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Investigations in the Refractrometric Study of S-trizinothiocarbamides in Dioxane-water Systems

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ABSTRACT

Refractrometric measurements of recently synthesized drugs viz. 1-(4-Hydroxy-6-phenyl)-s-triazino-3-phenylthiocarbamide (L_1), 1-(4-Hydroxy-6-phenyl)-s-triazino-3-ethylthiocarbamide (L_2), 1-(4-Hydroxy-6-phenyl)-s-triazino-3-methylthiocarbamide (L_3) were carried out at various percentage composition of solvent 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. Taking all these things, this research work was carried out.

Key words: 1-(4-Hydroxy-6-phenyl)-s-triazino-3-phenylthiocarbamides (L_1), 1-(4-Hydroxy-6-phenyl)-s-triazino-3-ethylthiocarbamide (L_2), 1-(4-Hydroxy-6-phenyl)-s-triazino-3-methylthiocarbamide (L_3), Dioxane-Water percentage composition, Refractrometry study.

INTRODUCTION

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]. Some of them are used in industries such as finishing and brightening agents[14]. They are also be used as herbicidals[15-23], sea water algicidals[24], fungicidal[25], insecticidal[26] and pesticidal[27]. Thus, the s-triazino compounds initiated the new branches of development in the medicinal, pharmaceutical, agricultural and biochemical fields. The s-triazino compounds possess their own identity and also play an immense role in industrial fields. The drug absorption, transmission, activity and effect will directly predicted by the refractometric measurements of the solute (drug) and solvent in the human anatomy. This information is essential for deciding dose of drug to the patient, drug activity and effect of drug in pharmaceutical and medicinal sciences. Results of refractometric measurements directly gave information regarding solute-solvent, solvent-solvent interactions. This study is an

important tool for pharmaceutical and medicinal sciences. Taking all these things into consideration and as a wider programme of this laboratory in the synthesis of nitrogen, sulphur and nitrogen and sulphur containing heteroacycles and heterocycles, it was thought interestingly to carry out the refractrometric measurements of newly synthesized drugs in this laboratory.

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 practitioners. 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 angle of refraction changes and ultimately the refractive index gets 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. From this point of view the present investigation was carried out. L_1, L_2 and L_3 in dioxane were studied at various percentage compositions. This is hither to unknown. This study becomes milestone in the drug, medicinal, pharmaceutical of triazinothiocarbamido molecules.

EXPERIMENTAL

The 0.1M solution of ligands in different percentage of dioxane-water and the solutions of different concentration of ligands (0.1M, 0.075M, 0.056M, 0.042M) 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 caliberated with glass piece (n=1.5220) provided with the instrument.

Observation and calculation

The present work deals with the study of molar refraction and polarizability constant of ligand (L_1), ligand (L_2) and ligand (L_4) in 60% dioxane-water, 70% dioxane-water and 80% dioxane-water mixtures at different composition at 303.15°K (30°c). The data obtained have been used to compute intermolecular interactions. The refractometric reading were taken as described in literature. Here, (L_1) is 1-(4-Hydroxy-6-phenyl)-s-triazino-3-phenylthiocarbamide, (L_2) is 1-(4-Hydroxy-6-phenyl)-s-triazino-3-ethylthiocarbamide and (L_3) is 1-(4-Hydroxy-6-phenyl)-s-triazino-3-methylthiocarbamide.

RESULTS AND DISCUSSION

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

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

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,

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

Where,

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

Table 1: Molar Refraction of Different Percentage of Dioxane-Water Mixture

% of Dioxane-Water	Molar Refraction (RM) (cm^3mole^{-1})
100	20.5977
90	14.4584
80	10.9390
70	10.6564
60	9.0551

A] Molar Refraction and Polarizability constant at different concentration for L_1

Table 2:

System: 60% Dioxane –Water Temp : 30±0.1°c

Concentration C(M)	DensityPx10^3 (Kg-m^{-3})	Refractive Index(η)	R_{mix} (m^{3}mole^{-1})	R_{Lig} (m^{3}mole^{-1})	αx10^{-23} (cm^3)
0.1	1.0234	1.4020	8.4887	0.4347	0.01722
0.075	1.0232	1.4016	8.4407	0.3856	0.01527
0.056	1.0229	1.4010	8.3991	0.3440	0.01362
0.042	1.0226	1.4004	8.3954	0.3403	0.01347

Table 3:

System: 70% Dioxane –Water Temp : 30±0.1°c

Concentration C(M)	DensityPx10^3 (Kg-m^{-3})	Refractive Index(η)	R_{mix} (m^{3}mole^{-1})	R_{Lig} (m^{3}mole^{-1})	αx10^{-23} (cm^3)
0.1	1.0286	1.4030	9.9844	0.3280	0.01328
0.075	1.0279	1.4018	9.9148	0.2584	0.01023
0.056	1.0269	1.4010	9.8659	0.2095	0.00829
0.042	1.0257	1.4399	9.8272	0.1711	0.00676

Table 4:

System: 80% Dioxane –Water Temp : 30±0.1°c

Concentration C(M)	DensityPx10^3 (Kg-m^{-3})	Refractive Index(η)	R_{mix} (m^{3}mole^{-1})	R_{Lig} (m^{3}mole^{-1})	αx10^{-23} (cm^3)
0.1	1.0312	1.4086	12.2639	0.3249	0.01286
0.075	1.0291	1.4078	12.2081	0.2691	0.01065
0.056	1.0279	1.4070	12.1581	0.2146	0.00849
0.042	1.0263	1.4058	12.1059	0.1669	0.00661

B] Molar Refraction And Polarizability constant at different concentration for L_2

Table 5:

System: 60% Dioxane –Water Temp : 30±0.1°c

Concentration C(M)	DensityPx10^3 (Kg-m^{-3})	Refractive Index(η)	R_{mix} (m^{3}mole^{-1})	R_{Lig} (m^{3}mole^{-1})	αx10^{-23} (cm^3)
0.1	1.0338	1.4058	8.4677	0.4316	0.01713
0.075	1.0295	1.4056	8.4490	0.4129	0.01637
0.056	1.0266	1.4042	8.4242	0.3861	0.01522
0.042	1.02120	1.4148	8.4101	0.3730	0.01466

Table 6:

System: 70% Dioxane –Water Temp : 30±0.1°c

Concentration C(M)	DensityPx10^3 (Kg-m^{-3})	Refractive Index(η)	R_{mix} (m^{3}mole^{-1})	R_{Lig} (m^{3}mole^{-1})	αx10^{-23} (cm^3)
0.1	1.0350	1.4098	10.0217	0.3653	0.01448
0.075	1.0310	1.4082	9.9867	0.3303	0.01309
0.056	1.0259	1.4068	9.9732	0.3168	0.01256
0.042	1.0207	1.4054	9.9712	0.3148	0.01247

Table 7:

System: 80% Dioxane –Water Temp : 30±0.1°c

Concentration C(M)	DensityPx10^3 (Kg-m^{-3})	Refractive Index(η)	R_{mix} (m^{3}mole^{-1})	R_{Lig} (m^{3}mole^{-1})	αx10^{-23} (cm^3)
0.1	1.0356	1.4124	12.2528	0.3138	0.01243
0.075	1.0313	1.4114	12.2316	0.2926	0.01160
0.056	1.0261	1.4096	12.2090	0.2700	0.01070
0.042	1.0225	1.4080	12.1825	0.2435	0.00965

C] Molar Refraction And Polarizability constant at different concentration for L_3

Table 8:

System: 60% Dioxane –Water Temp : 30±0.1°c

Concentration C(M)	DensityPx10^3 (Kg-m^{-3})	Refractive Index(η)	R_{mix} (m^{3}mole^{-1})	R_{Lig} (m^{3}mole^{-1})	αx10^{-23} (cm^3)
0.1	1.0360	1.4112	8.5028	0.4477	0.01774
0.075	1.0330	1.4098	8.4709	0.4158	0.01648
0.056	1.0290	1.4074	8.4357	0.3806	0.01508
0.042	1.0240	1.4058	8.4255	0.3704	0.001468

Table 9:

System: 70% Dioxane –Water Temp : 30±0.1°c

Concentration C(M)	DensityPx10^3 (Kg-m^{-3})	Refractive Index(η)	R_{mix} (m^{3}mole^{-1})	R_{Lig} (m^{3}mole^{-1})	αx10^{-23} (cm^3)
0.1	1.0385	1.4120	10.0242	0.3658	0.01456
0.075	1.0332	1.4110	10.0176	0.3612	0.01430
0.056	1.0288	1.4102	10.0128	0.3564	0.01411
0.042	1.0255	1.4086	9.9901	0.3336	0.01321

Table 10:

System: 80% Dioxane –Water Temp : 30±0.1°c

Concentration C(M)	DensityPx10^3 (Kg-m^{-3})	Refractive Index(η)	R_{mix} (m^{3}mole^{-1})	R_{Lig} (m^{3}mole^{-1})	αx10^{-23} (cm^3)
0.1	1.0394	1.4150	12.2618	0.3228	0.01278
0.075	1.0356	1.4138	12.2336	0.2945	0.01166
0.056	1.0313	1.4126	12.2203	0.2813	0.01113
0.042	1.0274	1.4112	12.2050	0.2660	0.01053

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

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

Where, N_o is Avogadro's number.

The values of molar refraction of Dioxane-Water mixture were presented in Table 1. The values of molar refraction and polarizability constant of ligand L_1, L_2, L_3 in 60%, 70% and 80% of Dioxane-Water mixtures were presented in Table 2 to 10.

The values of molar refraction and polarizability constant at different concentrations of ligands L_1, L_2, L_3 at 60%, 70% and 80% Dioxane-Water mixtures were given in Table 2 to 10. It was observed from these tables that, the molar refractions and polarizability constants of the ligands decreases in the concentration of ligand.

From the data, it can be predicted that, when the percentage of dioxane increases, the molar refractivity (true molar volume) continuously increases. At the same time the polarizability constant of ligand (á) decreases. This may be attributed to the fact that with the increase in percentage of dioxane it causes decrease in dielectric constant of medium and also considerable dipole association (intermolecular attraction) take place, which would be accompanied by decrease in polarizability. It was observed from Table 2-10 when concentration of dioxane increases the refractive index also increases for L_1,L_2,and L_3. It was also observed that the refractive index was increase from L_1 to L_3. The increase in refractive index in L_3 is due to –methyl group on thiocarbamido moiety. Refractive index of L_2 is more than L_3 because -ethyl group is present on thiocarbamido moiety. Refractive index of L_1 is more than L_2 because -phenyl group is present on thiocarbamido moiety. This clearly indicated that when the substituent on thiocarbamido group is bulkier like –phenyl or –ethyl, then the refractive index decreases.The bulky nature as well as resonance stabilization in the ring or in the molecule directly affect the solute –solvent interactions which affect on the result refractive index.At the same time the –phenyl as well as –ethyl groups directly affect the polarisability constant and dipole association propertise of the solution.From this investigation it was clear that L_3 is more suitable drug than L_1 and L_2 at preliminary stage.Much more anatomical, biochemical and medicinal study is required for these synthesized drugs. Then these drugs will renovate the old drug therapies in malaria typhoid, ulcer and cancer diseases.

It means that when the percentage of dioxane increases the solute-solvent interactions i.e. interactions of ligands (drugs) and dioxane increases, which may stabilize the drug activity at higher percentage of dioxane. From this it can be concluded that the drug absorption, drug transmission and drug effect of L_1, L_2 and L_3 is more effective at higher concentration of dioxane.

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