Available online at www.scholarsresearchlibrary.com

Scholars Research Library

Der Pharmacia Lettre, 2014, 6 (6):158-164
(http://scholarsresearchlibrary.com/archive.html)

ISSN 0975-5071
USA CODEN: DPLEB4

Viscometric study of substituted thiopyrimidine drugs at different temperature

Murlidhar P. Wadekar*, Amol S. Shrirao and Rajendra R. Tayade

Applied Chemistry Division, Govt. Vidarbha Institute of Science and Humanities, Amravati, Maharashtra, India

---

ABSTRACT

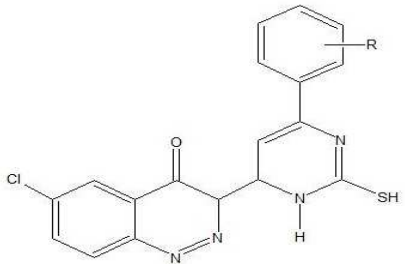
The measurement of densities, specific viscosities of substituted thiopyrimidine drugs of different concentration in the range ($1x10^{-2}$ M to $6x10^{-4}$ M) in 70% (DMF+water) solvent at 303K are reported. The experimental data shows, the effect of concentration of solute on viscosity in DMF-water mixtures which gives idea about the molecular interactions present in different solutions. Appreciable molecular interactions have been observed between the substituted thiopyrimidine and binary mixture. The themodynamic properties such as free energy change(ΔG), enthalpy change(ΔH) and entropy change (ΔS) of substituted thiopyrimidine drugs have been investigated in 70% (DMF+water) mixture at different temperature such as 308K, 313K and 318K. The experimental data gives the idea about effect of temperature on the molecular interaction and structural changes in solute.

Key words: specific viscosity, Density, thermodynamic parameters, substituted thiopyrimidine

---

INTRODUCTION

Physicochemical and thermodynamic investigation attract the inquisitive minds of researchers owing to the important role that drugs play. Physicochemical and thermodynamic investigations play an important role in understanding the nature and the extent of the patterns of molecular aggregation that exist in binary liquid mixtures and their sensitivities to variations in composition and the molecular structure of the pure components[1]. In biophysical chemistry, drug–macromolecular interaction is an important phenomenon involving a complex mechanism[2]. Since most of the biochemical processes occur in aqueous media, the studies on the thermodynamic and transport properties of drugs in the aqueous phase provide useful information in pharmaceutical and medicinal chemistry[3]. The drug-solvent molecular interaction and their temperature dependence play an important role in the understanding of drug action. Viscometric properties provide valuable clues for solute–solvent interactions in the solution phase. Such results can be helpful in predicting the absorption of drugs and transport of drugs across the biological membranes. Therefore, it may be interesting to investigate variation of their properties with temperature for understanding the mechanism of drug action. The detailed literature survey reveals that thermodynamic and transport properties of the above mentioned drugs in binary medium are scarce. This prompted us to investigate the thermodynamic and transport properties of four pharmacologically significant binary solutions of selected thiopyrimidine drugs.



L_1: R = -H
L_2: R = -2-Choro
L_3: R = -3-Chloro
L_4: R = -3-Bromo

L_1: 6-chloro-3-(2-mercapto-6-phenyl-3,4-dihydropyrimidin-4-yl)cinnolin-4(3H)one
L_2: 6-chloro-3-(6-(2-chlorophenyl)-2-mercapto-3,4-dihydropyrimidi-4-yl) cinnolin-4(3H) one
L_3: 6-chloro-3-(6-(3-chlorophenyl)-2-mercapto-3,4-dihydropyrimidin-4-yl) cinnolin-4(3H) one
L_4: 3-(6-(3-bromophenyl)-2-mercapto-3,4-dihydropyrimidin-4-yl)-6-chlorocinnolin- 4(3H)one

A survey of literature has shown that compounds having a pyrimidine nucleus possess a broad range of biological activities such as anticancer[4], antiviral[5], antibacterial[6], antimalarial[7], antihypertensive[8] and anti-inflammmatory activities[9,10]. The present work represents the continuation of a systematic investigation of the viscometric properties of drugs in binary solutions at various temperatures. Viscosity is one of the important physical property owned by the liquid. Shearing effect in the liquid is responsible for the viscous nature of the liquid which is nothing but the movement of liquid layers over each other.

The study of molecular interaction of an electrolyte in binary mixture of liquids by viscometrically plays an important role[11-14]. Many researcher study the biologically important drug at different temperature[15-19]. The Jones-Doles equation[20] helps to evaluate the observed viscosity concentration dependence of dilute electrolyte solutions.

MATERIALS AND METHODS

The ligands of which physical parameters is to be explore are synthesized by using reported protocol. The chemicals of AR grade were used. The densities of pure solvent and solutions of various concentrations were measured at different temperature using a precalibrated bicapilary pycnometer. All the weighings were made on one pan digital balance (petit balance AD_50B) with an accuracy of (±0.001)gm. Viscosities of the solutions were determined with the help of calibrated Ostwald viscometer (± 0.1% $Kgm^{-1}s^{-1}$). The flow time of solutions were measured by using digital clock of racer company having error (±0.01sec).

Calculation

To determine the relative and specific viscosity, in the different concentration of the substituted thiopyrimidine solution were prepared and there viscosities are measured with help of the following mathematical relation

$(\eta_r)=(ds \times ts/dw \times tw)\times \eta_w$.....(1)

Where

η_r	= Relative viscosity,	η_w	= Viscosity of water
ds	= Density of solution,	dw	= Density of water
ts	= Flow time for solution,	tw	= Flow time for water.

From the calculated values of relative viscosities (η_r) and the temperature (T),the graph between log (η_r) vs 1/T are plotted.

The relative viscosities of solution at different concentration are presented in table 1. The viscosity data have been analyzed by Jones –Dole equation[21]

$(\eta_r -1) /\sqrt{C}= \eta_{sp}/\sqrt{C} = A + B \sqrt{C}$ ---------- (3)

Where
A = Falkenhagen coefficient

B= Jones-Dole coefficient
C = concentration of solutions

The Falkenhagen coefficient (A) measures the solute-solute interation while Jones-Dole coefficient (B) measures the solute-solvent interaction.

The thermodynamic parameters i.e. free energy change(ΔG), enthalpy change(ΔH) and entropy change (ΔS) are determined by using following relation,

$\Delta G = -2.303 \times R \times slope$ ……. (4)
$\log \eta_{r1} - \log \eta_{r2} = (\Delta H/2.303) \times (1/T1 - 1/T2)$ ……(5)
$\Delta S = (\Delta G - \Delta H)/T$ …… (6)

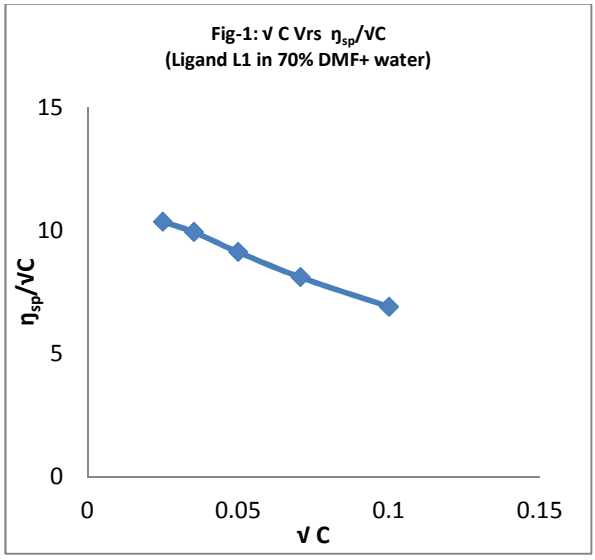
Table-1 Densites (d) gm/cc and specific viscosities (ŋsp) of substituted thiopyrimidines of different concentration in 70% (DMF+ water) solvent at 303K.

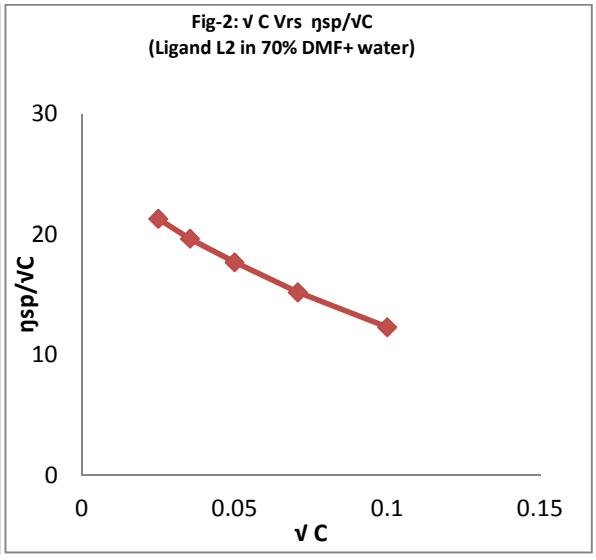
Conc. mole/lit	L_1		L_2		L_3		L_4	
	Density (d) (Kgm^{-3})	Rel. Viscosity η_r	Density (d) (Kgm^{-3})	Rel. Viscosity η_r	Density (d) (Kgm^{-3})	Rel. Viscosity η_r	Density (d) (Kgm^{-3})	Rel. Viscosity η_r
0.01	1.1263	1.6913	1.2253	2.2311	1.2246	2.0303	1.2532	2.3752
0.005	1.1253	1.5734	1.2243	2.0751	1.2224	1.8978	1.2502	2.2855
0.0025	1.1252	1.4568	1.2242	1.8845	1.2192	1.7135	1.2433	2.0604
0.00125	1.1241	1.3517	1.2231	1.6941	1.2185	1.5536	1.2402	1.8166
0.000625	1.1229	1.2592	1.2221	1.5323	1.2179	1.4251	1.2396	1.6221

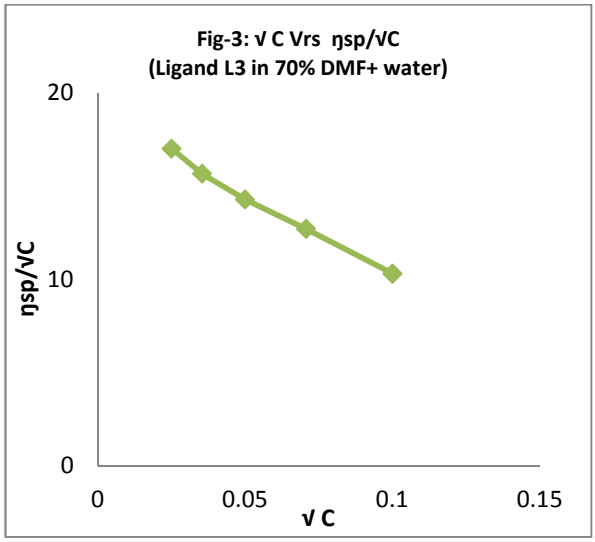
The value of A = Falkenhagen coefficient, B= Jones-Dole coefficient is calculated by ploting the graph between of √C Vs ŋsp/√C of all substituted thiopyrimidines.

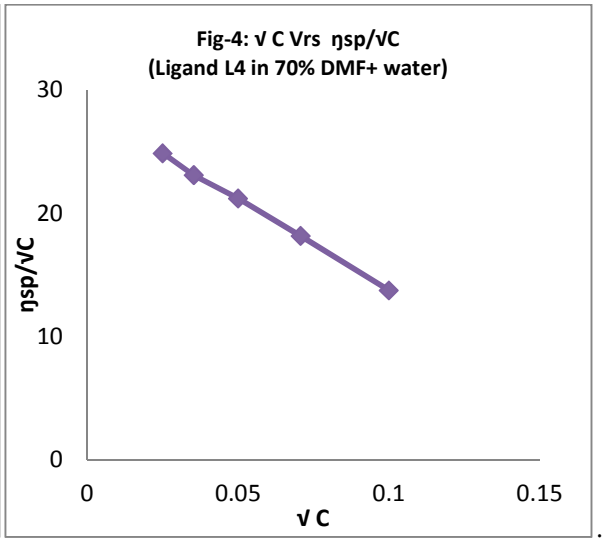
Table-2 A = Falkenhagen coefficient, B= Jones-Dole coefficient values

Ligand + 70%DMF-Water	A	β (Lit/mol)
L_1	11.52	-46.86
L_2	23.90	-118.7
L_3	18.87	-86.92
L_4	28.47	-146.7









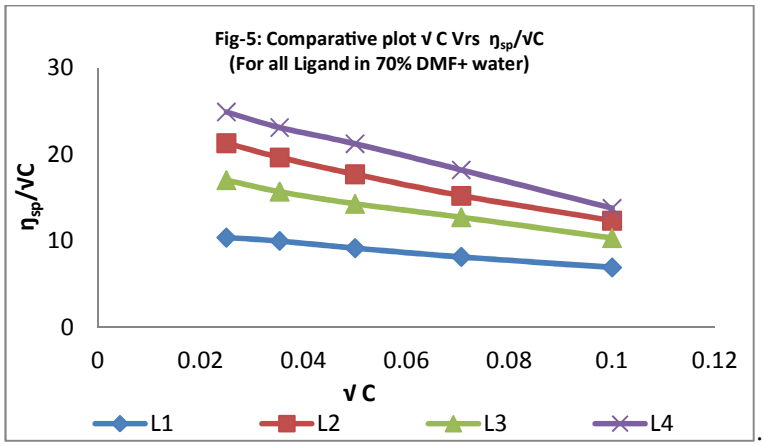


Table 3 Densites (d) gm/cc Relative and relative viscosities (ηr) of substituted thiopyrimidinea of 0.01M concentation in 70% (DMF+ water) solvent at different temperature (303, 308,313 and 318) K

Temp. in K	L_1		L_2		L_3		L_4	
	Density (d) (Kgm^{-3})	Rel. Viscosity η_r	Density (d) (Kgm^{-3})	Rel. Viscosity η_r	Density (d) (Kgm^{-3})	Rel. Viscosity η_r	Density (d) (Kgm^{-3})	Rel. Viscosity η_r
303	1.1263	1.6767	1.2253	2.1742	1.2245	2.1321	1.2532	2.4924
308	1.1154	1.6293	1.2144	2.1021	1.2136	2.0598	1.2427	2.4076
313	1.1047	1.5899	1.2035	2.0416	1.2027	2.0026	1.2321	2.3375
318	1.0930	1.5617	1.1987	1.9982	1.1965	1.9572	1.2216	2.2752

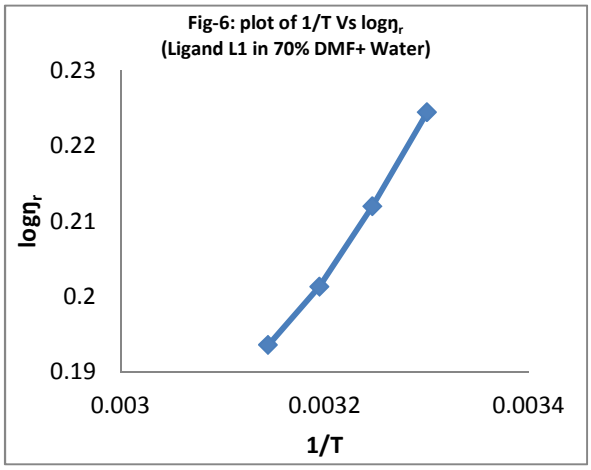


Fig-6: plot of 1/T Vs logη,
(Ligand L1 in 70% DMF+ Water)
0.23
0.22
0.21
0.2
0.19
logηr
0.003
0.0032
0.0034
1/T

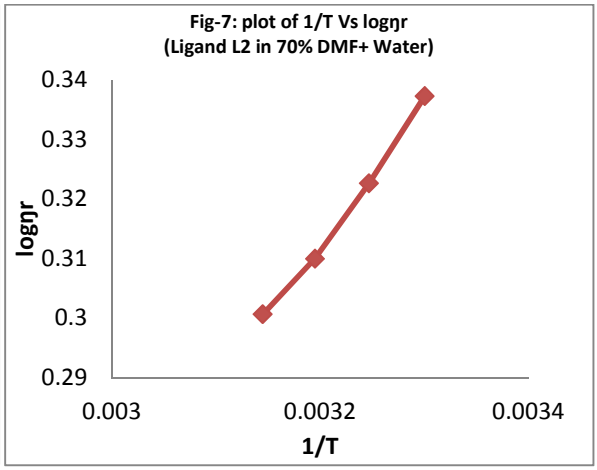


Fig-7: plot of 1/T Vs logηr
(Ligand L2 in 70% DMF+ Water)
0.34
0.33
0.32
0.31
0.3
0.29
logηr
0.003
0.0032
0.0034
1/T

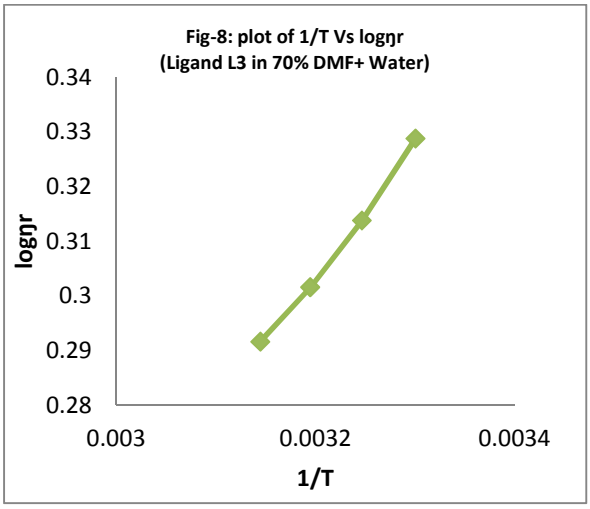


Fig-8: plot of 1/T Vs logηr
(Ligand L3 in 70% DMF+ Water)
0.34
0.33
0.32
0.31
0.3
0.29
0.28
logηr
0.003
0.0032
0.0034
1/T

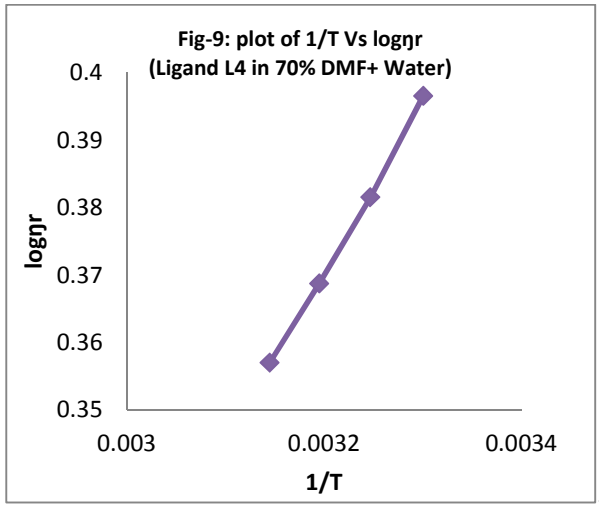


Fig-9: plot of 1/T Vs logηr
(Ligand L4 in 70% DMF+ Water)
0.4
0.39
0.38
0.37
0.36
0.35
logηr
0.003
0.0032
0.0034
1/T

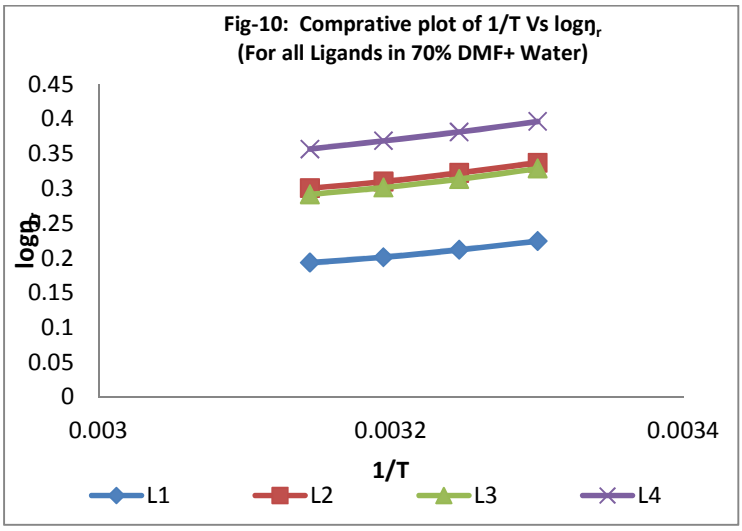


Fig-10: Comprative plot of 1/T Vs logη,
(For all Ligands in 70% DMF+ Water)
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
logηr
0.003
0.0032
0.0034
1/T
L1
L2
L3
L4

Table 4 Values of Thermodynamic Parameters for temperature difference 308K – 303°K

System	ΔG ($J\ mol^{-1}\ K^{-1}$)	ΔH ($J\ mol^{-1}\ K^{-1}$)	ΔS ($J\ mol^{-1}\ K^{-1}$)
L_1	-3812.20	-4448.63	-2.0663
L_2	-4528.30	-5234.14	-2.2916
L_3	-4570.42	-5352.79	-2.5401
L_4	-4859.54	-5370.30	-1.6583

RESULTS AND DISCUSSION

In the present investigation, the relative viscosity of solution of thiopyrimidine decreases with decrease in concentration of solutions. The increase in viscosity with increase in concentration may be ascribed to the increase in the interactions of solute-solvent. The relation between viscosity ($\eta_{sp}/\sqrt{C}$) and concentration of solution ($\sqrt{C}$) represented by plotting the graph (fig.1-5). The plotted graphs prove the validity of Jones-Dole equation for all systems by giving linear straight line. The values of Jones-Dole coefficients especially β -coefficients are the slope of graph ($\eta_{sp}/\sqrt{C}$) Vs ($\sqrt{C}$) while the values of Falkenhagen coefficient i.e. A-Coefficient are the intercept of graph of ($\eta_{sp}/\sqrt{C}$) Vs ($\sqrt{C}$). The order or disorder introduced by solute in solvent is measured by the values of β coefficient which shows either positive or negative values. β coefficient is in turn measures the effective hydrodynamic volume of solute, which accounts for the ion-solvent interaction.

In this work, the values of β -coefficients for all systems are negative. It is apparent from table-2 that β -coefficient is found to be negative for all system and is measure the effective thermodynamic volume of solute which accounts for solute-solvent interaction. It is known as a measure of disorder introduced by a solute in to the solvent. From data of table 2, it is conclude that, the order of Falkenhagen coefficient (A) are $L_2 > L_4 > L_3 > L_1$.

From table-1 the value of relative viscosity and density decreases for all system as the concentration of solution decreases. Polar nature of substituent depend upon its electronegativity and its position of attachment. Hence, ligand having more polar character shows high value of relative viscosity. The order of decreasing the relative viscosity all ligands are as $L_4 > L_2 > L_3 > L_1$. Density of solution also change in same order.

As the temperature increases the value of relative viscosity and density decreases shown in table 3. Due to increase in temperature the interaction between solute-solute and solute-solvent decreases. The themodynamic parameter such as free energy change(ΔG), enthalpy change(ΔH) and entropy change (ΔS) of different substituted thiopyrimidine drugs are calculated by plotting graph between 1/T Vrs log η_r are shown in (fig 6-10). Thermodynamic parameters are mentioned in table-4, indicate variation of their values with changing substituent on ligands. The negative value free energy change(ΔG) shows reaction is feasible in all cases. Enthalpy change(ΔH) interpreted that reaction of ligands and solvent are spontaneous and exothermic and negative value of entropy change (ΔS) interpreted that, randomness of solute molecule in solvent decreases i.e. there is association of solute molecule.

Acknowledgment
The Authors are thankful to Principal and Head of Chemistry department , Govt. College of Engineering, Amravati for providing laboratory facilities.

REFERENCES

[1] H. A. Zarei, F. Jalili, *J.Chem.Thermodyn*., **2007**, 39, 55.
[2] M. J. Iqbal, S. Mahrukh, *J.Braz.Chem*., **2006**, 5, 851.
[3] M. J. Iqbal, M. A. Chaudhry, *J.Chem.Thermodyn*., **2009**, 4, 221.
[4] S. J. Haggarty, T. U. Mayer, S. L.Schreiber, *Chem.Biol*., **2000**, 7, 275
[5] R. Kumar, M. Nath, D. L. Tyrrell, *J.Med.Chem*., **2002**, 45, 2032.
[6] A. A. Bekhit, H. T. Y. Fahmy, A. M. Baraka, *Eur.J.Med.Chem*., **2003**, 38, 27.
[7] A. Agarwal, K. Srivastava, Bioorg. *Med.Chem.Lett*., **2005**, 15, 3130.
[8] M. M. Ismail, N. A. Al-Sayed, Y. A. Ammar, *Arzneimittel-Forsch*., **2006,** 56, 322.
[9] S. M. Sondhi, N. Singh, A. Kumar, *Bioorg.Med.Chem*., **2005**, 13, 6158
[10] P. F. Ferri, A. Ubeda, I. Guillen, J. S. Arques, *Eur.J.Med.Chem*., **2003**, 38, 289.

[11] K. N. Mehrotra, K. Tandon, *J.Ind.Chem.Soc*., **1992**, 69, 193.
[12] S. Das, D. Hazra, *Ind.J.Chem*., **1988**, 27, 898.
[13] U. P. Kapadi, P. P. Hankare, *J.Ind.Chem.Soc*., **1994**, 72, 269
[14] R. B. Barry, F. M. Irving. *J.Phys.Chem.*, **1969**, 73, 2060.
[15] S. S, Dhondge, S. P. Zodape, D. V. Parwate, *J.Chem. Thermodynamics*, **2012**, 48, 207.
[16] A. G. Peshwe, B. R. Arbad, *Ind.StreamsRes.J.*,**2011**,1(5), 1.
[17] B. R. Breslan, J. F. Miller, *J.Phys.Chem*.,**1970**, 74, 1956.
[18] V. Vand, *J.Phys.Colloid.Chem*., **1948**, 52, 277.
[19] K. Rajagopal, S. S. Jayabalakrishnan., *J.Serb.Chem.Soc.*, **2011**, 76 (1) 129.
[20] G. Jones, M. J. Dole, J.*Am.Chem.Soc.*, **1929**, 51, 2950
[21] J. Jones, M. Dole, *J.Am.Chem.Soc*., **1929**, 5 (1), 2950.