

EFFECT OF TEMPERATURE ON VISCOSITY OF S-SUBSTITUTED TRIAZINOTHIOCARBAMIDES IN 60% DIOXANE WATER MIXTURE

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Abstract:

S-triazine and thiocarbamide group containing drug create their own identity in the drug, pharmaceutical and medicinal sciences in last four decades. Hence, the viscometric measurements of recently synthesized drugs viz. 1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide (L₁) and 1-(4-hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide (L₂), were carried out at 60% various percentage of solvent to investigate effect of structure, on group of S-triazinothiocarbamides. The result obtained during this investigation directly through light on the dipole association of compound, intermolecular attraction between solute and solvent, dielectric constant of medium, polarizability and mutual compensation of dipoles and useful for drug absorption, transmission, stability, activity and effect of drug.

Keywords:

1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide (L_1) and 1-(4-hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide (L_2), dioxane-water mixture, viscometric measurements.

Introduction:

The information regarding the transport property of drugs and the ion solvent interactions can be obtained from viscometric measurements. Viscosity measurement provides useful information about solute-solute and solute-solvent interactions. These interactions have been studied in aqueous and non aqueous solutions by many workers [1-3]. These interactions of electrolyte in binary mixtures of two liquids have been studied in terms of β -coefficient of viscosity [4-6]. Drug action has been widely recognized to be the ultimate consequence of physicochemical interactions between the drug and receptor. Drug receptors are the enzymes and directly hamper the drug activity and drug effects. It makes direct or indirect physical and chemical reactions with drug i.e. solute-solute interactions in the presence of solvent which changes viscosity of the phase during drug action and before testing and applying that drug to the patients, drug activity and drug effect must be evaluated. Most of the modern drugs contain heterocyclic nucleus [7, 8]. S-triazino and thiocarbamido nucleus containing drugs create its own identity and significance in the medicinal, drug [9-11] and pharmaceutical chemistry [12-18], biochemical fields [19-28]. Hence for studying the potency of recently synthesized drugs in this laboratory, the viscosity measurements of 1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide (L_1) and 1-(4-hydroxy-6-methyl)-S-triazino-3-methylthiocarbamides (L_2) were studied at various temperatures.

Experimental:

The entire chemical used of A.R. grade and doubly distilled water was used. All weighing were made on Mechaniki Zaktady Preczyzing Gdansk Balance [Poland make, (± 0.001 g)]. The density of solutions were determined by a bicapillary Pyknometer ($\pm 0.2\%$) having a bulb volume of about 10 cm^3 and capillary having an internal diameter of 1mm and calibrated with deionised doubly distilled water. The accuracy of density measurements were within $\pm 0.1\text{K.gm}^{-3}$. 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 at 25°C , 30°C and 35°C (± 0.1) for each measurement, sufficient time was allowed to attain thermal equilibrium between viscometer and water bath.

Observations and Calculations:

The present study deals with the viscosity investigation of Ligand (L_1) and Ligand (L_2) in 60% dioxane–water mixture at different compositions at 25°C , 30°C and 35°C respectively. The viscometric readings were taken as described in literature [29]. The results obtained were mentioned in Table 1-2. A and β -coefficient values calculated in Table 3.

**Determination of Relative and Specific Viscosities at Different Concentrations for 60% in
 Dioxane-Water mixture:**

A] For Ligand L₁

Table-1

Temperature T (°C)	Conc. (M)	Time flow t (sec)	Density $\rho \times 10^3$ (Kg.m ⁻³)	Relative Viscosity η_r	Specific Viscosity $\eta_{sp} = \eta_r - 1$	$\eta_r - 1/\sqrt{C}$
25	0.100	433.80	1.024	1.5864	0.7864	2.48682
	0.075	410.77	1.0238	1.4912	0.6912	2.52391
	0.056	394.24	1.0234	1.4225	0.6225	2.63054
	0.042	376.82	1.0230	1.3502	0.5502	2.68470
30	0.100	370.70	1.0236	1.5529	0.5529	1.74842
	0.075	357.76	1.0234	1.4984	0.4984	1.81990
	0.056	343.96	1.0231	1.4402	0.4402	1.86018
	0.042	334.12	1.0228	1.3986	0.3986	1.94497
35	0.100	330.34	1.0232	1.4176	0.4176	1.32057
	0.075	330.17	1.0229	1.4165	0.4165	1.52084
	0.056	319.40	1.0222	1.3693	0.3693	1.56058
	0.042	313.72	1.0218	1.3445	0.3445	1.68099

B] For Ligand L₂

Table-2

Temperature T (°C)	Conc. (M)	Time flow t (sec)	Density $\rho \times 10^3$ (Kg.m⁻³)	Relative Viscosity η_r	Specific Viscosity $\eta_{sp} = \eta_r - 1$	$\eta_r - 1/\sqrt{C}$
25	0.100	501.67	1.03682	2.0917	1.0917	3.45226
	0.075	471.36	1.03104	1.95440	0.95440	3.48498
	0.056	446.64	1.02754	1.84560	0.84560	3.57331
	0.042	422.98	1.0241	1.74200	0.74200	3.62059
30	0.100	473.62	1.03600	2.00800	1.00800	3.18758
	0.075	472.59	1.03300	1.99783	0.99783	3.64356
	0.056	447.44	1.02900	1.88420	0.88420	3.73643
	0.042	430.18	1.02400	1.80272	0.80272	3.91687
35	0.100	447.36	1.03588	1.9436	0.9436	2.98393
	0.075	428.63	1.03212	1.8555	0.8555	3.12384
	0.056	404.43	1.02845	1.7445	0.7445	3.14609
	0.042	385.60	1.02382	1.6558	0.6558	3.19998

Plot between $\sqrt{C} \times 10^{-2}$ Vs $\eta_r - 1/\sqrt{C}$ for Ligand L_1 and L_2 in 60%, Dioxane-Water mixture

Fig. - 1. L_1 in 60%D-W at 25°C

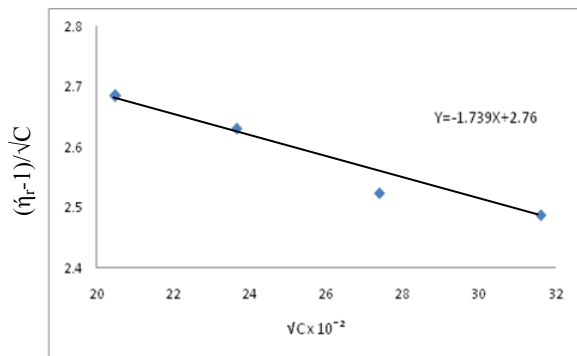


Fig. - 2. L_1 in 60%D-W at 30°C

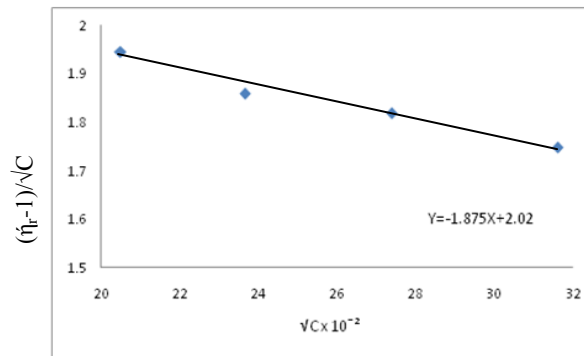


Fig. - 3. L_1 in 60%D-W at 35°C

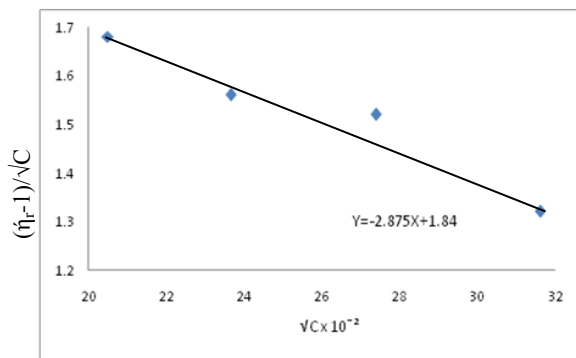


Fig. - 4. L_2 in 60%D-W at 25°C



Fig. - 5. L_2 in 60%D-W at 30°C

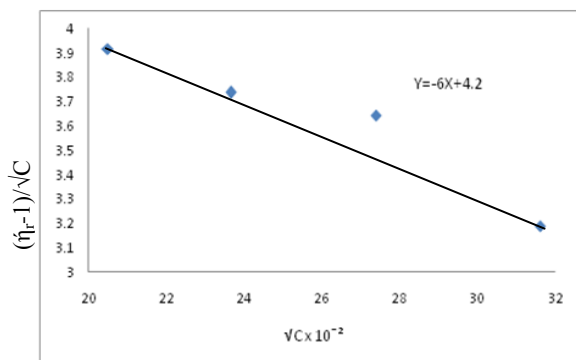


Fig. - 6. L_2 in 60%D-W at 35°C

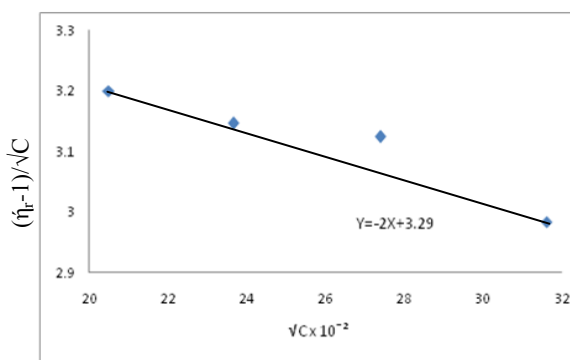


Table-3 – A and β Coefficient value in 60% Dioxane-Water mixture at 25°C, 30°C and 35°C

Ligand	Temperature (°C)	A- coefficient	β- coefficient
L ₁	25	2.76	-1.7390
	30	2.02	-1.8750
	35	1.84	-2.8750
L ₂	25	3.68	-1.5714
	30	4.2	-6.0000
	35	3.29	-2.0000

Result and Discussion:

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

$$\eta_r = D_s \times t_s / D_w \times t_w \quad \text{----- (1)}$$

Where, η_r = Relative viscosity of ligand solution

D_s and D_w = Density of ligand solution and water

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

And the relative viscosities have been analyzed by Jone’s-Dole equation [29],

$$(\eta_r - 1)\sqrt{C} = A + \beta\sqrt{C} \quad \text{----- (2)}$$

Where, C-is molar concentration of the ligand solution.

A-is the Falkenhagen coefficient

β-is the Jones’s –Dole coefficient

The graphs are plotted between \sqrt{C} versus $\sqrt{(\eta_r - 1)/\sqrt{C}}$. The graph for each system gave linear straight line showing validity of Jones's -Dole equation. The slope of straight line gave value of β coefficient.

In the present work, non specific solute-solvent association caused by the dielectric enrichment in the solvent shell of solute takes place resulting weak molecular interaction. The presence of weak solute-solvent interaction may be due to strong hydrogen bonding is present and in a dilute solution, solute molecules can disrupt this H-bonding to lesser extent.

From the results, it is observed that, the concentration of ligand is directly proportional to density and relative viscosity for ligand L_1 and L_2 at temperature 25°C , 30°C and 35°C for 60% dioxane-water mixture. This may be due to the weak solvation effect which interprets weak molecule interaction.

In this investigation, the value of relative viscosity of L_2 is greater than L_1 . 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 but when we compare, relative viscosity of L_1 and L_2 , the relative viscosity of bulkier group must be greater this may be due to the donating capacity of $-\text{CH}_3$ group to the thiocarbamido molecule. As the thiocarbamido molecule is highly electron rich moiety and $-\text{CH}_3$ group is also electron donating group, hence in L_2 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 the reactivity and stability and 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.

The negative values of “A” and β -coefficient characterized as ‘structure-breaker’ indicating a weak solute-solvent interaction which is good for interactions in between the drug and the drug receptors shows best drug activity and drug effect and it favors pharmacokinetics and pharmacodynamics of drug. At the same time, both ligands are hydrophilic in nature and they disrupted the hydrogen bonding in the mixture of solvent causing lesser molecular interaction. Thus, these factors plays important role during designing of any drug. The value of A coefficient show that, the solute-solvent interaction is highest among the molecules of ligand L₂ at 30°C for 60% Dioxane-water mixture and so they tend to interact with solvent molecules to lesser extent leading decrease in solute-solvent interaction.

From the table, it is observed that, the temperature of solution is inversely proportional to the density and relative viscosity for ligand L₁, L₂ at all concentration. It is due to the temperature increase, randomness of solute molecule in solution also increases shows weak the molecular interactions.

Finally we can predict that, both compounds are suitable at lower concentration and higher temperature in 60% dioxane-water mixture medium. Out of which phenyl substituted thiocarbamide plays important role in drug synthesis and drug designing process 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 when the temperature of dioxane increases, weak solute-solvent interactions i.e. interaction of compounds (drugs) and

dioxane increases, which may be stabilize the drug activity. From this it can be concluded that the drug absorption, drug transmission and drug effect of compounds L₁, L₂ 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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