Scientific Reviews
&
Chemical Communications

Sci. Revs. Chem. Commun.: 2(3), 2012, 503-509
ISSN 2277-2669

REFRACTROMETRY STUDY OF s-TRIZINOTHIOCARBAMIDES IN 80% DIOXANE-WATER MIXTURE AT DIFFERENT TEMPRATURE

A. M. KSHIRSAGAR*

Department of Chemistry, Alamurai Ratnamala Institute of Engineering & Technology, Sapgaon, ASANGAON, Tal. Shahapur, Dist. Thane (M.S.) INDIA

(*Received : 01.03.2012; Revised : 19.03.2012; Accepted : 25.03.2012*)

ABSTRACT

Refractrometric measurements of recently synthesized drugs viz.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) were carried out at 70% percentage composition of dioxane-water mixture as solvent to investigate effects of structure, groups on s-triazinothiocarbamides at different temperature. 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-methyl)-s-triazino-3-phenylthiocarbamides(L_1); 1-(4-Hydroxy-6-methyl)-s-triazino-3-ethylthio-carbamide(L_2);1-(4-Hydroxy-6-methyl)-s-triazino-3-methylthiocarbamide (L_3); Dioxane-Water percentage composition; Refractrometry study.

INTRODUCTION

In the recent era, the heterocycles and drugs are both interconnected with each other. The medicinal field is undefined without heterocycles. Most of the modern drugs contain heterocyclic nucleus[1,2] The s-triazino compounds initiated the new branches of development in the medicinal, pharmaceutical, agricultural and biochemical fields and used as drugs as hypoglycemic agent[3], blood pressure depressant[4], anti-tumor properties[5], anti-bacterial[6,7]. Anti-inflammetry[8], antipsychotic agent[9], herbicidals[10,11], insecticidal.[12] As results of refractometric measurements directly gave information regarding solute-solvent, solvent-solvent interactions so we selected the compounds as shown in Fig. 1, 2 and 3 for Refractrometric study

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. These results are much more useful for transmission, stability, activity and effect of drug.

Available online at www.sadgurupublications.com
*Author for correspondence; E-mail: ashwinikshirsagar2@gmail.com

EXPERIMENTAL

Materials

1-(4-Hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamides(L_1);1-(4-Hydroxy-6-methyl)-S-triazino-3-ethylthiocarbamide (L_2); 1-(4-Hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide (L_3). These compounds were prepared by Dr. D.T. Tayade, Associate Professor, and G.V.I.S.H. Amaravati. India.[13 7]0 ml pure dioxane mixed with 30 ml double distilled water prepared in laboratory, used to prepare 80% Dioxane-Water mixture. The 0.1M concentrated solution of compound 1-(4-Hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamides (L_1) was prepared in 80% Dioxane-Water mixture. Similarly, the solutions for 1-(4-Hydroxy-6-methyl)-S-triazino-3-ethylthiocarbamide(L_2); 1-(4-Hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide (L_3) were also prepared in 80% Dioxane-Water mixture. In the same way, 0.075M, 0.056M and 0.042M solutions for the compounds L_1, L_2 and L_3 were prepared. All weighing were made on Mechaniki Zaktady Precyzying Gdansk Balance [Poland make, (±0.001g)] The 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 1mm.

The compounds used during investigations are as depicted below -

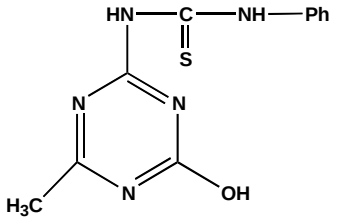

Fig. 1: 1-(4-Hydroxy-6-methyl)-S-triazino-3-phenylthicarbamide

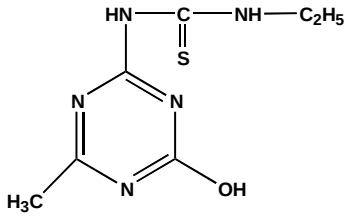

Fig. 2: 1-(4-Hydroxy-6-methyl)-S-triazino-3-ethylthiocarbamide

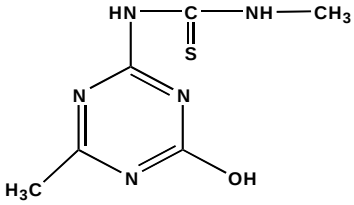

Fig. 3: 1-(4-Hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide

Refractrometric procedure

The refractive indices of solvent mixture and solutions were measured by Abbe's refractrometer (± 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. For evaluating the molar refraction and

polarizability constant of the compounds, we prepared 0.1 M, 0.075 M, 0.56 M and 0.042 M solutions in 80% Dioxane-Water mixture at 20˚C, 25˚C, 30˚C, 35˚C and 40˚C. The temperature was maintained by using the thermostat. The data obtained was used to compute intermolecular interactions. The Refractrometric readings were taken as described in literature.

Observation and calculation

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

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

Where,

ή 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 compound is calculated as -

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

Where,

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

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

$$\mathbf{R_{lig} = (4/3)\ \pi\ No\ \alpha} \quad \mathbf{\ldots(3)}$$

Where, No is Avogadro's number.

The values of molar refraction of Dioxane in different percentage of Dioxane-Water mixture are presented in Table 1. The values of molar refraction and polarizability constant of compound L_1, L_2, L_3 in 80% of Dioxane-Water mixture are presented in Table 2 to 4.

Table 1: Molar refraction of dioxane in different percentage of dioxane-water mixture

% of Dioxane in dioxane-water mixture	Molar refraction (RM) (cm^3mole^{-1})
100	21.5977
90	15.4584
80	11.9390
70	9.6564
60	8.0551

Table 2: **Molar refraction and polarizability constant at different concentration for L_1 System: 80% dioxane –water**

Temperature T (^oC)	Concentration C (M)	Density ρ	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	1.4124	12.2663	0.3273	0.01297
	0.0750	1.0356	1.4110	12.2126	0.2736	0.01084
	0.0560	1.0319	1.4098	12.1771	0.2381	0.00944
	0.0420	1.0292	1.4082	12.1320	0.1930	0.00765
25	0.1000	1.0352	1.4104	12.2612	0.3222	0.01277
	0.0750	1.0312	1.4096	12.2279	0.2889	0.01145
	0.0560	1.0284	1.4080	12.1713	0.2323	0.00920
	0.0420	1.0201	1.4054	12.1662	0.2272	0.00900
30	0.1000	1.0314	1.4088	12.2641	0.3251	0.01288
	0.0750	1.0293	1.4080	12.2083	0.2693	0.01067
	0.0560	1.0281	1.4072	12.1538	0.2148	0.00851
	0.0420	1.0265	1.4060	12.1061	0.1671	0.00662
35	0.1000	1.0304	1.4078	12.2495	0.3105	0.01231
	0.0750	1.0245	1.4070	12.2390	0.3000	0.01189
	0.0560	1.0209	1.4060	12.2077	0.2687	0.01065
	0.0420	1.0182	1.4044	12.1624	0.2234	0.00885
40	0.1000	1.0298	1.4072	12.2408	0.3018	0.01196
	0.0750	1.0281	1.4066	12.1856	0.2466	0.00977
	0.0560	1.0269	1.4054	12.1205	0.1815	0.00719
	0.0420	1.0259	1.4040	12.0606	0.1216	0.00482

Table 3: Molar refraction and polarizability constant at different concentration for l_2 system: 80% dioxane –water

Temperature T (^oC)	Concentration C(M)	Density ρ	Refractive index η	R_{mix} $cm^3.mole^{-1}$	R_{Ligand} $cm^3.mole^{-1}$	$\alpha x10^{-23}$ cm^3
20	0.1000	1.0369	1.4138	12.2739	0.3349	0.01327
	0.0750	1.0341	1.4126	12.2298	0.2908	0.01152
	0.0560	1.0312	1.4114	12.1956	0.2566	0.01017
	0.0420	1.0298	1.4092	12.1275	0.1885	0.00747
25	0.1000	1.0357	1.4132	12.2725	0.3335	0.01322
	0.0750	1.0330	1.4120	12.2271	0.2881	0.01142
	0.0560	1.0284	1.4108	12.2134	0.2744	0.01087
	0.0420	1.0260	1.4086	12.1567	0.2177	0.00863

Cont…

Temperature T (^oC)	Concentration C(M)	Density ρ	Refractive index η	R_{mix} $cm^3.mole^{-1}$	R_{Ligand} $cm^3.mole^{-1}$	$\alpha x10^{-23}$ cm^3
30	0.1000	1.0356	1.4124	12.2528	0.3138	0.01243
	0.0750	1.0313	1.4114	12.2316	0.2926	0.01160
	0.0560	1.0261	1.4096	12.2090	0.2700	0.01070
	0.0420	1.0225	1.4080	12.1825	0.2435	0.00965
35	0.1000	1.0354	1.4118	12.2395	0.3005	0.01191
	0.0750	1.0312	1.4106	12.2119	0.2729	0.01081
	0.0560	1.0260	1.4090	12.1945	0.2555	0.01012
	0.0420	1.0218	1.4074	12.1750	0.2360	0.00935
40	0.1000	1.0352	1.4112	12.2261	0.2871	0.01138
	0.0750	1.0310	1.4100	12.1985	0.2595	0.01028
	0.0560	1.0260	1.4084	12.1787	0.2397	0.00950
	0.0420	1.0211	1.4068	12.1676	0.2286	0.00906

Table 4: Molar refraction and polarizability constant at different concentration for L3 system: 70% dioxane –water

Temperature T (^oC)	Concentration C (M)	Density ρ	Refractive index η	R_{mix} $cm^3.mole^{-1}$	R_{Ligand} $cm^3.mole^{-1}$	$\alpha \times 10^{-23}$ cm^3
20	0.1000	1.0402	1.4168	12.2964	0.3574	0.01416
	0.0750	1.0371	1.4156	12.2599	0.3209	0.01272
	0.0560	1.0332	1.4142	12.2355	0.2965	0.01175
	0.0420	1.0300	1.4134	12.2276	0.2886	0.01144
25	0.1000	1.0398	1.4160	12.2804	0.3414	0.01353
	0.0750	1.0361	1.4148	12.2510	0.3120	0.01236
	0.0560	1.0324	1.4132	12.2190	0.2800	0.01110
	0.0420	1.0281	1.4120	12.2137	0.2747	0.01089
30	0.1000	1.0396	1.4152	12.2620	0.3230	0.01280
	0.0750	1.0358	1.4140	12.2337	0.2947	0.01168
	0.0560	1.0314	1.4128	12.2205	0.2815	0.01115
	0.0420	1.0275	1.4114	12.2052	0.2662	0.01055
35	0.1000	1.0386	1.4144	12.2530	0.3140	0.01245
	0.0750	1.0356	1.4134	12.2205	0.2815	0.01116
	0.0560	1.0294	1.4118	12.2181	0.2791	0.01106
	0.0420	1.0267	1.4110	12.2042	0.2652	0.01051
40	0.1000	1.0381	1.4140	12.2485	0.3095	0.01227
	0.0750	1.0354	1.4128	12.2073	0.2683	0.01063
	0.0560	1.0280	1.4108	12.2086	0.2696	0.01069
	0.0420	1.0242	1.4096	12.1973	0.2583	0.01024

From the data, it can be predicted that, when the temperature of mixture increases, the molar refractivity (true molar volume) continuously decreases. At the same time, the polarizability constant of compound (α) decreases. This may be attributed to the fact that with the increase in temperature of dioxane, there is decrease in dielectric constant of medium and also considerable dipole association (intermolecular attraction) take place, which would be accompanied by decreases in polarizability. It is observed from Table 2 to 4 when fraction of dioxane increases the refractive index also increases for compounds L_1, L_2, L_3 respectively.

RESULTS AND DISCUSSION

Literature survey reveals that when there is bulkier group, the molar refraction is greater. But in this investigation the value of molar refraction of compound L_3 was greater than L_2 as well as L_1. It was observed that only the bulkiness of the group as a substituent was not only interfere the values of molar refraction but also the reactivity and stability; tautomeric properties also interfair the values of molar refraction. It was clear from the result that in L_1, there was resonance stabilization in benzene ring which was substituted on one nitrogen of thiocarbamide at the same time on nitrogen of the same molecule; there was S-triazino moiety which restricts the tautomeric changes in L_1 molecule. While in case of L_2, a methylenic group in ethyl moiety become more reactive which directly and easily involved in tautomeric conversion of whole molecule such type of greater interference of methyl group will not involved in L_3 hence molar refraction of L_2 was smaller than L_3. But when we compared the molar refraction of L_1 and L_3, L_3 was greater than L_1, it was due to electron donating capacity of $–CH_3$ group to the thiocarbamide molecule hence in L_3 molecule there occurs compactness in the bond which was greater than L_1 molecule.

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 the 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 L_1, L_2, L_3 is more effective at higher concentration of dioxane. This study may become a milestone in the drug, medicinal and pharmaceutical chemistry of triazino thiocarbamides.

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