Original Research Paper Chemistry

MOLECULAR INTERIONIC STUDIES OF 4-OXO-2-THIOXO PYRIMIDINE CARBONITRILES IN 60 % AQUEOUS DMSO AT 298.15 K

Jairaj S. Aher Department of Chemistry, K.T.H.M College, Nashik.

ABSTRACT Density, Viscosity of 4-oxo-2-thioxo pyrimidine carbonitriles have been measured in 60% aqueous dimethyl sulphoxide (DMSO) at 298.15 K. From the experimental data the related parameters such as apparent molar volume, limiting apparent molar volume, semi-empirical parameter, Falkenhagen coefficient and Jones Dole coefficient were evaluated. Such parameters gives identification of molecular interactions such as ion-ion, ion-solvent and solvent-solvent.

KEYWORDS : 4-oxo-2-thioxo pyrimidine carbonitrile, density, viscosity, aqueous DMSO.

Introduction:
Compounds contains heteroatoms such as oxygen, nitrogen and sulphur are termed as heterocyclic compounds. These compounds may be aliphatic or aromatic in nature. Pyrimidine ring system belongs to important heterocyclic conpounds in nature due to many biological significant compounds including nucleosides, nucleotides and biological activity[1-13] such as antiviral, antibacterial, anticancer, antifungal, antioxidant, antimalerial, anti HIV, sedatives, anticonvulsant, antihistamic agent, antihypertensive, anti-inflammatory, anticancer and calcium channel blockers. The parameters like apparent molar volume, density, viscosity, 'A' and 'B' parameters of Jones Dole equation are useful to focus the solute solvent interactions and to understand different biochemical aspects at 298.15 K. The results are interpreted in terms of solute-solvent and solute-solute molecular interactions in these systems.

Dimethyl sulphoxide (DMSO) is aprotic and is strongly associated due to highly polar S=O group. It has high miscibility in water and used for dissolving many organic as well as inorganic compounds. The study of DMSO is important because of its application in medicine.[14] It easily penetrates the biological membrane, facilitates chemical transport into biological tissues and is well known to have protective effects in biological systems.[15] It is also used as an inflammatory agent and for cancer treatment.16 Therefore the unique property of DMSO gives rise to wide use as solvent.

Also the drug water molecule interactions and its temperature dependence plays an important role in understanding drug action[17] ie drug reaching the blood stream, its extend of distribution, its binding to the receptor and producing the physiological action.

Material: 4-oxo-2-thioxo pyrimidine carbonitriles were synthesized and purified by recrystallization technique in laboratory.[18-25] Triple distilled deionized water was used for preparation of solution at room temperature in a molar range of 2 x 10^{-3} to 1 x 10^{-3} mol L^{-1}. DMSO used is of analytical reagent grade (AR) of minimum assay of 99.9% obtained from SD Fine Chemicals, Mumbai.

Density measurements: The pycknometer was calibrated by measuring the densities of triple distilled water. The densities of distilled organic liquids like acetone, toluene and carbon tetrachloride were evaluated with respect to density of water.

Viscosity measurement: The solution viscosities were measured by using Ubbelohde viscometer at 298.15 K. The temperature of thermostat was maintained to desired temperature by using demerstat. The flow time was recorded by using digital stop watch.

The different concentrations of solution were prepared in 60 % aqueous DMSO.

Data evaluation: The apparent molar volumes, Øv were obtained from the following equation[26-29]

$$\Phi v = \frac{1000\,(\rho_o - \rho)}{C\,\rho_o} + \frac{M2}{\rho_o}$$

where M_2, C, , **po** and **P** are the molar mass of 4-oxo-2-thioxo pyrimidine carbonitriles derivatives, concentration (mol. L^{-1}) and densities of the solvent and the solution respectively.

The apparent molar volumes Φv were plotted against the square root of concentration ($C^{1/2}$) in accordance with the Masson's equation[30]

$$\Phi v = \Phi^{\circ}_{v} + S_v\, C^{1/2}$$

where $\Phi^{\circ}V$ is the limiting apparent molar volume and Sv is semi empirical parameter or associated constant which depends on the nature of solvent, solute and temperature.

The viscosity results for the aqueous solutions of 4-oxo-2-thioxo pyrimidine carbonitriles were plotted in accordance with John Dole equation[31]

$$\frac{\eta_r - 1}{C^{1/2}} = A + B\,C1/2$$

Where $\eta_r = (\eta/\eta_o)$ and η, ηo are viscosities of the solution and solvent respectively. C is the molar concentration. The linear plot for $(\eta r-1)/C^{1/2}$ vs $C^{1/2}$ were obtained. The intercept (A) coefficient shows solute-solute interaction and the slope (B) reflect the solute-solvent interaction.

Table 1: Densities, molar volumes, viscosities and relative viscosities of 4-oxo-2-thioxo pyrimidine carbonitriles in 60 % aqueous DMSO solution at 298.15 K temperature.

Densities (ρ) (g.cm^{-3}), Apparent molar volumes (Φv) (cm^3.mol^{-1}), Viscosities (η) (cP) and Relative Viscosities (η_r)

Compound	Conc mol L-1	ρ	Φv	η	ηr
A-1	0.002	1.08527	-1086.4143	3.70105	1.098043
	0.004	1.08547	-483.6206	3.70728	1.099891
	0.006	1.08562	-274.9909	3.71334	1.101689
	0.008	1.08585	-179.9143	3.71968	1.103569
	0.010	1.08623	-136.7256	3.72653	1.105602
A-2	0.002	1.09076	-3580.7328	3.79084	1.124682
	0.004	1.09188	-1922.4729	3.79696	1.126498
	0.006	1.09385	-1500.5943	3.79766	1.126705
	0.008	1.09456	-1144.1531	3.80988	1.130329
	0.010	1.09586	-984.7939	3.81716	1.13249
A-3	0.002	1.08957	-3044.9162	3.76793	1.117885
	0.004	1.09102	-1737.7086	3.77488	1.119947
	0.006	1.09156	-1161.8597	3.78107	1.121783
	0.008	1.09189	-849.6850	3.79258	1.125198
	0.010	1.09387	-814.8107	3.7985	1.126955

Table 2: $(\eta r\text{-}1)/C^{1/2}$ and $C^{1/2}$ values of 4-oxo-2-thioxo pyrimidine carbonitriles in 60 % aqueous DMSO solution at 298.15 K temperature.

Compound	$C^{1/2}$ mol L^{-1}	$(\eta_r^{-1})/C^{1/2}$
A-1	0.04472	2.19232
	0.06325	1.57942
	0.07746	1.31280
	0.08944	1.15793
	0.10000	1.05601
A-2	0.04472	2.78798
	0.06325	2.00012
	0.07746	1.63576
	0.08944	1.45712
	0.10000	1.32490
A-3	0.04472	2.63600
	0.06325	1.89653
	0.07746	1.57221
	0.08944	1.39976
	0.10000	1.26955

Table 3: Masson's and Jones-Dole parameters of 4-oxo-2-thioxo pyrimidine carbonitrile5 in 60 % aqueous DMSO solution at 298.15 K temperature.

Compound	ΦoV	Sv	A ($dm^{3/2}mole^{-1/2}$)	B (dm^3mole^{-1})
A-1	-1691.9	16801	2.9793	-20.269
A-2	-5227.5	45362	3.7998	-26.124
A-3	-4565.8	40601	3.5773	-24.309

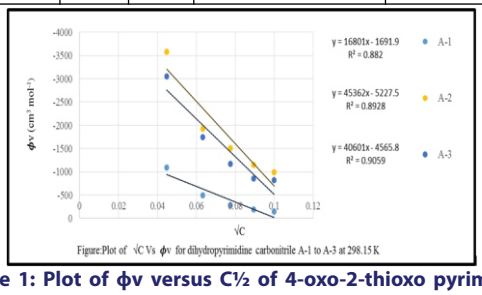


Figure 1: Plot of ϕv versus C½ of 4-oxo-2-thioxo pyrimidine carbonitriles in 60 % aqueous DMSO solution at 298.15 K temperature.

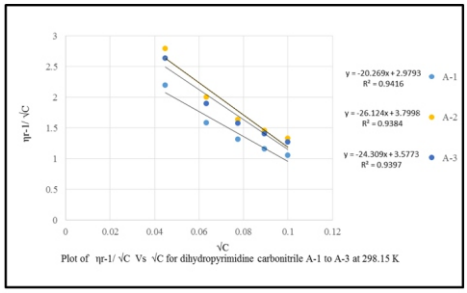
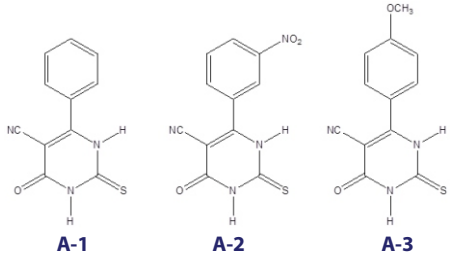


Figure 2: Plot of (ηr-1)/C½ versus C½ of 4-oxo-2-thioxo pyrimidine carbonitriles in 60 % aqueous DMSO solution at 298.15 K temperature.

Structure:



A-1 **A-2** **A-3**

Result and Discussion:

The values of the densities, molar volumes, viscosities and relative viscosities of 4-oxo-2-thioxo pyrimidine carbonitrile in 60 % aqueous DMSO solution at 308.15 K temperature are shown in Table 1. From A-1 to A-3, the densities increases with increase in concentration. The Φv values increases as the concentration increases. The negative value indicate the electrostrictive salvation of ions. The Φv values are more negative in A-2 as compared to A-3 and A-1 which suggest that there is strong molecular association in A-2 than A-3 and A-1 ie presence of electrostriction and hydrophilic interaction (solute solvent interactions).

Figure 1 shows linear plots of Φv vs $C^{1/2}$ of 4-oxo-2-thioxo pyrimidine carbonitriles in 60 % aqueous DMSO solution at 298.15 K temperature. Masson's parameter ΦoV (limiting apparent molar volume) and Sv (experimental slope or semi empirical parameter or associated constant) were obtained from linear plots in Table 3. The values of ΦoV are negative shows weak or absence of ion solvent interactions. In other words hydrophobic-hydrophobic group interactions are present. The values of ΦoV follow the trend A-2 > A-3 > A-1. The positive value of Sv indicates the presence of solute-solute interactions. A-2 has high solute-solute interactions than A-3 and A-1.

The values of the viscosities and relative viscosities of 4-oxo-2-thioxo pyrimidine carbonitriles in 60 % aqueous DMSO solution at 308.15 K temperature. The viscosities of solution increases with increase in concentration of solution. The value of $(\eta r^{-1})/C^{1/2}$ vs $C^{1/2}$ studied at 308.15 K. is shown in Table 2. Figure 2 shows variation of $(\eta r^{-1})/C^{1/2}$ against $C^{1/2}$ at 308.15 K.

'A' is constant independent of concentration and represent Falkenhagen coefficient (solute-solute interactions) while 'B' is Jones-Dole coefficient representing measure of order and disorder introduced by solute in solvent (solute-solvent interactions). Positive 'A' coefficient shows strong solute-solute interactions. The Jones-Dole parameters are shown in Table 3. The negative values of 'B' shows weak solute-solvent interactions. The value of 'A' in A-2 are high than A-3 and A-1 indicates presence of strong solute-solute interactions in A-2.

Conclusions:

From the present studies we have systematically reported densitometric and viscometric study of 4-oxo-2-thioxo pyrimidine carbonitriles in 60 % aqueous DMSO solution at 308.15 K temperature. It has been observed that negative values of (Φv) indicates strong molecular associations in A-2.

The values of ΦoV are negative which are high in A-2 suggests weak ion-solvent interactions. The value of Jones-Dole coefficient 'B' indicates strong interactions between solute and solvent while Falkenhagen coefficient 'A' indicates strong solute-solute interaction in A-2. The Jones Dole and Masson's equations are found to be obeyed for study of 2,4 dioxopyrimidine carbonitrile and derivatives in 60 % aqueous DMSO solution system at 298.15 K temperature.

Acknowledgement: The authors are thankful to UGC WRO, Pune and BCUD Savitribai Phule Pune University, Maratha Vidya Prasarak Samaj Nashik for providing infrastructure and Principal, K. R. T. Arts B. H. Commerce and A. M. Science College, Gangapur Road, Nashik-422 002, (MS), India for providing the research facilities.

References:

1 Kappe C. Tetrahedron , 49, 6937, 1993 and references cited therein.
2 (a) Patil A, Kumar N, Kokke W., Bean M., Freyer J., Brosse C., Mai S., Truneh A., Faulkner D., Carte B., Breen A., Hertzberg R., Johnson P. R., Westley J., Potts B., J. Org. Chem., 60, 1182, 1995. (b) Snider B., Chen J., Patil A., Freyer A., Tetrahedron Lett., 37, 6977 1996.
3 Clark J. , Shahhet M., Korakas D., Varvounis G., Heterocyclic Chem., 30, 1065-1072, 1993.

4 Ogowva K., Yamawaki I., Matsusita Y., Nomura N., Kador P., Kinoshita J., Eur. J Med Chem., 28, 769-781, 1993.
5 Tozkoparan B. , Ertan M., Kelicen P., Demirdar R., Farmaco, , 54, 588-593, 1999.
6 Santagati M. , Modica M., Santagati A., Russo F., Sampinato S., Pharmazie,, 51, 7-11, 1996.
7 Ahluwalia V., Chopra M., Chandra R., J Chem. Res. S., 162-163, 2000.
8 Van M., Volkerts E., Verbaten M., Psychopharmacology, 154, 189-197, 2001.
9 Danel K., Pedersen E., Nielsen C., J Med Chem., 41, 191-198, 1998.
10 Fathalla O., Awad S., Mohamed M., Arch Pharm Res., 28, 1205–1212, 2005.
11 Fathalla O., Zaghary A., Radwan H., Awad S., Mohamed M., Arch Pharm Res., 25, 258-269, 2002.
12 Ding Y., Girardet J., Smith K., Prigaro G., Wu J., Yao N., Bioorg Chem., 34, 26–38, 2006.
13 Azza T., Sahar M., Molecules, 17, 9868-9886, 2012.
14 Jacob S., Rosenbanm E., Wood D., Dimethyl Sulphoxide, Marcel Dukker, New York, 1971.
15 Lal J., et al, J. Sol. Chem., 24(1), 89–102, 1995.
16 Scaduto R., Free Radic. Biol. Med., 18(2), 271–277, 1995.
17 Muhammad J., Chaudhry M., J. Chem. Therm., 41, 221–226, 2009.
18 Kambe S., Saito K., Kishi H., Synthesis, 287-289, 1979.
19 Patel A., Pasha T., Modi A., Inter. J. Phar Tech Res, 8, 136-143, 2015.
20 Murthy Y., Saveri L. R., Parimi A., Nareesh S., Org Commun, 6(1), 47-54, 2013.
21 Eweas A., Qasem M., Emad A., Hassan S., J. App. Phar. Sci., 4(12), 102- 111, 2014.
22 Mohamed M., Awadn S., Ahmed A., Acta Pharm, 61, 171-185, 2011.
23 Chitre T., Bothara K., Der Chem. Sinica, 2(2), 187-193, 2011.
24 Muftah M., Abuhamrah S., Int. J. Adv. Res. Bio. Sci., 1(9), 259-262, 2014.
25 Desai S., Bhatia M., Choudhari P., Ingale K., Inter. J. Phar. Sci Res, 5(6), 241-248, 2014.
26 Das M, Das S. Patnaik A., J. Phy. Sci, 24(1), 37-50, 2013
27 Sumathi T., Varalakshmi M., Rasayan. J. Chem., 3(3), 550-555, 2010.
28 Sikarwar S., Chourey V. Ansari A., Inter. J. Chem. Phy. Sci., 4(1), 115-120, 2015.
29 Das M., Pradhan S., Das S., Patnaik A., Der Pharma Chemica., 7(2), 315–322, 2015.
30 Chauhan S., Syal V., Chauhan M., Sharma P., J. Mol. Liqs., 136, 161-164, 2007.
31 Jones G., Dole M., J. Am. Chem. Soc., 51, 2950-2964, 1929.