Research Journal of Pharmaceutical, Biological and Chemical Sciences

Experimental study on Density, Viscosity, Derived Properties and Theoretical viscosities of Binary liquid mixtures of 2- Ethylhexanol + Hexane at T = (303.15, 313.15 and 323.15) K.

Venkatesan D[1]*, Joshua Amarnath D[1], and Saravanakumar K[2].

[1]Department of Chemical Engineering, Sathyabama Institute of Science and Technology , Chennai-600119, India.
[2]Department of Engineering, College of Applied Sciences, Sohar, Ministry of Higher Education, Oman.

ABSTRACT

Viscosity deviation ($\Delta\eta$), Excess molar volume (V^E) and Excess Gibb's free energy for viscous flow (ΔG^{*E}) are worked out from the experimental values. The values obtained were associated with the aid of Redlich-Kister polynomial to obtain the coefficients. Quantitative analysis was carried using modified Kendall-Monroe ($E\eta_m$) to understand the molecular interactions of the liquid-liquid binary system. Theoretical viscosities of 2 Ethylhexanol (1) + Hexane (2), were calculated by using various models like Frenkel, Hind–Mclaughlin Ubbelohde, Katti–Chaudhary, Grunberg–Nissan, and Kendall–Monroe and compared with the experimental values. It was observed that the calculated data was found to be quite reasonable and satisfactory.

Keywords: Viscosity, Density, 2 Ethyl hexanol, Hexane ,Excess properties

*Corresponding author

INTRODUCTION

In industrial flow applications wherein heat, mass and fluid flow is concerned it is essential to understand the molecular interactions. The study of transport (density, viscosity, etc.) and thermodynamic properties (excess molar volume) of liquid-liquid binary system at different temperatures give an insight into industrial flow problems [1,2]. The Thermophysical properties of liquid systems are complex because it depends on solvent-solute interactions and also the structural effects due to interstitial accommodation [3].

In the recent years, the studies on the intermolecular interactions have received significant attention among the scholars. The thermo physical properties data for binary liquid-liquid systems is useful in the theory of solutions and molecular dynamics [10]. Also, the experimental outcomes and interpretation of data of transport and thermodynamic properties are essential in biochemical, chemical, and electrochemical kinetic studies [2]. In particular, the studies on excess properties of binary systems are useful to understand the intermolecular forces [3,4]. Again, densities and viscosities at various temperatures for pure substance and binary liquid systems for whole range in composition are important in industrial flow applications associated with the fluid flow, heat and mass transfer processes [5]. In design of chemical process plants, very precise data are necessary on the transport and thermodynamic properties and reliable models to correlate when there is lack of experimental data. Therefore accurate predictive models are required as they are simple, powerful and attractive.

In the previous research paper, it is considered that the Thermophysical properties of binary liquid mixtures [3-6]. In continuation of this research, it is presented in the previous research paper that the experimentally measured viscosity and density values of 2-Ethylhexanol and Hexane (binary mixture) at three diverse temperatures T=(303.15, 313.15 and 323.15) K . Using the density(ρ) and viscosity(η) data, deviations in transport and thermodynamic properties like $\Delta\eta$, V^E and ΔG^{*E} are calculated. For viscosity correlation modified Kendall-Monroe equations with zero parameters are for the liquid-liquid mixture. Redlich-Kister [7] polynomial is used for fitting the calculated deviations of excess functions and viscosity .The consequences are then scrutinized in terms of molecular interactions.

In the manufacture of low-volatility esters, 2-Ethylhexanol mainly is used as a feed stock, 2-ethylhexyl phthalate (DOP and DEHP) is the most important, as a plasticizer for Poly Vinyl Chloride (PVC) and copolymers of vinyl chloride. It is also used as a common solvent of low volatility. 2-Ethylhexanol is also used as the octane riser upon reaction with nitric acid. In industries, hexane finds application in the formulation of glues that are applied for shoes, leather products and roofing. It is also used as a non-polar solvent in chromatography.

EXPERIMENTAL

In this present study, analytical grade chemicals are used and these chemicals are procured from M/s. Lobo Chemicals, India. The purity in terms of mass fraction is ≥ 0.998. Using molecular sieves the chemicals used are dried and degassed. [8,9]. The purity of chemicals used in the present study are analyzed for densities and viscosities in comparison with published literature data. With the help of Teflon coated air sealed glass bottle, liquid-liquid mixtures are well mixed for suitable volumes.   The weight of the liquid mixtures are measured using electronic balance model type BL 2205 (Shimadzu Corporation Japan) with a accuracy of 0.0001 g. The density and viscosity are gauged immediately after preparing samples with different composition [10, 11]. A thermostat with water circulation is employed for all the cases to control the temperature fluctuations and maintain ± 0.03K.

Density

To determine the density of pure binary liquid- mixtures a pycnometer of bi-capillary of 25 cubic centimeter is used. The double distilled water of deionized has density of 0.996 g/cm^3 is used to calibrate pycnometer at standard condition. The pycnometer is placed in a see-through water bath wherein the temperature is retained steady with ± 0.01 K in order to acquire thermal equilibrium. The liquid level in the bath is attained by using microscope that could read 1/100 mm. The density measurement precision is likely to be ± 0.0003 g/cm^3.

Viscosity

Ostwald viscometer is employed to measure the viscosities of pure liquid. Time and viscosity is assessed with an exactness of 0.01 s and 0.0002 mPa.s respectively. The relationship given below is used to obtain the viscosity [12].

$$\eta = (at - b/t)\rho \tag{1}$$

where 'a' and 'b' are the constants of the viscometer, 't'(s) is the flow time and ρ is the density (g/cm^3).

RESULTS AND DISCUSSION

The experimental data from this present work is matched up with the published data from literature. Table 1 gives the experimental and the literature data and Table 2 lists the densities and viscosities data from the experiments from 303.15 K to 323.15 K at different mole fractions.

The equations 2 - 6 are used to calculate the transport and thermodynamic properties like Viscosity deviation($\Delta\eta$), Molar volume(V_m), Excess molar volume(V^E), Excess Gibbs free energy of activation of viscous flow (ΔG^{*E}) [16] and Modified Kendall –Monroe ($E\eta m$) from the experimental data. The data obtained are presented in Table 3.

$$\Delta\eta = \eta_m - (x_1\eta_1 + x_2\eta_2) \tag{2}$$

$$V^E = \frac{x_1M_1 + x_2M_2}{\rho_m} - \frac{x_1M_1}{\rho_1} - \frac{x_2M_2}{\rho_2} \tag{3}$$

$$V_m = \frac{x_1M_1 + x_2M_2}{\rho_m} \tag{4}$$

$$E\eta_m = x_1x_2\left(\eta_1 x_1^{1/3} + \eta_2 x_2^{1/3}\right)^3 \tag{5}$$

$$\Delta G^{*E} = RT\left[\ln(_mV_m) - x_1\ln(_1V_1) - x_2\ln(_2V_2)\right] \tag{6}$$

Where x_1 and x_2 - mole fractions; ρ_1 and ρ_2 - densities; M_1 and M_2 - molar masses; η_1 and η_2 viscosities; V_1 and V_2 - molar volumes of 2 Ethylhexanol(1) and Hexane(2) respectively. T is the total temperature, and R is universal gas constant. The subscript m represents the properties of mixtures. Redlich–Kister polynomial [7] was used to correlate the Excess properties.

$$Y = x_1x_2 \sum_{K=0}^{m} A_k(x_1 - x_2)^k \tag{7}$$

Where Y= $\Delta\eta$, V^E, ΔG^{*E} and A_k are the coefficient parameters that were computed by least-squares method. Table 4 gives the parameter values of Redlich–Kister polynomial.

Theoretical viscosities of 2 Ethylhexanol (1)+Hexane (2), were calculated by using various models (Frenkel, Hind–Mclaughlin Ubbelohde , Katti–Chaudhary , Grunberg–Nissan, and Kendall–Monroe) and the values are listed in Table 5.

1. Based on zero adjustable parameters, Kendall-Monroe [17] derived Eqn.(8) for analysis of viscosity of binary mixtures.

$$\eta = \left(\eta_1 x_1^{1/3} + \eta_2 x_2^{1/3}\right)^3 \tag{8}$$

2. For non-ideal binary mixtures, Frenkel used Eyring's model [18] and considering molecular interaction Frenkel developed an algorithmic equation as given Eqn. 9.

$$\ln\eta = x_1^2\ln\eta_1 + x_2^2\ln\eta_2 + 2x_1x_2\ln\eta_{12} \tag{9}$$

where, η_{12} is the constant, η_{12} is attributed to, distinct pair exchanges. The value of this constant can be computed using the following relation:

$$\eta_{12} = 0.5\,\eta_1 + 0.5\,\eta_2 \qquad (10)$$

3. Hind et al. [19] have proposed the model

$$\ln\eta = x_1^2\eta_1 + x_2^2\eta_2 + 2x_1x_2H_{12} \qquad (11)$$

where, H_{12} - Interaction parameter and is attributed to distinct pair exchanges, and other terms have their usual meaning.

4. Katti-Chaudhri relation is expressed as [19]:

$$\ln\eta V = x_1\ln[\eta_1 V_1] + x_2\ln[\eta_2 V_2] + x_1x_2(W/RT) \qquad (12)$$

where, W -interaction energy parameter, V - mixture volume, V_1 and V_2 pure volumes of component 1 and component 2, respectively.

5. To assess the molecular interaction that leads to viscosity changes, Grunberg and Nissan [20] formulated an equation as given below:

$$\ln\eta = x_1\ln\eta_1 + x_2\ln\eta_2 + x_1x_2G_{12} \qquad (13)$$

where, G_{12} –proportional constant, η - dynamic viscosity and the subscripts 1,2 stands for pure components.

It is observed that in the whole composition variety, V^E- Excess molar volume in Fig 1. exhibits the positive values of V^E are due to the contributions from many opposing effects [21]. Positive V^E be capable of attributing the weak interactions between distinct molecules and V^E rises with increase in temperature [22]. The viscosity deviations seen in Fig 2 are negative over the whole range of composition and this suggest the existence of weak intermolecular interactions for the reason that of mixing in 2 Ethylhexanol and Hexane [23,24]. The figure also clearly shows a general viscosity deviation that decreases with rise in temperature. For calculating and forecasting vapor liquid equilibrium [25] Fig.3, the excess properties supply information on the macroscopic behavior and molecular interactions of fluid mixtures that will be supportive to test the advance thermodynamic models Fig.3. ΔG^{*E} are found to be positive and the magnitude of it stands for the potency of interaction among distinct molecules [26 ,27 ,28]. The given Fig.4 clearly exhibits that the altered Kendall-Monroe viscosity at different temperatures proves decrease with rise in temperature.

Table 1. Densities (ρ), and viscosities (η) data acquired from the present work in comparison with the literature data for pure components.

Substance	T/K	$\rho(g/cm^3)$		$\eta(mPa.s)$	
		Expt.	*Lit.*	Expt.	*Lit.*
2 Ethylhexanol	303.15	0.8258	0.8253[14]	5.5340	5.5345[14]
Hexane	298.15	0.6548	0.6549[15] 0.6547[12]	0.2926	0.2930[13]
	303.15	0.6518	0.6502[12]	0.2814	0.2830[12]

Table 2. Experimental densities and viscosities of 2 Ethylhexanol (1) and Hexane (2).

x_1	ρ (g/cm^3)			η(mPa.s)		
	303.15 K	313.15 K	323.15 K	303.15 K	313.15K	323.15 K
0.0000	0.6518	0.6425	0.6330	0.2814	0.2595	0.2408
0.0850	0.6691	0.6600	0.6506	0.3625	0.3277	0.2984
0.1729	0.6865	0.6774	0.6682	0.4710	0.4172	0.3727
0.2639	0.7039	0.6949	0.6858	0.6175	0.5356	0.4689
0.3580	0.7213	0.7124	0.7034	0.8174	0.6935	0.5948
0.4554	0.7387	0.7300	0.7211	1.0930	0.9064	0.7608
0.5564	0.7561	0.7476	0.7389	1.4760	1.1960	0.9820
0.6612	0.7735	0.7652	0.7567	2.0170	1.5950	1.2790
0.7699	0.7909	0.7828	0.7745	2.7880	2.1500	1.6840
0.8827	0.8084	0.8005	0.7924	3.9020	2.9310	2.2390
1.0000	0.8258	0.8181	0.8104	5.5340	4.0450	3.0110

Table 3. Deviation in Viscosity (Δη), Excess Molar Volume (V^E), Molar Volume (V$_m$), Excess Gibbs free energy (ΔG*^{E}) and modified Kendall-Monroe viscosity (Eη$_m$) for 2 Ethylhexanol (1) + Hexane (2).

x_1	$\Delta\eta$ (mPa.s)	V^E (cm^3/mol)	V_m (cm^3/mol)	ΔG^{*E} (J/mol)	$E\eta m$ (mPa.s)
303.15 K					
0.0000	0.0000	0.0000	132.2108	0.0000	0.0000
0.0850	-0.3655	0.0043	134.3906	3.3581	0.0328
0.1729	-0.7187	0.0082	136.6253	5.9243	0.0872
0.2639	-1.0498	0.0112	138.9388	7.9355	0.1661
0.3580	-1.3443	0.0136	141.3353	9.3658	0.2690
0.4554	-1.5806	0.0150	143.8191	10.0810	0.3896
0.5564	-1.7282	0.0153	146.3946	9.8254	0.5114
0.6612	-1.7373	0.0138	149.0670	8.7536	0.6036
0.7699	-1.5372	0.0109	151.8415	6.9133	0.6131
0.8827	-1.0160	0.0062	154.7049	3.8805	0.4551
1.0000	0.0000	0.0000	157.7016	0.0000	0.0000
313.15 K					
0.0000	0.0000	0.0000	134.1245	0.0000	0.0000
0.0850	-0.2537	0.0058	136.2435	2.5354	0.0289
0.1729	-0.4969	0.0099	138.4606	5.1813	0.0741
0.2639	-0.7227	0.0132	140.7383	7.2445	0.1369
0.3580	-0.9211	0.0156	143.1010	8.6171	0.2162
0.4554	-1.0771	0.0169	145.5331	9.2846	0.3064
0.5564	-1.1699	0.0172	148.0591	9.1667	0.3948
0.6612	-1.1674	0.0158	150.6839	8.0863	0.4584
0.7699	-1.0238	0.0129	153.4127	6.1766	0.4590
0.8827	-0.6701	0.0082	156.2316	3.3214	0.3365
1.0000	0.0000	0.0000	159.1859	0.0000	0.0000
323.15 K					
0.0000	0.0000	0.0000	136.1374	0.0000	0.0000
0.0850	-0.1779	0.0067	138.2120	1.9178	0.0258
0.1729	-0.3471	0.0120	140.3670	4.3047	0.0638
0.2639	-0.5028	0.0152	142.6058	6.2902	0.1147

0.3580	-0.6376	0.0169	144.9320	7.9079	0.1768
0.4554	-0.7416	0.0179	147.3293	8.6175	0.2454
0.5564	-0.8003	0.0182	149.8024	8.6085	0.3104
0.6612	-0.7934	0.0173	152.3765	7.3976	0.3547
0.7699	-0.6895	0.0149	155.0568	5.4159	0.3501
0.8827	-0.4471	0.0101	157.8286	2.6553	0.2534
1.0000	0.0000	0.0000	160.6984	0.0000	0.0000

Table 4. Coefficients of Redlich–Kister polynamial and standard deviations (σ) for 2 Ethylhexanol (1) + Hexane (2).

Property	A_0	A_1	A_2	A_3	A_4	σ
303.15 K						
$\Delta\eta$(mPa.s)	-6.639	-3.0685	-1.1035	-0.3376	-0.0818	0.0831
V^E(cm^3/mol)	-0.002	0.0964	0.1008	-0.3645	-0.0900	0.0122
ΔG^{*E}(J/mol)	39.119	-1.3036	-1.9873	-5.8107	1.5916	0.1213
313.15 K						
$\Delta\eta$(mPa.s)	-4.5117	-1.9416	-0.6411	-0.1827	-0.0493	0.0852
V^E(cm^3/mol)	-0.036	-0.0896	0.3358	0.0763	-0.7877	0.0123
ΔG^{*E}(J/mol)	35.378	-3.2480	19.579	4.1041	-37.951	0.1751
323.15 K						
$\Delta\eta$(mPa.s)	-3.098	-1.2378	-0.3748	-0.0970	-0.0291	0.0853
V^E(cm^3/mol)	0.0135	0.0238	-0.1580	0.2558	0.1649	0.0135
ΔG^{*E}(J/mol)	35.617	-3.8352	15.863	16.011	-33.041	0.1425

Table 5. Experimental Viscosity η values and Theoretical viscosity values by different models of 2 Ethylhexanol (1) + Hexane (2).

x_1	η_{exp}	Frenkel	Hind	Katti	G. & N.	K. & M.
303.15 K						
0.0000	0.2814	0.2814	0.2814	0.2814	0.2814	0.2814
0.0850	0.3625	0.3924	0.3725	0.3841	0.3624	0.4218
0.1729	0.4710	0.4910	0.4821	0.4815	0.4708	0.6095
0.2639	0.6175	0.6375	0.6379	0.6269	0.6175	0.8549
0.3580	0.8174	0.8398	0.8376	0.8371	0.8173	1.1706
0.4554	1.0930	1.1925	1.1335	1.1230	1.0920	1.5707
0.5564	1.4760	1.5605	1.5010	1.4960	1.4858	2.0722
0.6612	2.0170	2.2170	2.1178	2.1141	2.0708	2.6945
0.7699	2.7880	2.9580	2.8985	2.8185	2.8715	3.4604
0.8827	3.9020	4.2528	4.2140	4.1020	3.9312	4.3966
1.0000	5.5340	5.5340	5.5340	5.5340	5.5340	5.5340
0.0000	0.2814	0.2814	0.2814	0.2814	0.2814	0.2814
313.15 K						
0.0000	0.2595	0.2595	0.2595	0.2595	0.2595	0.2595
0.0850	0.3277	0.3872	0.3577	0.3987	0.3417	0.3718
0.1729	0.4172	0.4678	0.4575	0.4356	0.4275	0.5179
0.2639	0.5356	0.6252	0.5657	0.5958	0.5582	0.6049
0.3580	0.6935	0.8024	0.7593	0.8132	0.7136	0.7108
0.4554	0.9064	1.2062	1.0964	1.1842	1.0865	1.1354
0.5564	1.1960	1.3910	1.3095	1.2658	1.2563	1.2996
0.6612	1.5950	1.7050	1.6942	1.7984	1.6814	1.8465
0.7699	2.1500	2.2046	2.2015	2.2548	2.2050	2.3908
0.8827	2.9310	3.0342	3.0142	3.0542	3.0350	3.2502
1.0000	4.0450	4.0450	4.0450	4.0450	4.0450	4.0450

323.15 K					
0.0000	0.2408	0.2408	0.2408	0.2408	0.2408	0.2408
0.0850	0.2984	0.3252	0.3104	0.3004	0.2995	0.3014
0.1729	0.3727	0.3957	0.3982	0.4015	0.3821	0.4164
0.2639	0.4689	0.5141	0.5061	0.4925	0.4808	0.5406
0.3580	0.5948	0.6594	0.6645	0.6354	0.5997	0.6869
0.4554	0.7608	0.8360	0.8501	0.8615	0.8060	0.9089
0.5564	0.9820	1.0985	1.1024	1.0810	1.0120	1.1478
0.6612	1.2790	1.3765	1.4012	1.3273	1.3079	1.3834
0.7699	1.6840	1.9054	1.8220	1.8852	1.7281	1.9760
0.8827	2.2390	2.3454	2.4035	2.3254	2.2910	2.3474
1.0000	3.0110	3.0110	3.0110	3.0110	3.0110	3.0110
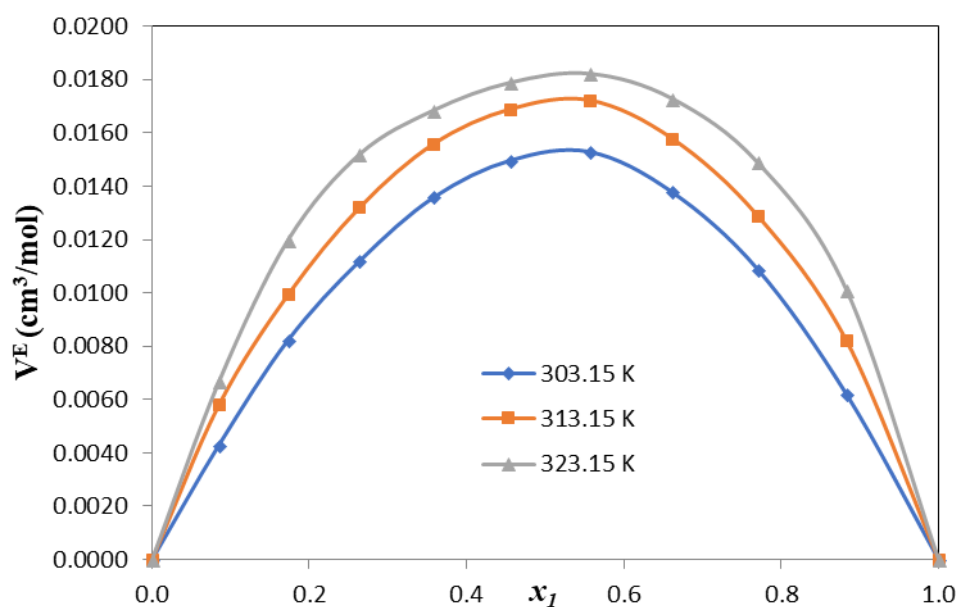
Figure 1. Excess molar volume versus mole fraction of 2 Ethylhexanol (1)+ Hexane (2).
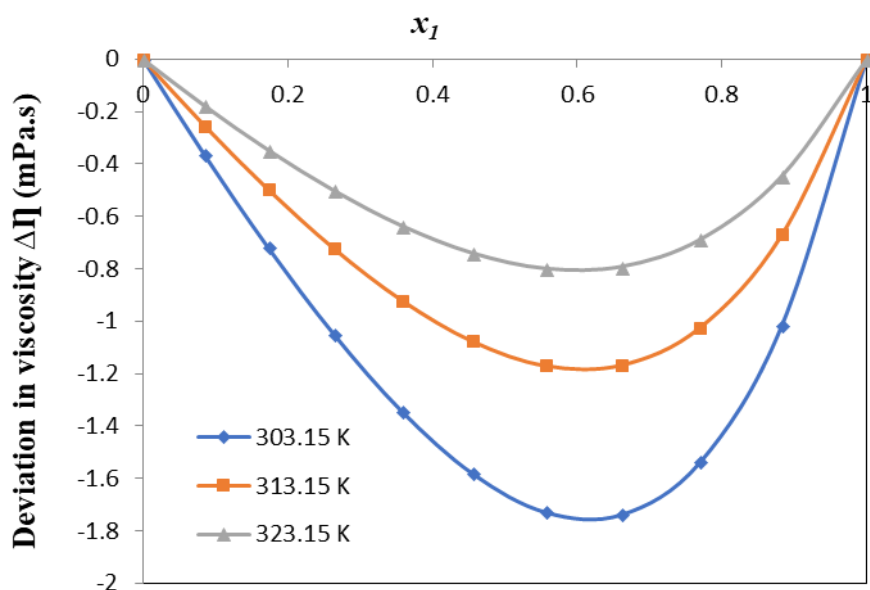

Figure 2. Viscosity Deviation versus mole fraction of 2 Ethylhexanol (1) + Hexane (2).
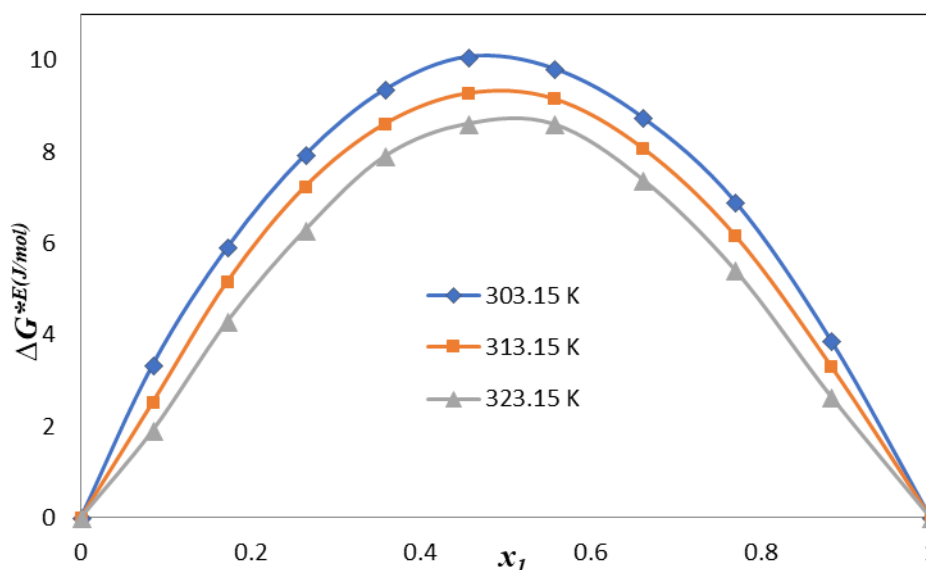
Figure 3. Excess Gibbs free energy versus mole fraction of 2 Ethylhexanol (1) + Hexane (2).
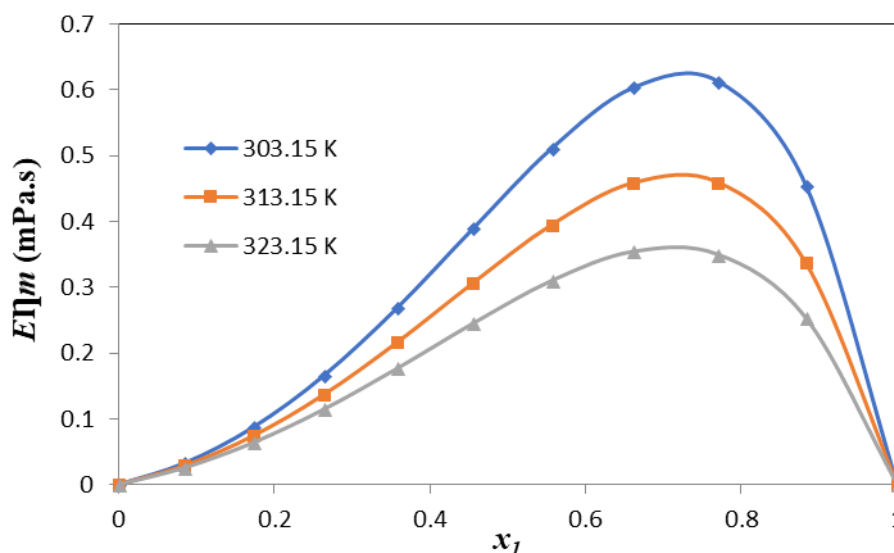

Figure 4. Modified Kendall and Monroe viscosity versus mole fraction of 2 Ethylhexanol (1) + Hexane (2).

CONCLUSION

Viscosities and Densities and viscosities) for liquid-liquid mixtures are measured. The viscosity variations and Excess molar volumes of 2 Ethylhexanol and Hexane are acquired from the experimental outcomes, and the outcomes are fitted in the Redlich-Kister equation. The outcomes are analyzed in terms of molecular interactions between the components. For the liquid-liquid binary system (2 Ethylhexanol and Hexane) the altered Kendall-Monroe viscosity correlation and Excess Gibbs free energy of viscous flow at different T =(303.15, 313.15 and 323.15) K are reported. Theoretical viscosities of 2 Ethylhexanol (1) + Hexane (2), are calculated by using various models and the results are quite satisfactory.

REFERENCES

[1]   Mchaweh.A,Alsaygh.A and Mosh-Feghian.M.A, Fluid Phase Equilib.,2004;224:157-165.
[2]   Kenart.C.M and Kenart.W, Phys. Chem. Liq.,2000;38:155-161.
[3]   Saravanakumar.K,Venkatesan.D and Gokulakrishnan.M,Research Journal of Pharmaceutical, Biological and Chemical Sciences.,2014;5:1392-1402.

[4] Saravanakumar.K, Baskaran. R and Kubendran.T.R, J.Kor. Chem. Soc.,2012;56: 424-434.

[5] Saravanakumar.K,Lavanya T.G, Baskaran.R and Kubendran.T.R, J. Iran Chem. Soc.,2012;9: 277-290.

[6] Saravanakumar.K,Baskaran.R and Kubendran.T.R. Russ. J. Phys.Chem.,2012;86: 1947-1959

[7] Redlich.O, Kister. A. T, Ind. Eng. Chem.,1948;40: 345-354.

[8] Xin-Xue Li, Gui-Chen Fan,Yan-Wei Wang,Min Zhang and Yi-Qiang Lu, Journal of Molecular Liquids.,2010;151: 62-75.

[9] Ezekiel D. Dikio, Simphiwe M. Nelana, David A. Isabirye, Eno E. Ebenso Int. J. Electrochem. Sci.,2012;7:11101-11117.

[10] Pal.A and Gaba.R, J, Chem. Thermodyn.,2008;40: 750-762.

[11] Fenn.E.E, Moilanen.D.E, Levinger.N.E and Fayer.M.D, J.Am. Chem. Soc.,2009;131:5530-5542.

[12] Nandhibatla V. Sastry , and Mahendra M. Raj, *J. Chem. Eng. Data.,*1996;41: 612-622.

[13] Jagan Nath and Jai Gopal Pandey *J. Chem. Eng. Data.,42(*1997;42:1133-1145.

[14] Edward Zore-bski, Marzena Dzida, and Ewa WysockaJ. Chem. Eng. Data.,2011;56:2680-2692.

[15] Pereiro.A.B and Rodrı´guez.A, J. Chem. Thermodynamics.,2007;39:1219–1230

[16] Singh.S, Sethi.B.P.S, Katyal.R.C and Rattan,V.K, J. Chem. Eng. Data.,2004;49: 1373-1381.

[17] Clara.R.A,Marigliano.A.C.G, Campos.V.V and Solimo,H.N, Fluid Phase Equilib.,2010;293:151-163.

[18] Gonzalez.B,Calvar.N,Gomez.E,and Dominguez.A, J. Chem. Thermodyn.,2007;39: 1578-1590.

[19] Dubey.G.P, Sharma.M and Dubey.N, J. Chem. Thermodyn.,2008;40: 309-320.

[20] Liu,J, Zhu,C and Ma.Y, J. Chem. Eng, Data.,2011;56:2095-2120.

[21] Bhatia.S.C,Sangwan.J and Bhatia.R, J. Mol. Liq.,2011;161: 95-108.

[22] Azhagiri.S,Jayakumar.S,Padmanaban.R,Gunasekaran.S,and Srinivasan.S, J Solution Chem .,2009;38:441-452 .

[23] Akanksha Saini,Hrishikesh Joshi, Kratrika Kukreja and Ranjan Dey, Journal of Molecular Liquids.,2016;223:165-180.

[24] Jyoti N. Nayak, Mrityunjaya.I,Aralaguppi and Tejraj M. Aminabhavi, J. Chem. Eng. Data.,2003;48:1152-1164.

[25] Ohji.H,Tamura.K and Ogawa. H,   J. Chem. Thermodyn.,2000;32:319-329.

[26] Aminabhavi.T. M, Aralaguppi.M. I,Bindu.G and Khinnavar,R, J. Chem. Eng. Data.,1994;39:522-532.

[27] Marquardt,D. W, J. Soc. Ind. Appl. Math.,1963;11:431-443.

[28] Antonio Aucejo,Cruz Burguet.M and Rosa Muñoz , J. Chem. Eng. Data.,1996;41: 1131-1143.