Interferometric Study 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, density and sound velocity of some biologically important substituted triazinothiocarbamides were measured at 30°C in 60% dioxane-water mixture. The interferometric measurements of recently synthesized drugs have been carried out for solutions of 1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide(L_1), 1-(4-hydroxy-6-methyl)-S-triazino-3-ethylthiocarbamide (L_2) and 1-(4-hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide (L_3) at various concentrations. This data have been used to determine various acoustic / thermodynamic parameters viz. adiabatic compressibility (β), apparent molal compressibility (ϕ_k), apparent molal volume (ϕ_v), intermolecular free length (L_f), relative association (R_A) and specific acoustic impedance (Z). These properties are used to interpret weak molecular solute-solvent, solute-solute interactions in the system. The data and result obtained during this investigation gave detail information regarding drug absorption, transmission, activity and effect of these drugs which is base of pharmacokinetics and pharmacodynamics of any drug. Taking all these things into consideration this research work was carried out. These properties are used to interpret weak molecular solute-solvent, solute-solute interactions in the system.

Keywords

1-(4-Hydroxy-6-methyl)-S-triazino-3-substitutedthiocarbamides; Dioxane-water mixture; Interferometric measurements; Pharmacokinetics; Pharmacodynamics.

1. Introduction

Most of the modern drugs contain heterocyclic nucleus [1,2]. The S-triazino compounds initiated the new branches of development in the medicinal [3,4], pharmaceutical, agricultural and biochemical fields [7-9]. The successful application of acoustic methods to physiochemical interactions of solution becomes possible after the development of adequate theoretical approaches and methods for precise ultrasonic velocity measurements in small volumes of liquids [10-12]. Most of the information procured from ultrasonic study of fluids is confined to the determination of hydration number and compressibility [13-15]. In the basic sciences, these waves are used to provide information on the behaviour of microscopic particle of matter [16]. The use of ultrasound was proved to be useful probe for generating more information on oregano metallic chemistry, biotechnology, polymerization medicinal use [17-19].

While studying the pharmacokinetics and pharmacodynamics of any drug the interferometric measurements play an important role in medicinal and drug chemistry [20-22]. 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 transmission, stability, activity and effect of drug.

Hence we were studied the potency of recently synthesized drugs in G.I.S.H., Amravati laboratory in the month of May 2012. The interferometric 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-methylthiocarbamides (L_3) were studied in 60% dioxane water mixture. S-triazino and thiocarbamido nucleus containing drugs create its own identity and significance in drug, pharmaceutical and agricultural chemistry [23-30].

2. Experimental

2.1 Materials

1-(4-Hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide(L_1), 1-(4-hydroxy-6-methyl)-S-triazino-3-ethylthiocarbamid (L_2), 1-(4-hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide (L_3) were synthesized which were used as ligand [31]. The general structures of substituted thiocarbamides as shown in Fig.1. All the solutions of ligand were prepared fresh in the present investigation.

2.2 Methods

Carbon dioxide free double distilled water was used. Extra pure (E. Merck) dioxane was further purified by the prescribed procedure [31] and used for preparation of ligand solutions. The densities of the solutions were determined by a bicapillary Pyknometer (±0.2%). Weighing was made on electronic balance, made by Mechaniki Zaktady Precyzyjnej Gdansk Balance, made in Poland (±0.001 gm). A special thermostatic arrangement was done for density.

Single crystal interferometer (Mittal Enterprises, Model MX-3) with accuracy ±0.03% and frequency 1 MHz was used in the present work. The working of the ultrasonic interferometer [32, 33] was checked by measuring ultrasonic velocity of pure water at 30°C. The measured value is in good agreement with literature value 1510 check value ms^{-1}.as shown in Table No 1. The ultrasonic velocity was calculated for all three ligands the concentration of ligands at various concentration at 30°C in 60% dioxane-water mixture. The molecular interactions were studied with solutes, the effect of these specially related to protic-aprotic nature of solvent, polarity-non polarity of solvent and hydrogen boding in solvent, dielectric constant, density, viscosity and

surface tension of solvent on solute-solvent, ion-solvent and ion-ion interactions in this investigation.

2.3. Data analysis:

Various acoustic properties were calculated by using following equations,

1. **Adiabatic Compressibility (β)**
   $\beta = 1/ V_s^2 d$ …….. 1
2. **Apparent Molar Compressibility (ϕ_K)**
   $\phi_K = [1000 (\beta_s d_0 - \beta_0 d_s) / m d_s d_0] + ((\beta_s M/d_s)$ …….. 2
3. **Intermolecular Free Length (L_f)**
   $L_f = K. (\beta_s)^{1/2}$ …… 3
4. **Relative association (R_A)**
   $R_A = d_s /d_0 [V_0/V_S]^{1/3}$ …… 4
5. **Specific Acoustic Impedance (Z)**
   $Z = V_s d_s$ …… 5
6. **Apparent Molar Volume (ϕ_v)**
   $\phi_V = [1000(d_0 - d_s) / m d_0 d_s]+(M/ d_s)$…6

Where,

d_0 = density of pure solvent

d_s = density of solution

m = molality of solution

M = molecular weight of solute

β_0 = adiabatic compressibility of pure solvent and

β_s = adiabatic compressibility of solution

L_f = Intermolecular Free Length

K = Jacobson's constant

V_0 = ultrasonic velocities in a solvent

V_s = ultrasonic velocity of solution

M = molecular weight of solute

m = molality of solution

3. Result

An addition of polar solute having a partial positive charge on hydrogen atom, there is every likely hood that there can be a weak interactions between this positive charge and negative charge on oxygen atom (due to electro negativity) of dioxane. This weak interaction of the wonder wall's forces is expected to introduce the structuredness in the solution i.e. specific arrangement of dioxane molecule may be occurring due to attached solute molecule. Thus, spaces may be created making the solution more compressible as it appears from the higher apparent molar compressibility value in dioxane solvent. Using the values in Table no 1 and 2, we can calculated the values of all acoustic parameter using the equation 1 to 6 which are shown in Table No. 3 for L_1, L_2 and L_3. The adiabatic compressibility shows the increase association of molecules by lower β value. Whereas, apparent molar compressibility also shows the increase association but at the same time the structuredness of the solution by higher ϕ_K values. It is also observed that positive values of ϕ_K for ligands indicates electro static force in the vicinity of ions [34, 35].

From the difference in trends in two compressibility's, adiabatic & apparent molar, it may be predicted that adiabatic compressibility can detect gross changes in interactions but minute changes due to change in structure may only be noticed by apparent molar compressibility (ϕ_K). It is clear from the graphs shown in Fig 7, Fig. 8, Fig 9. Thus, the structure of solute and the number of atoms present in it will have direct effect on ϕ_K value. The parameters of solvents which directly affect the values of β are due to high density of dioxane as compare to protic nature, polarity, high dielectric constant (24.6).

Similarly on increasing the concentration of ligands, β decreases continuously. The increased concentration of solute will require more and more number of solvent molecules to dissolve it resulting in breaking the electrostriction/ structuredness of solvent consequently decreasing the compressibility. Thus in both the system solute-solvent and solvent-solvent interactions are

involved which are reflected in the compressibility values.

The conventional approach based on compressibility is both useful and fundamental; In fact it constitutes an additional probe for studying molecular interactions. Specific acoustic impedance is the complex ration of the effective sound pressure at a point to the effective particle velocity at that point [18].

In case of dioxane, because of its non-polar nature, the compact packing of molecules is already there and when polar solute is added because of its association again free space decreases. Therefore, the L_f values in dioxane must be smaller. When the metal ions are added, the polar-polar associations still increases and the L_f decreases Ultrasonic velocity depends upon intermolecular free length L_f with decrease in free length velocity increases.

Relative association R_A is an acoustic property of understanding interaction, which is influenced by two opposing factors,

- Breaking of solvent structure on addition of solute to it satisfy decreases in values when concentration of ligand L_1, L_2, L_3 in 60% dioxane-water mixture increases for 30^0C. It was observed that, the value of R_A of ligand L_1 get affected by the resonance stabilization in benzene while the value of ligand L_2 get affected by the methylene group attached.
- Solvation of solute that is simultaneously present by the free solvent molecules. It was clearly observed that the high concentration of solute. The values of R_A at high percentage of dioxane are very well explained by second factor.

In general it is observed that, the value of β, ϕ_v, L_f of ligand L_1, L_2, L_3 clearly indicates effects of resonance stabilization in benzene ring which is a substituent on thiocarbamido nucleus as shown in Fig 4, Fig 5, Fig 6. At the same time bulkier nature of ethyl group may also interfere during these interactions. This clearly indicates that not only the bulkier nature and nature of ligand will affect but the molecular weight of solute is also one of an important factor which directly affects the solute-solvent interaction. The change in values of L_f may be due to stronger interaction between ions and solvent molecules at that particular percentage combination of dioxane-water mixture decrease in L_f values indicated weaker interaction between ions and solvent molecules. The intermolecular free length goes on decreasing with increase in concentration of solute indicates decrease in free space between the molecules because of stronger solute-solvent interaction which is in a agreement with on observed value of β.

4. Discussion

These factors may directly interfere the solute-solvent interaction. Measurement of ultrasonic velocity is the best tool to investigate solute-solvent, solute-solute and ion-solvent interactions. Therefore, in last four decades ultrasonic interferometric study created its own identity for determining solute-solvent interactions. By this study β, ϕ_v, ϕ_K, L_f, R_A, Z, etc. acoustic properties were determined which explain how these interactions occur and responsible for breaking and making of the structure in the solution. So in the present work these acoustic parameters were studied for newly synthesized ligands, which were used as solutes.

To study the pharmacokinetics and pharmacodynamics of any drug relating these ligands, the acoustic parameters of dioxane helps to find out the property of solvent interfere in breaking and making of structure of solvent. From this study it is clear that properties, which are directly or indirectly responsible for these are protic-aprotic nature of solvents, dielectric constant, polarity, density, tendency of forming hydrogen bonding, surface tension, viscosity of solvent, bulkier nature, resonance, reactivity of

group, size and molecular weight of ligand. All these parameters plays important role in pharmaceutical and medicinal drug chemistry.

From this study it can be concluded that interferometric technique requires minimum efforts, solutions and is somewhat a direct method and has its own identity and significance in material sciences, which can give idea about effectiveness of solvent. By knowing these parameters the selection of solvent during synthesis in organic and coordination chemistry can be predicted. This study is an important basic tool for pharmaceutical, medicinal and biochemical sciences which directly focus on drug activity and drug effect at primary level and then onwards only the characteristics of drug can be decided. This study gave detail information regarding pharmacokinetics and pharmacodynamics of drug.

5. Observations and Calculations

Table No.1: Average Ultrasonic Velocity of Water at 30˚C

Sr. No.	No. of Rotation of Screw	Micrometer Reading (mm)	Difference Between Reading (mm)	Distance Travelled By Screw in One Rotation	Average Ultrasonic Velocity (m/sec)
1	5	26.7843	3.7654	1.50616	1501.2914
2	10	23.0189	3.7584	1.50336	
3	15	19.2605	3.7544	1.50176	
4	20	15.5061	3.7002	1.48008	
5	25	11.8059	3.7468	1.49872	
6	30	8.0591	3.7583	1.50332	
7	35	4.3008	3.7891	1.51564	
8	40	0.5117		10.50904	

Table No.2: Average Ultrasonic Velocity of Dioxane at 30˚C (β_0)

D-W %	Sr. No.	No. of Rotation of Screw	Micrometer Reading (mm)	Difference Between Reading	Distance Travelled By Screw in One Rotation	Average Ultrasonic Velocity (v_0) (m/sec)	Density (d_0) ($Kg.m^{-3}$)	$\beta_0 \times 10^{-10}$ (Pa^{-1})
60	1	5	20.0328	3.7055	1.4822	1477.72	1026.2	4.4625
	2	10	16.3273	3.7255	1.4902			
	3	15	12.6018	3.6907	1.4763			
	4	20	8.9111	3.6555	1.4622			
	5	25	5.2556					
					5.9109			

Table No.3: Acoustic Parameters at Different Concentration of Ligand L_1, L_2, L_3 at 30˚C

Ligand	Conc. C (Mole/lit)	Average Ultrasonic Velocity V (m/sec)	Density d_s ($Kg.m^{-3}$)	$\beta sx10_{-10}$ (pa^{-1})	ϕ_V ($m3mol^{-1}$)	ϕ_k $x10^{-10}$	L_f (A_0)	R_A	$Z * 10^4$ ($Kgm^{-2}sec^{-1}$)
L_1	0.1	1683.89	1023.6	3.4454	0.2797	-8.9475	0.0117	0.9550	172.3630
	0.075	1582.9	1023.4	3.8998	0.2817	-6.1779	0.0125	0.9747	161.9940
	0.056	1434.675	1023.1	4.7487	0.2846	6.4420	0.0138	1.0069	146.7816
	0.042	1286.695	1022.8	5.9055	0.2876	35.4424	0.0153	1.0438	131.6032
L_2	0.1	1583.89	1033.9	3.8554	0.1799	-5.4015	0.0124	0.9845	163.7584
	0.075	1421.975	1029.4	4.8043	0.2233	5.2410	0.0138	1.0161	146.3781
	0.056	1278.675	1026.1	5.9606	0.2085	27.3144	0.0154	1.0493	131.2048
	0.042	1130.175	1021.8	7.6620	0.2504	76.5963	0.0175	1.0888	115.4813
L_3	0.1	1734.53	1036	3.2083	0.0999	-11.9013	0.0113	0.9570	179.6973
	0.075	1620.3	1033	3.6873	0.1285	-9.6772	0.0121	0.9762	167.3770
	0.056	1417.525	1029	4.8364	0.1669	7.2126	0.0139	0.9939	156.1533
	0.042	1356.765	1024	5.3051	0.2153	20.8428	0.0145	1.0267	138.9327

6. Figures

The Ligands used during investigation are as below,

Figure-1: L_1: 1-(4-Hydroxy-6-methyl)-S-triazino-3-phenylthicarbamide

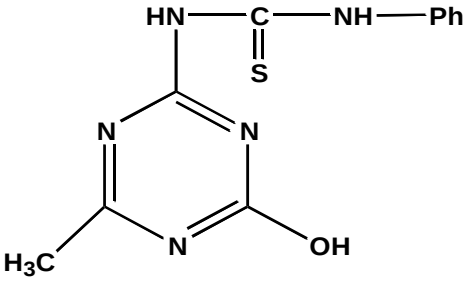


Figure-2: L_2: 1-(4-Hydroxy-6-methyl)-S-triazino-3-ethylthiocarbamide

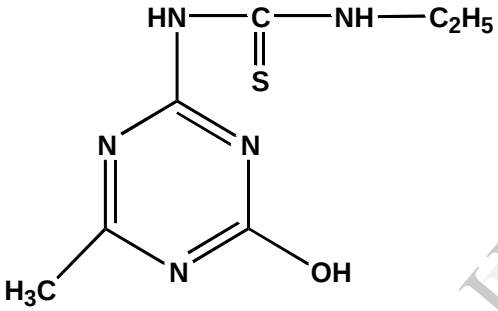
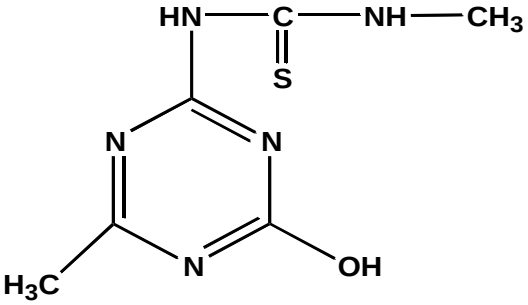


Figure-3: L_3: 1-(4-Hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide



7. Graphs

Plot Between Apparent molar volume (ϕ_v) V_s concentration ($\sqrt{C}$) for Ligand L_1, L_2 and L_3 at 30˚C in 60% dioxane-water mixture

Figure 4 : L_1 at 30˚C for ϕ_V

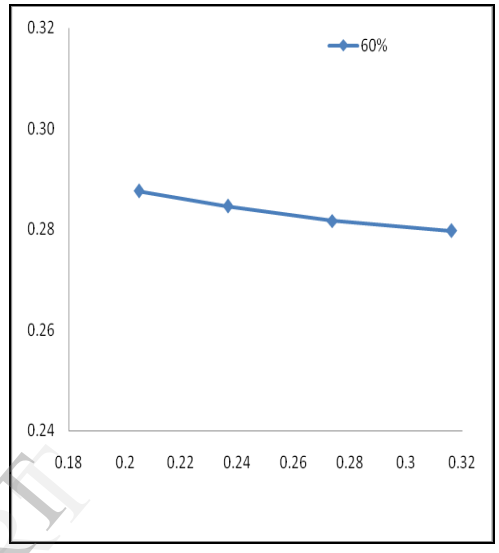


Figure 5 : L_2 at 30˚C for ϕ_V

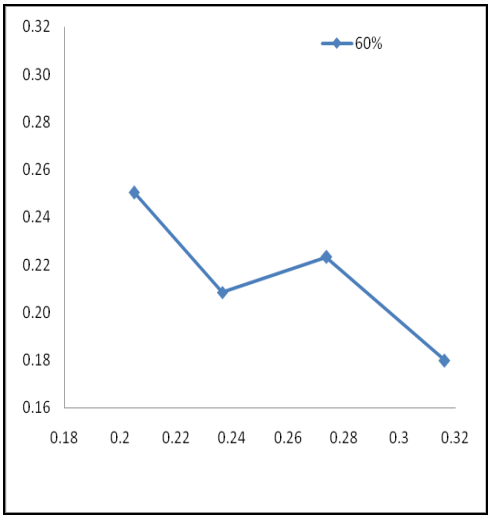
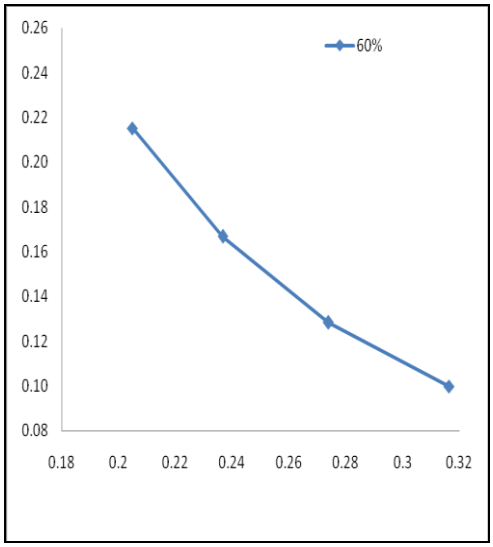


Figure 6 : L_3 at 30˚C for ϕ_V



Plot between Apparent molar compressibility (ϕ_k) V_s concentration ($\sqrt{C}$) for Ligand L_1, L_2 and L_3 at 30˚C in 60% dioxane-water mixture

Figure 7 : L_1 at 30˚C for ϕ_K

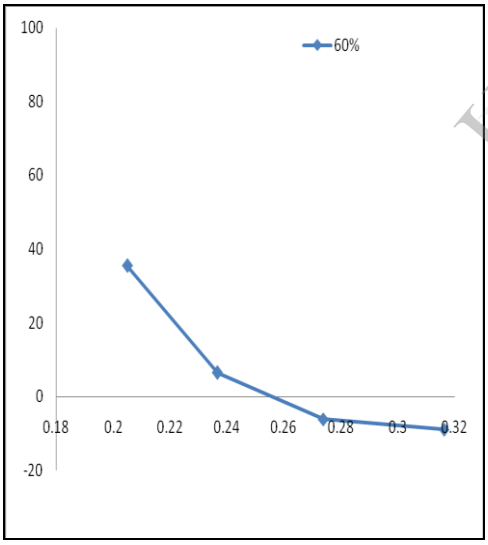


Figure 8 : L_2 at 30˚C for ϕ_K

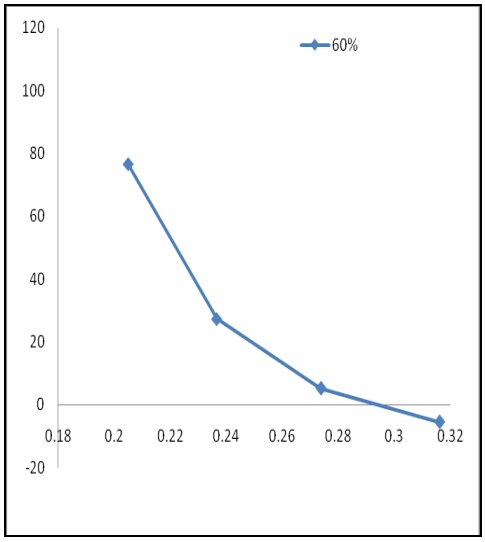
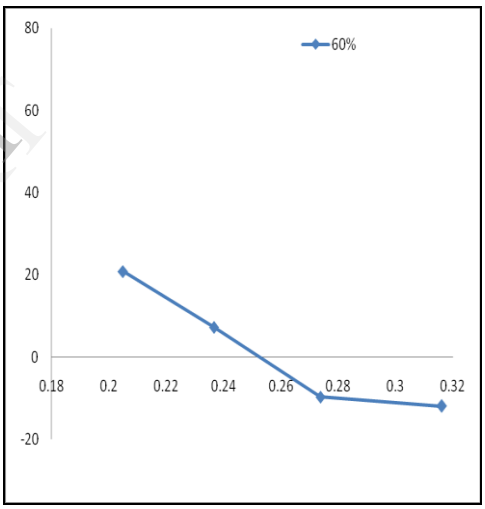


Figure 9 : L_3 at 30˚C for ϕ_K



8. Conclusion

As at high percentages of dioxane in dioxane-water system indicate the protic nature, polarity, dielectric constant and tendency of formation of hydrogen bonding in solvent in the system decreases. Hence, it may cause decreases values of β for L_1, L_2 and L_3.

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. It means that when the high percentage of dioxane in the solute-solvent interactions i.e. interaction of compounds (drugs) and dioxane which may be stabilize the drug activity. This consider as basic study for any drug through the point of medicinal chemistry From this it can be concluded that the drug absorption, drug transmission and drug effect of compounds L_1, L_2 and L_3 is effective at high concentration of dioxane. This study may become a milestone in the drug, medicinal and pharmaceutical chemistry of triazino thiocarbamides.

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10. Reference

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