity investigation of ligand (L_1), ligand (L_2), ligand (L_3) in 60% dioxane-water mixture at different compositions and at 20°C, 30°C, 40°C. The data obtained have been used to determine the thermodynamic parameters ΔG, ΔH and ΔS. From this data, the structure breaking and making properties of liquids have been considered as a measure of solute-solute and solute-solvent interaction. The thermodynamic parameters were determined by measuring the viscosity at different temperatures.

Table 1: Determination of relative viscosities at 0.1 M concentration for ligand L_1, L_2 and L_3 at 60% dioxane-water mixture

Ligand	Temp. (°C)	Time sec.	Density ρ x 10^3 (Kg/m^3)	η_r
	20	451.98	1.0246	1.8465
L_1	30	370.70	1.0236	1.5529
	40	298.23	1.0228	1.3422
	20	415.15	1.03412	1.7118
L_2	30	392.49	1.03391	1.6607
	40	354.60	1.03380	1.6131
	20	527.43	1.03712	2.1810
L_3	30	473.62	1.036	2.0080
	40	403.46	1.03579	1.8385

Table 2: Determination of ΔG, ΔH and ΔS at 0.1 M concentration for ligand L_1, L_2 and L_3 at 60% dioxane-water mixture

Ligand	Temp. (°C)	ΔG KJ	ΔH $J.mole^{-3}K^{-1}$	ΔS $KJ.K^{-1}$
	20	-60688.69	12799.8212	-250.6857
L_1	30	-62317.78	11503.9080	-243.5154
	40	-63994.10	17670.6853	-260.7849

Cont…

Ligand	Temp. (°C)	ΔG KJ	ΔH J.mole^{-3}K^{-1}	ΔS KJ.K^{-1}
	20	-61499.91	2239.4732	-217.4292
L_2	30	-62487.29	2295.7116	-213.6995
	40	-64472.83	2741.1258	-214.6382
	20	-61090.40	6116.6796	-229.2583
L_3	30	-62966.00	6959.1256	-230.6618
	40	-64813.50	5610.2872	-224.8884

The relative viscosity of each solution during study was determined by formula depicted below :

$$\eta_r = \rho_s \times t_s / \rho_w \times t_w \quad \ldots(1)$$

Where, η_r = Relative viscosity of ligand solution.

ρ_s and ρ_w = Density of ligand solution and density of water.

t_s and t_w = Time of flow for ligand solution and water respectively.

The thermodynamic parameters can be evaluated from the following expressions,

$$\eta = \left(\frac{h\ No}{V}\right) \exp\left(\frac{-\Delta G}{RT}\right) \quad \ldots(2)$$

Where,

h is Plank's number,

No is Avogadro's number,

R is Gas constant,

T is Temperature in Kelvin and

ΔG is Standard free energy of activation

$$\left(\frac{\delta \ln n_r}{\delta (1/T)}\right)_p = \frac{\Delta H}{R} \quad \ldots(3)$$

Where,

ΔH is Enthalpy change of activation process and

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

Where,

ΔS is Entropy of activation.

Few researchers have studied the viscosities at different temperature and evaluated the thermodynamic parameters.[14-18] In the present work, 0.1 M solution of 1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide (L_1), 1-(4-hydroxy-6-methyl)-S-triazino-3-ethylthiocarbamide(L_2), 1-(4-hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide (L_3) in 70% dioxane-water mixture were subjected to viscosity measurement at 20°C, 30°C, 40°C. The values of viscosities are depicted in Table 1.

From the Table 1, it is also observed that viscosities of all the ligand solutions have direct correlation with temperature. This correlation favors 'hole theory' of liquid. The liquid molecules keep on moving continuously into vacancies. The motion of liquid molecules need some energy to move into hole. At increasing temperature, the energy becomes increasingly available and so a liquid can flow more easily. Thus, the viscosity falls appreciably with rise in temperature. At the same time when the temperature increases the intermolecular force of attraction in the ligand also decreases this will directly affect the viscosity. This shows decrease in solute-solvent interactions which is the best property of drug. It means that triazino or thiocarbamido nucleus containing drugs which are newly synthesized possess best drug activity and drug effect which is very advantageous. Also, the decrease is appreciable being about ten percentage degree rise of temperature. The negative ΔG values indicate the spontaneity of reaction which is clear from the values in Table 2.

From the values of L_1, L_2 and L_3, it was observed that, the value of relative viscosity of L_3 is greater than L_2 and L_1. Only the bulkiness of the group as substituent not only interfere the values of relative viscosity but the reactivity and stability and tautomeric properties also interfere the values of relative viscosities. It is clear from the result that, in L_1 there is a resonance stabilization in the benzene ring, while S-triazino moiety which restrict the tautomeric changes in the molecule for L_1 while in case of L_2, S-triazine and ethyl group is substituted. A methylenic group in ethyl moiety becomes more reactive which directly and easily involved in tautomeric conversion of whole molecule. Such type of greater interference of methyl will not involved in L_3 but when we compare, relative viscosity of L_1 and L_3, the relative viscosity of bulkier group must be greater but in this investigation, the relative viscosity of L_3 is greater than that of L_1, this may be due to the donating capacity of $-CH_3$ group to the thiocarbamido molecule. As the thiocarbamido molecule is highly electron rich moiety and $-CH_3$ group is also electron donating group, hence in L_3 molecule there occur compactness in the bond which is greater than L_1 molecule.

From this discussion, it is clear that bulky substituent on the molecule is not only factor in trend of relative viscosity but tautomeric conversion as well as electron donating nature, electron clouds, nature of hetero atom present in ligands and the compactness in the molecule will directly hampered results and trends in the relative viscosity. So ligand with lower viscosity shows good results at higher temperature which favors the concept of pharmacokinetics and pharmacodynamics in pharmaceutical field.

CONCLUSION

Hence from the above discussion, it was clear that bulky substituent on the molecule was not only factor in trend but tautomeric conversion as well as electron donating nature, electron clouds, nature of hetero atom present in compounds and compactness in the molecule will directly hampered results and trends in the molar refraction. It means that at 60% percentage of dioxane, the solute-solvent interactions i.e. interaction of compounds (drugs) and dioxane shows good results with rise in temperature, which may be stabilize the drug activity. From this it can be concluded that the drug absorption, drug transmission and drug effect of compounds L_1, L_2, L_3 is more effective at higher temperature of dioxane. This study may become a milestone in the drug, medicinal and pharmaceutical chemistry of triazino thiocarbamides.

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