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Refractrometry Study of S-Trizinothiocarbamides in Different Percentage of 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. Refractrometric measurements of recently synthesized drugs viz. 1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide (L1) is carried out at various percentage composition of solvent and at different temperatures to investigate effects of structure, groups on S-triazino thiocarbamides. The data and the results obtained during this investigation gave detail information regarding drug absorption, transmissions activity and effect of these drugs. This study explores the potency of newly synthesized drugs, stability of drug and also to renovate and modify the traditional drugs which are used by medicinal practioners. Taking all these things in to consideration this research work was carried out.

Index Terms- 1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamides, Dioxane-Water mixture, Refractrometry study.

I. Introduction

One of a unique and important property of liquid is refractive index. When a ray of light passes from less dense to denser medium then there is a change in the direction of refraction and also angle of refraction changes and ultimately the refractive index changed. The result obtained during this investigation directly through light on the dipole association of ligand, intermolecular attraction between solute and solvent, dielectric constant of medium, polarizability and mutual compensation of dipoles. These results are much more useful for transmission, stability, activity and effect of drug hence this study is essential. Pharmaceutical, medicinal and biochemical literature survey reveals that S-triazino and thiocarbamido nucleus containing drugs have their own identity in drug chemistry. Many of them are used as drugs as muscle relaxant[1], hypoglycemic agent[2], blood pressure depressant[3], anti-diabetic drug[4]. With the development in medical field, it is reported that the drug having S-triazino nucleus possess anti-tumor properties[5-6], anti-bacterial[7-9], anti-inflammetry[10] and anti-cancer properties[11]. These drugs were also be used as hormone antagonists[12] and antipsychotic agent[13]. The S-triazino compounds possess their own identity and also play an immense role in industrial[14] fields. Results of refractometric measurements directly gave information regarding solute-solvent, solvent-solvent interactions. Taking all these things into consideration the present investigation was carried out in various percentage compositions and at different temperatures. This is hither to unknown. This study becomes milestone in the drug, medicinal, pharmaceutical of triazinothiocarbamido molecules.

II. Experimental

The 0.1M solution of ligand in different percentage of dioxane-water and the solutions of different concentration of ligands in 60%, 70% and 80% dioxane-water mixture were prepared. All weighing were made on Mechaniki Zaktady Precyzying Gdansk Balance [Poland make, (±0.001gm)]. The densities of solutions were determined by a bicapillary Pyknometer (±0.2%) having a bulb volume of about 10cm^3 and capillary having an internal diameter of 1mm. The refractive indices of solvent mixture and solutions were measured by Abbe's refractometer (±0.001). The temperature of the prism box was maintained at 27°C. Initially, the refractometer was calibrated with glass piece (n=1.5220) provided with the instrument.

III. Observation and Calculation

The present work deals with the study of molar refraction and polarizability constant of ligand (L_1) in 60%, 70% and 80% dioxane-water mixtures at different composition at different temperatures. The data obtained have been used to compute intermolecular interactions. The refractometric reading were taken as described in literature.

Table No. I- Molar Refraction of Different Percentage of Dioxane - Water Mixture	
% of Dioxane-Water Mixture	**Molar Refraction (RM) (cm^3 . $Mole^{-1}$)**
100	21.5977
90	15.4584
80	11.9390
70	9.6554
60	8.0551

Determination of Molar Refraction and Polarizability Constant at Different Concentrations and Temperature for 60%,70% and 80% of Dioxane-Water Mixture

Table No. II For L_1 at 60% D-W Mixture

Temp (°C)	Concentration (M)	Density $\rho x10^3$ ($kg.cm^{-3}$)	Refractive Index η	R_{mix} ($cm^3.mole^{-1)}$	R_{Ligand} ($cm^3.mole^{-1}$)	$\alpha x10^{-23}$ (cm^3)
20	0.1000	1.0246	1.4110	8.8577	0.8026	0.03180
	0.0750	1.0243	1.4102	8.7976	0.7425	0.02942
	0.0560	1.0241	1.4098	8.7556	0.7005	0.02776
	0.0420	1.0239	1.4088	8.7059	0.6508	0.02579
30	0.1000	1.0236	1.4102	8.8427	0.7876	0.03121
	0.0750	1.0234	1.4082	8.7597	0.7046	0.02796
	0.0560	1.0231	1.4070	8.7029	0.6478	0.02567
	0.0420	1.0228	1.4052	8.6385	0.5834	0.02312
40	0.1000	1.0228	1.4084	8.8086	0.7535	0.02986
	0.0750	1.0224	1.4072	8.7408	0.6857	0.02717
	0.0560	1.0219	1.4052	8.6691	0.6140	0.02433
	0.0420	1.0213	1.4032	8.6008	0.5457	0.02162

Table No. III For L_1 at 70% D-W Mixture						
Temp (°C)	**Concentration (M)**	**Density $\rho x10^3$ ($kg.cm^{-3}$)**	**Refractive Index η**	**R_{mix} ($cm^3.mole^{-1)}$**	**R_{Ligand} ($cm^3.mole^{-1}$)**	**$\alpha x10^{-23}$ (cm^3)**
20	0.1000	1.0291	1.4124	10.4785	0.8221	0.03257
	0.0750	1.0281	1.4112	10.3991	0.7427	0.02943
	0.0560	1.0271	1.4102	10.3337	0.6773	0.02684
	0.0420	1.0264	1.4088	10.2728	0.6164	0.02442
30	0.1000	1.0288	1.4116	10.4604	0.8040	0.03186
	0.0750	1.0281	1.4094	10.3588	0.7024	0.02783
	0.0560	1.0271	1.4076	10.2760	0.6196	0.02455
	0.0420	1.0259	1.4062	10.2154	0.5590	0.02215
40	0.1000	1.0279	1.4108	10.4427	0.7863	0.03116
	0.0750	1.0269	1.4088	10.3455	0.6891	0.02730
	0.0560	1.0253	1.4062	10.2450	0.5886	0.02332
	0.0420	1.0246	1.4044	10.1753	0.5189	0.02056

Table No. IV For L_1 at 80% D-W Mixture						
Temp (°C)	**Concentration (M)**	**Density $\rho x10^3$ ($kg.cm^{-3}$)**	**Refractive Index η**	**R_{mix} ($cm^3.mole^{-1)}$**	**R_{Ligand} ($cm^3.mole^{-1}$)**	**$\alpha x10^{-23}$ (cm^3)**
20	0.1000	1.0392	1.4152	12.8257	0.8867	0.03510
	0.0750	1.0356	1.4138	12.7231	0.7841	0.03107
	0.0560	1.0319	1.4124	12.6358	0.6968	0.02761
	0.0420	1.0292	1.4114	12.5725	0.6335	0.02510
30	0.1000	1.0314	1.4134	12.7746	0.8356	0.03311
	0.0750	1.0293	1.4122	12.6798	0.7408	0.02935
	0.0560	1.0281	1.4108	12.5926	0.6536	0.02590
	0.0420	1.0265	1.4096	12.5241	0.5851	0.02318
40	0.1000	1.0298	1.4118	12.7364	0.7921	0.03139
	0.0750	1.0281	1.4104	12.6311	0.6921	0.02742
	0.0560	1.0269	1.4096	12.4873	0.5483	0.02172
	0.0420	1.0259	1.4074	12.4622	0.5232	0.02073

Graph Plotted Between Refractive Index (η) Versus C at Different Concentrations and Temperature for 60%, 70% and 80% Dioxane-Water Mixture.

Fig.1: FOR L_1 in 60% D-W at 20°C

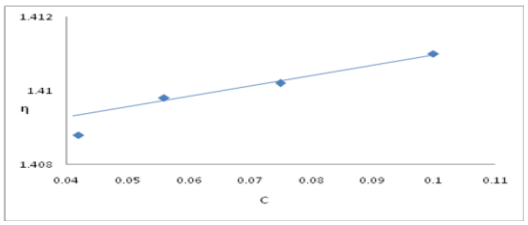


Fig.2: FOR L_1 in 60% D-W at 30°C

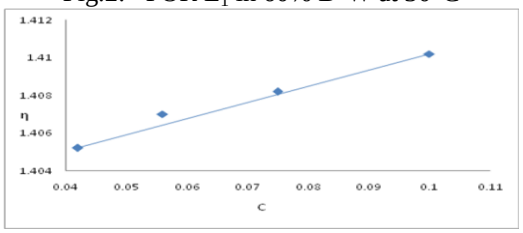


Fig.3: FOR L_1 in 60% D-W at 40°C

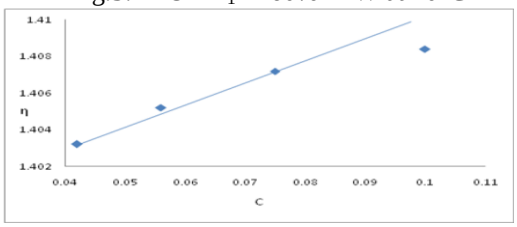


Fig.4: FOR L_1 in 70% D-W at 20°C

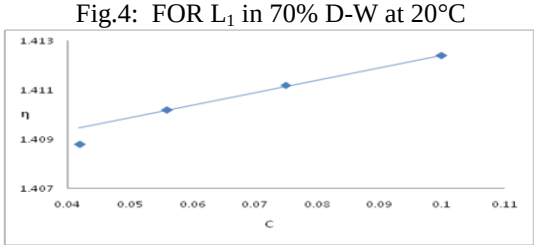


Fig.5: FOR L_1 in 70% D-W at 30°C

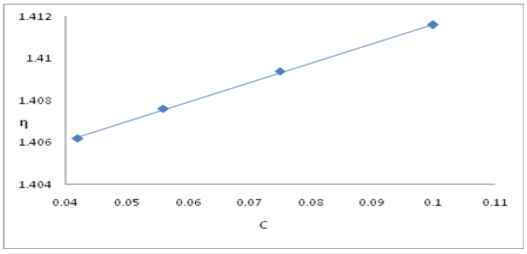


Fig.6: FOR L_1 in 70% D-W at 40°C

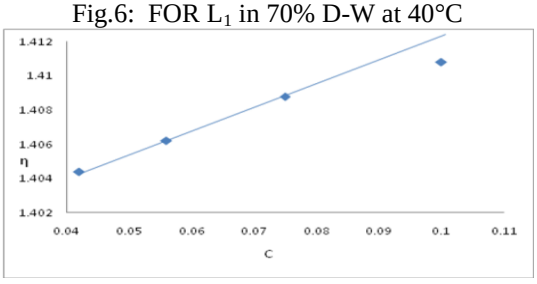


Fig.7: FOR L_1 in 80% D-W at 20°C

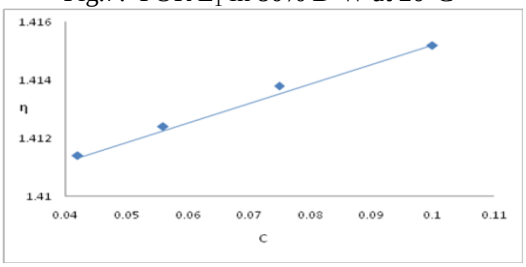


Fig.8: FOR L_1 in 80% D-W at 30°C

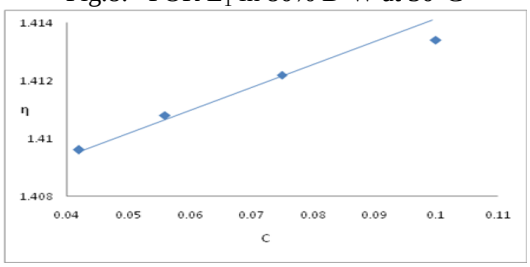
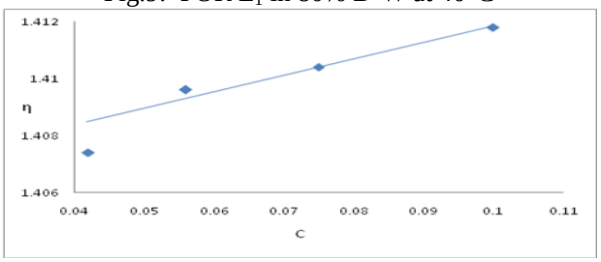


Fig.9: FOR L_1 in 80% D-W at 40°C



IV. Result and Discussion

The molar refraction of solutions of ligand in Dioxane-Water mixture were determined by a following equation,

$$R_{mixture} = [(\eta^2-1)/(\eta^2+2)]\{[X_1M_1+X_2M_2+X_3M_3]/d\} \quad \text{--------①}$$

Where,

η is the refractive index of solution,

X_1 is mole function of Dioxane,

X_2 is mole function of Water,

X_3 is mole function of Solute,

M_1, M_2, M_3 are molecular weights of Dioxane, water and solute respectively,

D is density of solution

The molar refraction of ligand is calculated as,

$$R_{lig} = R_{mixture} - R_{Dioxane\text{-}Water} \quad \text{---------②}$$

Where,

$R_{Dioxane\text{-}Water}$ - The molar refraction of solvent, Dioxane-Water mixture

The polarizability constant (α) of ligand is calculated from the following relation,

$$R_{lig} = (4/3)\ \pi\ N_o\ \alpha \quad \text{---------③}$$

Where, N_o is Avogadro's number.

The values of molar refraction of Dioxane-Water mixture were presented in Table No I. The values of molar refraction and polarizability constant of ligand in 60%, 70% and 80% of Dioxane-Water mixtures were presented in Table No. II to IV.
From the results, it is observed that, the concentration of ligand is directly proportional to density and refractive index for ligand at temperature 20°C, 30°C and 40°C. This may be due to the weak solvation effect which interprets weak molecule interaction. The 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, ligand is 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.

From the table, it is observed that, the temperature of solution is inversely proportional to the density and refractive index for ligand at all concentration. It is due to the temperature increase, randomness of solute molecule in solution also increases shows weak the molecular interactions. From this discussion , it is clear that bulky substituent on the molecule is not only factor in trend of refractive index but the reactivity and stability and tautomeric conversion as well as electron donating nature, electron clouds, nature of hetero atom present in ligand and the compactness in the molecule will directly hampered results and trends in the refractive index.

It shows that, the molar refractivity (true molar volume) as well as the polarizability constant of ligand may be attributed to the fact that, the dipole in the ligand lies perpendicular to the longer axis of the molecules and in the presence of dioxane causing decrease in dielectric constant of medium, considerable dipole association (intermolecular attraction) take place which would be accompanied by decreases in polarizability as well as molar refractivity because of the mutual compensation of dipoles. In the present work, non specific solute-solvent association caused by the dielectric enrichment in the solvent shell of solute takes place result may be due to strong hydrogen bonding resulting weak molecular interaction and in a dilute solution, solute molecules can disrupt this H-bonding to lesser extent.

The literature survey on pharmaceutical, medicinal, biochemical and chemical sciences reveals that the pharmacokinetics and pharmacodynamics of that drug are governed by solute-solvent and solute-solute interactions. These interactions can be determined by refractrometric measurements. These studies become important and essential tool for these studies in medicinal and pharmaceutical sciences. The results obtained in refractrometric measurements directly focused and gave information regarding solute-solvent (drugs-solvent) interactions and also solute-solute (drug-drug receptor) interactions. Hence, refractrometric measurements create its own identity in medicinal, pharmaceutical and chemical sciences. At the same time methodology is very simple, easy and easily affordable and required learnt chemicals and low cost instruments. This study also maintains green chemistry parameters.

The results obtain in refractrometric study directly shows merits or demerits of that drug. The literature survey also shows that the transport of drug which is a part of pharmacokinetics which involved drugs absorption, drug distribution (transmission), drug metabolism and drug excretion in which solute-solvent interactions were studied. While in pharmacodynamics drug and drug interactions (solute-solvent interactions) were studied. Drug transport and drug receptor interactions were studied in pharmacokinetics and pharmacodynamics respectively. Pharmacokinetics and pharmacodynamics parameters can also be determined by refractrometric study. Interpretation of nature of chemical reactions involved in pharmacodynamics and pharmacokinetics can be easily predicted by obtaining results of refractrometric measurements as drug and drug receptor interactions is also depends upon refractive index[15-17] and transport of drug[18-21] also depends upon this factor. Hence, refractrometric study creates its own importance and identify in the medicinal, pharmaceuticals, biochemical and chemical sciences. So it become prior duty of chemist before giving final result and opinion about any drug, the result must be cross verified and then only result must be determined. Taking all these things into consideration, the molar refraction and polarizability constant of ligand 1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide L_1 was studied in various percentage of dioxane-water mixture at different and also at various concentrations and temperature.

V. 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 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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