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RESEARCH ARTICLE

Temperature Dependence and Molecular Interactions Studies from Refractive Indices of 6-(4-Chlorophenyl)-1, 2, 3, 4-Tetrahydro-4-Oxo-2-Thioxopyrimidine-5-Carbonitrile in 60% Aqueous Dimethyl Sulphoxide

Ankita M Rayate[1], **Manoj R Gaware**[2]*

1 Research Scholar, Chemistry Research Center, M. V. P. Samaj's G.M.D. Arts, B.W. Commerce and Science College, Sinnar, Nashik, 422 103, Maharashtra, India
2 Professor, Chemistry Research Center, M. V. P. Samaj's G.M.D. Arts, B.W. Commerce and Science College, Sinnar, Nashik, 422 103, Maharashtra, India

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* **Corresponding author**.

gawaremanoj@rediff.com

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Abstract

Objectives: To study the effect of molecular interactions present in ternary system on refractive index with respect to different concentration. To evaluate the optical parameters by examine the change in refractive index. **Methods:** The compound under study was synthesized and purified by recrystallization. DMSO used for preparation of different series of concentration was purchased as analytical reagent grade (AR) of minimum assay of 99.9%. Different concentration was prepared from stock solutions. For density measurement we have adopted used calibrated pycknometer. To measure refractive index we have used Abbes Refractometer (AR-56, COSLAB). For maintaining required desired temperature we have continuously circulated water through refractometer. **Findings:** In this article, we are reporting the measurement of density, refractive index, molar refraction and polarizability constant as function of temperature at different concentration. We found that density has inverse relationship with temperature which can be well explained with respect to molar volume effect. Moreover, refractive index also declines with rise in temperature due to weakening of solute-solvent and solute-solute interactions. Due to this optical property related to refractive index are found to change. **Novelty:** Work reported in this article is not studied earlier. Our work with study of refractive index in ternary mixture system helps to understand the electronic component of radiation with the molecules.

Keywords: 6-(4-chlorophenyl)-1, 2, 3, 4-tetrahydro-4-oxo-2-thioxopyrimidine-5-carbonitrile, Refractive index, Molar refraction, Molar polarizability, Molecular interactions

1 Introduction

Study of refractive indexes of organic compounds has gained more attentions due to its application in solid waste management[(1)], drug discovery[(2)], supramolecular chemistry[(3)], etc. It is the optical property describing the relative speed of light through medium. Today nearly, 70-80 % drugs are incorporated with amine functionality. Study of molecular interactions between organic compounds with polar aprotic solvent have been gained importance has been of priority important to study different physiological action, physiological effect, pharmacokinetic in living organism. Such intermolecular interaction can be studies by various properties such as density, viscosity, conductivity, refractive index[(4)]. Refraction is natural optical phenomenon in which the non- perpendicular incident light is bent towards the normal at the interface between two different mediums in such a way that Sin angle of incidence light to Sin angle of reflected light is found to be constant as given by Snell's Law. Refractive index on the other hand is termed as an additive property of molecule easy to measure using Abbe's Refractometer. This property arises due to arrangement of atoms in the molecule. The cause for refraction to occur arises due to change in concentration of microscopic particles namely atoms and structure in the molecule. This property finds an application to determine the geometry of molecule. Different parameters such as refractive index, molar refraction and polarizability constant help researchers to understand different interactions of various mixtures.[(5)]Pyrimidines are class of unsaturated compounds containing fused cyclic amide ring. It also plays a crucial role in different biochemical process and hence is considered as important Pyrimidines play an important role in many biochemical processes hence are considered to be important moiety in drug discovery and metathesis reactions. Synthesis of pyrimidine is well-known from Biginelli reaction. During last decades any revolutionary changes have been made for developing methodologies in asymmetric Biginelli reaction in connection to pyrimidine compounds due to different biological activities[(6)] and remarkable pharmacological properties. Heterocyclic compounds are vital compounds and have gain important role in living organism including plants, animals and human beings. Such compounds are present as essential metabolite in living organism.

Various methodologies have been followed for the synthesis of pyrimidine scaffolds. Generally synthesis of pyrimidines derivatives are usually carried out by one step condensation procedure. On literature survey for procedure to synthesis dihydropyrimidines and its derivatives we have found are some of the procedures from literature which are useful in preparation of dihydropyrimidines and its derivatives. The synthesis of dihydropyrimidine carbonitriles is started by condensation of aromatic aldehyde and ethyl cyanoacetate by nucleophilic attack of carbanion generated by weak base to produce α, β unsaturated ester. Further on reaction with urea/thiourea, elimination of alcohol and hydrogen molecule takes place to give product. Many of these methods involve long reaction time, anhydrous solvents, stoichiometric amount, hazardous radiations, use of costly apparatus and give unsatisfactory yields. Owing to this limitation we have developed a new protocol for synthesis of 2, 4 dihydropyrimidine carbonitrile using ammonium chloride as inexpensive, mild and neutral available catalyst with NH_4Cl under solvent free condition[(7)]. The reported procedure gives product in good yields and avoid the problems such as cost, handling and safety associated with the use of the solvent. This method has decreased reaction time due to enhancing the reactivity of the reactant in solid state at 100°C reaction temperature.

We thought to continue our research one step ahead by measuring temperature dependence of refractive index used to determine molar refractivity and polarizability constant of our compound namely 6-(4-chlorophenyl)-1, 2, 3, 4-tetrahydro-4-oxo-2-thioxopyrimidine-5-carbonitrile prepared in series of concentration using binary solvent mixture of 60% aqueous dimethyl Sulphoxide. We studied these parameters to know the interaction associated with the solute and solvent.

2 Methodology

The compound under study was synthesized by simple and effective method as discussed earlier by using ammonium chloride and purified by recrystallization technique in laboratory by chromatographic plate technique[(8)]. DMSO used for preparation of different series of concentration was purchased as analytical reagent grade (AR) of minimum assay of 99.9%. We have prepared required concentration from stock solutions of 0.02 (mol L^{-1}) of compound. The stock solution were prepared by dissolving calculated amounts of organic compound in 60% aqueous dimethyl sulphoxide solution using serial dilution method. For our study we have used concentration ranging from 0.002 to 0. 010(mol L^{-1}). For density measurement we have adopted used pycknometer. For accurate measurement of density, pycknometer has to be calibrated. For this purpose, we have measured densities of triple distilled water and compared with literature values. Similarly, the densities of different liquids such as ethyl alcohol, acetone, toluene and carbon tetrachloride were determined using standardized pycknometer. To measure refractive index, we have used Abbes Refractometer (AR-56, COSLAB) having refractive index ranging from 1.3000 to 1.7100. For maintaining required desired temperature we have continuously circulated water through refractometer.

3 Result and Discussion

In earlier work we have reported the refractive index of 6-(4-chlorophenyl)-1,2,3,4-tetrahydro-2, 4-dioxopyrimidine-5-carbonitrile[9] using Lorentz-Lorentz equation[10]. We have determined density and refractive index at concentration ranging from 0.0002 to 0.01 (mol L^{-1}) at different temperatures (298-313 K). The change in refractive index was correlated with the molecular interactions present in the molecule. The refractive index of molecule reported earlier contained highly electronegative oxygen atom. Hence, in this article we have reported the change in refractive index of molecule containing sulphur atom. Here we found that due to presence of sulphur atom the refractive index, molar refraction (Rm) and polarizability constant (α) increases with concentration and decreases with temperature. This can be well explained that high electronegative atom has strong molecular interactions than less electronegativity atom. The molar refraction and polarizability constant can be deduced by using following equations:

$$R_m = \frac{n^2\text{-}1}{n^2\text{+}2} \times \frac{M}{d} = \frac{4}{3}\pi N\alpha \quad (1)$$

Rm = molecular refraction, n = refractive index of solution, M = molecular weight of solution, N = Avogadro's constant, α = polarizability constant.

Molar refraction and polarizability constant values are indicated in Table 1 and are shown below. Dependence of refractive index with concentration change is given by plot between refractive index (n) to concentration (C) as highlighted in Figure 1. During the study we have found direct correlation of density, refractive index, molar refraction and polarizability constant with increase in concentration. The effect points out the correlation that change in these parameters can led to change in intermolecular attraction between solute and solvent molecules. The interaction between solute and solvent is found to weaken with elevating the temperature resulting in decline in the values of molar refraction and polarizability.

Concentration and refractive index are correlated by using the equation as shown below:

$$n = K\,x\,C + n^0 \quad (2)$$

n = refractive index of solution, K = slope and n^0 is the intercept.

Table 1. Values of Density, refractive index, molar refraction and polarizability constant for different concentration at 298 K

Temperature	Conc.molL^{-1}	Density (d)g cm^{-3}	Refractive Index (n)	Molar Refraction (R_m) cm^3mol^{-1}	Polarizability constant (α)x 10^{-23}	n_0	K (L mol-1)
	0.002	1.08736	1.4251	61.9762	2.45654		
	0.004	1.08772	1.4253	61.9812	2.45673		
298 K	0.006	1.08814	1.4255	61.9827	2.45680	1.4248	0.13
	0.008	1.0889	1.4259	61.9904	2.45710		
	0.010	1.08912	1.4261	62.0033	2.45761		
	0.002	1.08684	1.4240	61.8655	2.45215		
	0.004	1.08714	1.4243	61.8867	2.45300		
303 K	0.006	1.08793	1.4247	61.8927	2.45323	1.4236	0.17
	0.008	1.08823	1.4249	61.9012	2.45356		
	0.010	1.08910	1.4254	61.9154	2.45413		
	0.002	1.08600	1.423	61.7855	2.44898		
	0.004	1.08653	1.4233	61.7937	2.44930		
308 K	0.006	1.08694	1.4235	61.7959	2.44939	1.4228	0.11
	0.008	1.08723	1.4237	61.8050	2.44975		
	0.010	1.08755	1.4239	61.8123	2.45004		
	0.002	1.08585	1.4221	61.67886	2.44475		
	0.004	1.08600	1.4222	61.68314	2.44492		
313 K	0.006	1.08623	1.4224	61.69566	2.44542	1.422	0.065
	0.008	1.08635	1.4225	61.70163	2.44565		
	0.010	1.08650	1.4226	61.67525	2.44582		

By studying parameters like molar refraction (R_m), Polarizability constant (α) and extent of intermolecular forces we are able to its role in studying antagonistic effect and finds application to study drug design, QSRR and QSAR studies[8]. From above interpretative studies we have found that both molar refraction (Rm) and polarizability constant (α) have direct relationship

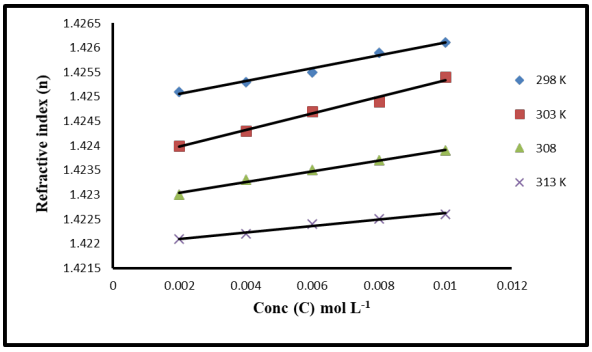

Fig 1. Variation of refractive index (n) with concentration (C) at different temperature

with concentration and inversely proportional with temperature ultimately resulting diminishing the interaction between solute and solvent [11]. The preferment is seen in the values of Rm and α at low temperature and concentration. We have systematically reported the variations in the values obtained by using above equations using graphical representation in Figure 2 and Figure 3.

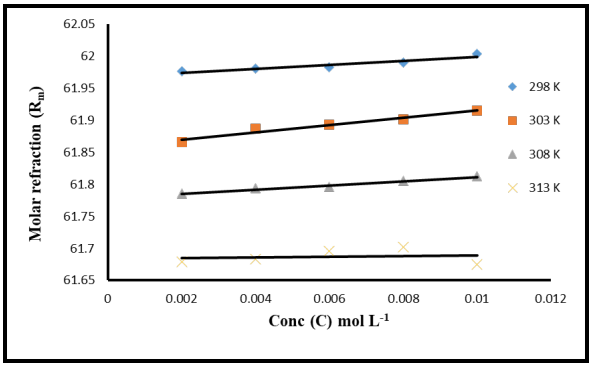

Fig 2. Variation of molar (R_m) at different concentration

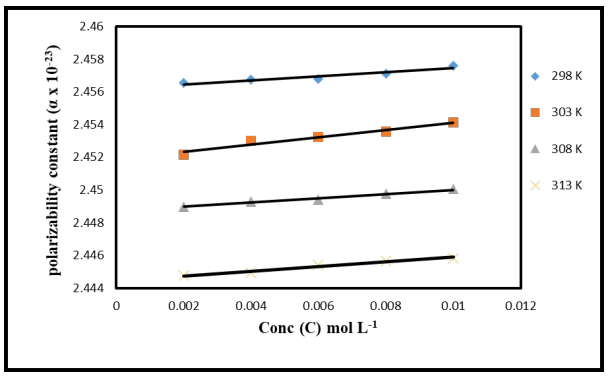

Fig 3. Variation of polarizability constant (α) at different concentration

4 Conclusion

We have measured refractive index of 6-(4-chlorophenyl)-1,2,3,4 tetrahydro-4-oxo-2-thioxopyrimidine-carbonitrile in series of solution prepared using 60 % aqueous dimethyl Sulphoxide as ternary mixture. This study reported the temperature dependence

of refractive index of this compound in term of molar refraction (Rm) and polarizability constant (α) ranging from 298 to 313 K. This study correlated density and refractive index with concentration, and we found that as concentration increases density and refractive index also increases. This study utilized the values obtained from measurement of refractive index to estimate the values of molar refraction and polarizability constant. This helps to understand the presence of interaction present between non polar atoms with molecules possessing electrical charge, dielectric constant and dipole moment. To understand in better ways we have correlated by means of graphical representation of refractive index against concentration, molar refractivity against concentration and molar refraction and polarizability constant against concentration. The graphical representation is studied for better understanding of formation and strength of intermolecular force constructed when organic compound is dissolved in polar solvent and it also gives a conceptual idea about the temperature dependence on the magnitude of intermolecular strength. This helps the researcher to understand the electronic component of radiation with the molecules. This study have predicted the strong dependence of density and refractive index with respect to molar concentration and temperature. The values determined by density and refractive index measurement points out the linear relationship with concentration. It is also found that polarizability enhances with linear rise in concentration which can be encountered due to molecular interactions present between solute and solvent and diminishes with temperature i.e. it is found to be high at low temperature and concentration while low at high temperature and concentration. This study have also reported the effect of electronegative atom on the magnitude of refractive index and its optical parameters which in turns show the nature of molecular interactions present in the molecule. This study will definitely will be useful to other pharmaceutically important molecules and will definitely bring revolutionary change in field of pharmaceutical industries.

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