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***Research Article***

# STUDY ON THE SOLUBILITY CHARACTERISTICS OF SOME QUINAZOLINE DERIVATIVES AND THERMODYNAMIC STUDY IN DIFFERENT ORGANIC SOLVENTS

***Shipra Baluja, Paras Ramavat and Kajal Nandha**
*Physical Chemistry Laboratory, Department of Chemistry, Saurashtra University, Rajkot-360005 (Gujarat), India*
**Author for Correspondence*

## ABSTRACT
Some new pyrazolo quinazoline derivatives were synthesized and their solubility data were determined at different temperatures under atmospheric pressure. Solubility study of all the compounds were studied by gravimetric method in N, N-dimethylformamide, dimethyl sulphoxide, tetrahydrofuran, 1, 4-dioxane and ethyl acetate. The modified Apelblat and Buchowski-Ksiazczak λh equations were used to correlate the experimental solubility data. Using Van't Hoff and Gibb's equations, some thermodynamic parameters such as Gibb's free energy, enthalpy and entropy of dissolution were evaluated from solubility data. It is found that solubility increases with temperature and found to be greater in DMF.

***Keywords:*** *Pyrazolo Quinazolines, Average Deviation, Relative Deviation, Apelblat Equation, Buchowski-Ksiazack λh Equation, Gibb′s Energy*

## INTRODUCTION
In recent years, quinazolines and their derivatives have drawn a great attention in the field of pharmacological medicinal chemistry (Eweas *et al.,* 2013). A vast number of quinazoline derivatives have been synthesized to design highly effective medicines (Dangi *et al.,* 2011). Literature survey shows that sulpher containing compounds of five-member and six-member rings possess various types of biological activities. The compounds which have quinazoline moiety shows various biological activities such as antidepressant agents (Shehata *et al.,* 2011), antimalarial (Verhaeghe *et al.,* 2008), antibacterial (Dangi *et al.,* 2011; Sharma *et al.,* 2004; Elkholy and Morsy, 2006), anticancer (Joseph *et al.,* 2010; Al-Obaid *et al.,* 2009), anti-inflammatory (Sondhi *et al.,* 2005; Kumar *et al.,* 2012; Chandrika *et al.,* 2008), anticonvulsant (Farghaly *et al.,* 2014; Abdel Gawad *et al.,* 2011; Kashaw *et al.,* 2009; Archana *et al.,* 2004), antifungal (Pandey *et al.,* 2005; Shivananda and Shivarama, 2011) etc.
Solubility of a heterocyclic compound is the most useful physical property that has been studied. The aqueous solubility plays an important role in industrial, pharmaceutical and environmental application (Morelock *et al.,* 1994). Solubility behavior of a compound is an important factor affecting their bioavailability. Drug design must be done by taking information of solubility as well as biological activity (Mitchell and Jurs, 1998).
Further, solubility data provides useful information for design process pharmaceutical dosage form and drug discovery process (Lipinski *et al.,* 2012). Such solubility data is also important for synthesis and evaluation of the separation process and equipments (Ding *et al.,* 2010). Study of temperature dependence solubility data provides the explanation of molecular mechanisms involved in the respective drug dissolution process (Kuhs *et al.,* 2013). Temperature dependent solubility data has been used in practical applications such as drug discovery, drug formulation, crystallization based on separation etc. Solubility data may be useful to understand various metabolic processes and for the drug design process of pharmaceutical industry. So, it will be interesting to study solubility of these derivatives in various solvents at various temperatures.
Because of containing interest about pyrazolo quinazoline derivatives, the solubility of synthesized compounds has been studied in different solvents and temperatures. The present work describes the synthesis and solubility of pyrazolo quinazolines in N, N-dimethyl formamide, 1, 4-dioxane, dimethyl sulphoxide, tetrahydrofuran and ethyl acetate at 298.15 K to 328.15 K temperature range. These data were

correlated with a modified Apelblat and Buchowski-Ksiazczak λh equations. And by these data some thermodynamic parameters were also evaluated.

## MATERIALS AND METHODS

### *Experimental*

*Materials*

α-tetralone and different substituted benzaldehydes used for the synthesis, were supplied from Spectrochem Pvt. Ltd. (Mumbai, India) and were used without any treatment. The solvents used to determine dissociation constant were of AR grade supplied by Spectrochem Pvt. Ltd. (Mumbai, India) and was purified according to the standard procedure (Riddick *et al.*, 1986). Dielectric constant and dipole moment of all the solvents used are given in Table 3. Distilled solvents were stored over molecular sieves. The purity of used solvents was confirmed by GC-MS (SHIMADZU-Model No.-QP-2010) equipped with column (DB-5MS, 25 m in length, 0.20 mm internal diameter and 0.33μm film) and was found to be 99.99%. The source and mole fraction purity of solvents are given in Table 1.

**Table 1: The Source and Mole Fraction Purity of Solvents**

| Solvents/Chemicals | Source | Mole Fraction Purity |
|---|---|---|
| DMF | Allied Chemical Corporation | 0.997[s] |
| DMSO | Allied Chemical Corporation | 0.994[s] |
| THF | Allied Chemical Corporation | 0.990[s] |
| 1,4-Dioxane | Allied Chemical Corporation | 0.992[s] |
| Ethyl Acetate | Allied Chemical Corporation | 0.998[s] |
| α-Tetralone | Spectrochem | 0.950[s] |
| KC-1 to KC-10 | Synthesis | 0.995[t] |

[s]: Analytical grade reagent dried over anhydrous sodium sulphate and kept over molecular sieves.
[t]: Gas Chromatography method.

**Table 2: Physical Constants of Synthesized Compounds**

| Compound Code | Substitution R | Molecular Formula | Molecular Weight | Yield (%) | $R_f$* Value | Melting Point $^0$C |
|---|---|---|---|---|---|---|
| KC-1 | -4-Cl | $C_{22}H_{17}ClN_4S$ | 404.09 | 78 | 0.66 | 243 |
| KC-2 | -4-$OCH_3$ | $C_{23}H_{20}N_4OS$ | 400.14 | 79 | 0.64 | 254 |
| KC-3 | -4-F | $C_{22}H_{17}FN_4S$ | 388.46 | 78 | 0.61 | 250 |
| KC-4 | -4-Br | $C_{22}H_{17}BrN_4S$ | 448.04 | 76 | 0.63 | 269 |
| KC-5 | -3,4-di$OCH_3$ | $C_{24}H_{22}N_4O_2S$ | 430.52 | 71 | 0.59 | 228 |
| KC-6 | -4-CN | $C_{23}H_{17}N_5S$ | 395.12 | 75 | 0.63 | 269 |
| KC-7 | -3-Cl | $C_{22}H_{17}ClN_4S$ | 404.09 | 72 | 0.65 | 248 |
| KC-8 | -3-$OCH_3$ | $C_{23}H_{20}N_4OS$ | 400.14 | 79 | 0.62 | 215 |
| KC-9 | -3-Br | $C_{22}H_{17}BrN_4S$ | 448.04 | 71 | 0.61 | 261 |
| KC-10 | -4-$CH_3$ | $C_{23}H_{20}N_4S$ | 384.14 | 69 | 0.65 | 285 |

*Hexane: Ethyl acetate = 0.6:0.4

**Table 3: Dielectric Constant and Dipole Moment of Studied Solvents at 293.15 K[40]**

| Solvent | Dielectric Constant | Dipole Moment | δH Hydrogen Bonding |
|---|---|---|---|
| DMF | 36.71 | 3.86 | 11.3 |
| DMSO | 47 | 3.96 | 10.2 |
| THF | 7.52 | 1.63 | 8.0 |
| 1,4-Dioxane | 2.22 | 0.45 | 9.0 |
| Ethyl acetate | 6.00 | 1.78 | 7.2 |

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***Synthesis***

*Synthesis of (Different Chalcones) Int.-I*

Equimolar mixture of α-tetralone and different substituted benzaldehydes in methanol were stirred for 4 h in presence of catalytic amount of potassium hydroxide. The completion of reaction was confirmed by analytical thin layer chromatography (TLC) (Performed on aluminum coated plates Gel $60F_{254}$ (E. Merck)) using (7:3-Hexane: Ethyl acetate) as mobile phase. After completion of reaction, the reaction mass was cooled and the resulting solid was filtered, washed with water and dried under vacuum to give crude product. The obtained crude product was purified by adding suitable solvent (diethyl ether) to remove colored, non polar impurity by scratching/stirring. The product was then allowed to settle down and the above solution was decanted. The procedure was repeated 3-4 times to remove impurities. The purity of Int.-I was 99.5 % as determined by gas chromatography.

*Synthesis of ((5-Amino-3-(Methylthio)-1H-Pyrazole-4-Carbonitrile) Int.-II*

A mixture of malanonitrile (0.01 mol) and dry $K_2CO_3$ (0.012 mol) were stirred in dry DMF at room temperature (RT) for 30 min. To this reaction mixture, 0.02 mole of carbon disulphide was added drop wise and the resulting solution was stirred for 2.5 hrs at room temperature. The solution was then cooled at 0 to $5^0$C. To this cooled solution, 0.02 mol dimethyl sulphate was added and the solution was again stirred for 5-6 hrs at room temperature. The progress of the reaction was monitored by thin layer chromatography. After completion of the reaction, it was poured into crushed ice to give solid product. The resulting solid was filtered, washed with cold water and dried under vacuum to give crude product.

Equimolar solution of this crude product and hydrazine hydrate in isopropyl alcohol (IPA) was refluxed for 30 min. The reaction mixture was then poured into crushed ice. The resulting solid was filtered, washed with water and dried under vacuum to give product. The obtained crude product was purified by trituration with hexane and was used in the next step without further purification.

*Synthesis of Pyrazolo Quinazoline Derivatives*

An equimolar mixture of Int-I (chalcones) and Int-II (5-amino-3-(methylthio)-1H-pyrazole-4-carbonitrile) were refluxed in n-butanol for 4-5 hrs. The completion of reaction was confirmed by Thin Layer Chromatography using (6:4- Hexane: Ethyl acetate) as a mobile phase. The reaction mixture was then allowed to cool and the resulting solid was filtered, washed with diethyl ether to remove impurities. The procedure was repeated 3-4 times to free the product from impurities. All the reaction schemes are given in Figure 1.

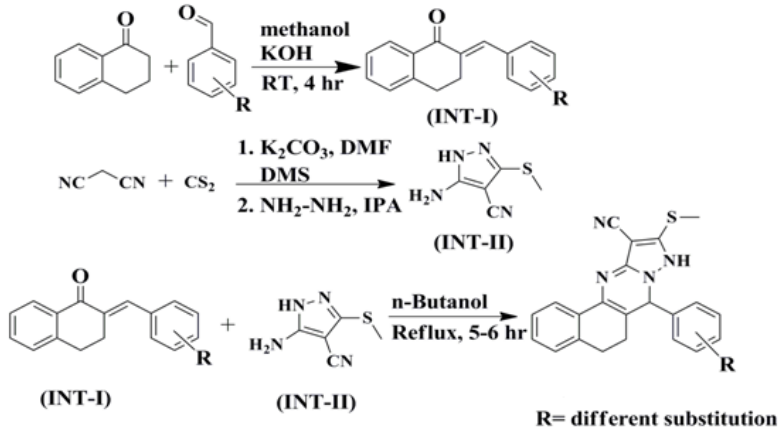



**Figure 1: Synthesis Scheme of Pyrazolo Quinazoline Derivatives**

***Solubility Measurement***

The solubility measurement was carried out by gravimetric method (Yu *et al.*, 2012; Zhu, 2001; Joly *et al.*, 1979). An excess mass of synthesized pyrazolo quinazolines derivatives were added to a known mass

of solvent. The solution was heated at constant temperature with continuous stirring until equilibrium established.

After few hours the stirring was stopped and the solution was kept at constant temperature for 2 hours. After 2 hours the change in concentration was less than 1%. So, this solution was filtered and 2 ml of the solution was taken in pre weighted measuring vial. This vial was instantly weighted to determine the mass of the sample and then kept in vacuum oven at 318.15 K to evaporate solvent present in it. When in the vial mass of residue reached to the constant value then the final mass of residue was recorded. The weights were taken in electronic balance (Mettler Toledo AB204-S, Switzerland) with uncertainty of ±0.0001 g.

During the whole experiment, at each temperature the measurement was conducted three times and average value was used to determine the mole fraction solubility of solute ($x_i$) in solvents by using equation 1 and given in Table 4.

$$x_i = \frac{m_2/M_2}{m_1/M_1 + m_2/M_2} \quad (1)$$

Where, $M_1$ and $M_2$ is the molecular weight of solvent and compound respectively. $m_1$ and $m_2$ are weights of solvent and synthesized compound in the solution respectively.

## RESULTS AND DISCUSSION

### *Solubility Data Correlation and Correlation Models*

The mole fraction solubilities $x_i$ in some selected solvents at different temperatures is given in Table 4. The diagrammatic variation of solubility of all the synthesized compounds in studied solvents is given in Figure 2 and Figure 3.

As evident from Figures that for all the compounds, solubility is maximum in DMF. However, in other solvents, order of solubility for different compounds varies. This may be due to electron withdrawing (-I) / electron donating (+I) effects of different substitutions.

Different solvents have different hydrogen donating capacity as shown in Table 3. This may affect solubility of compounds in these solvents. DMF has maximum δH (hydrogen donating capacity) as comparison to other solvents, which may be the reason for maximum solubility of studied compounds in DMF.

Further, for all the compounds, solubility increases with temperature. The temperature dependence solubility of compounds in solvents is described by modified Apelblat equation (Baluja *et al.*, 2009; Apelblat A and Manzurola, 1987).

$$ln\, x^a_i = A + B/T + C\, ln(T) \quad (2)$$

where $x^a_{ci}$ is the mole fraction solubility calculated by equation 2 and T is the absolute temperature. *A, B* and *C* are the empirical model parameters determined by least square method and the values are given in Table 5.

The values of *A* and *B* represent the variation in the solution activity and the solution behavior resulting from the non idealities on the solubility of solute, and the value of *C* represents the association between the temperatures and the enthalpy of fusion.

The solubility is also correlated with temperature by Buchowski–Ksiazczak λh equation (Buchowski *et al.*, 1980; Ksiazczak *et al.*, 1994) which describes the solid-liquid equilibrium behavior by only two adjustable parameters λ and h. The Buchowski equation can be written as:

$$\ln\left(1 + \frac{\lambda(1 - x^b_{ci})}{x^b_{ci}}\right) = \lambda h\left[\frac{1}{(T/K)} - \frac{1}{(T_m/K)}\right] \quad (3)$$

Where, $x^b_{ci}$ is calculated mole fraction solubility by equation 3. *T and* $T_m$ are experimental temperature and melting temperature of compound in K. λ and h are the parameters of Buchowski-Ksiazczak *λh* model which are given in Table 6.

**Table 4: Experimental Mole Fraction Solubilities ($x_i$), Calculated Mole Fraction Solubilities by Modified Apelblat Equation ($x^a_{ci}$), Calculated Mole Fraction Solubilities by Buchowski–Ksiazczak λh Equation ($x^b_{ci}$) and Relative Deviation (*RD*) of Synthesized Compounds in Selected Solvents at Different Temperatures**

| *T/K* | $x_i$ | $x^a_{ci}$ | $10^2$ *RD*$^a$ | $x^b_{ci}$ | $10^2$ *RD*$^b$ | $x_i$ | $x^a_{ci}$ | $10^2$ *RD*$^a$ | $x^b_{ci}$ | $10^2$ *RD*$^b$ |
|---|---|---|---|---|---|---|---|---|---|---|
| | ***DMF*** | | | | | | | | | |
| | ***KC-1*** | | | | | | ***KC-6*** | | | |
| 298.15 | 0.0047 | 0.0047 | -1.058 | 0.0047 | -1.782 | 0.0079 | 0.0080 | -0.712 | 0.0079 | 0.412 |
| 303.15 | 0.0067 | 0.0066 | -0.162 | 0.0066 | 0.785 | 0.0086 | 0.0086 | 0.430 | 0.0086 | 0.290 |
| 308.15 | 0.0087 | 0.0091 | -5.273 | 0.0090 | -3.302 | 0.0093 | 0.0092 | 1.199 | 0.0093 | 0.353 |
| 313.15 | 0.0125 | 0.0124 | -0.802 | 0.0122 | 1.346 | 0.0099 | 0.0099 | -0.391 | 0.0101 | -1.451 |
| 318.15 | 0.0164 | 0.0166 | 0.164 | 0.0163 | 1.927 | 0.0106 | 0.0107 | -1.050 | 0.0108 | -1.826 |
| 323.15 | 0.0220 | 0.0218 | -0.559 | 0.0217 | 0.257 | 0.0116 | 0.0116 | -0.398 | 0.0117 | -0.424 |
| 328.15 | 0.0277 | 0.0283 | -0.088 | 0.0285 | -0.802 | 0.0127 | 0.0126 | 0.605 | 0.0125 | 1.731 |
| | ***KC-2*** | | | | | | ***KC-7*** | | | |
| 298.15 | 0.0087 | 0.0087 | 0.164 | 0.0087 | 0.766 | 0.0060 | 0.0060 | -0.233 | 0.0061 | -1.872 |
| 303.15 | 0.0096 | 0.0096 | 0.007 | 0.0096 | -0.295 | 0.0077 | 0.0077 | 0.573 | 0.0077 | 0.662 |
| 308.15 | 0.0105 | 0.0106 | -0.531 | 0.0107 | -1.350 | 0.0095 | 0.0096 | -0.825 | 0.0095 | 0.234 |
| 313.15 | 0.0117 | 0.0117 | 0.133 | 0.0118 | -0.821 | 0.0119 | 0.0119 | 0.257 | 0.0117 | 1.571 |
| 318.15 | 0.0129 | 0.0129 | 0.167 | 0.0130 | -0.575 | 0.0144 | 0.0145 | -0.591 | 0.0144 | 0.351 |
| 323.15 | 0.0143 | 0.0142 | 0.405 | 0.0143 | 0.200 | 0.0176 | 0.0175 | 0.799 | 0.0175 | 0.742 |
| 328.15 | 0.0157 | 0.0157 | -0.316 | 0.0156 | 0.321 | 0.0207 | 0.0208 | -0.426 | 0.0211 | -2.079 |
| | ***KC-3*** | | | | | | ***KC-8*** | | | |
| 298.15 | 0.0045 | 0.0045 | 0.149 | 0.0045 | 0.042 | 0.0064 | 0.0065 | -0.143 | 0.0065 | -0.369 |
| 303.15 | 0.0055 | 0.0055 | 0.790 | 0.0056 | 0.619 | 0.0071 | 0.0071 | 0.269 | 0.0071 | 0.018 |
| 308.15 | 0.0064 | 0.0066 | -3.291 | 0.0066 | -3.507 | 0.0077 | 0.0077 | -0.046 | 0.0078 | -0.312 |
| 313.15 | 0.0080 | 0.0079 | 1.030 | 0.0080 | 0.814 | 0.0084 | 0.0084 | -0.460 | 0.0085 | -0.728 |
| 318.15 | 0.0096 | 0.0095 | 1.293 | 0.0095 | 1.094 | 0.0091 | 0.0092 | -0.647 | 0.0092 | -0.906 |
| 323.15 | 0.0114 | 0.0112 | 1.419 | 0.0113 | 1.260 | 0.0100 | 0.0100 | 0.474 | 0.0100 | 0.239 |
| 328.15 | 0.0131 | 0.0133 | -1.802 | 0.0133 | -1.901 | 0.0108 | 0.0108 | -0.052 | 0.0108 | -0.257 |
| | ***KC-4*** | | | | | | ***KC-9*** | | | |
| 298.15 | 0.0069 | 0.0069 | -0.325 | 0.0069 | -0.423 | 0.0072 | 0.0073 | -0.594 | 0.0072 | 0.033 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 303.15 | 0.0075 | 0.0075 | -0.470 | 0.0076 | -0.592 | 0.0077 | 0.0077 | 0.621 | 0.0077 | 0.375 |
| 308.15 | 0.0082 | 0.0082 | 0.565 | 0.0082 | 0.431 | 0.0081 | 0.0081 | 0.279 | 0.0081 | -0.460 |
| 313.15 | 0.0089 | 0.0089 | 0.272 | 0.0090 | 0.136 | 0.0085 | 0.0085 | -0.337 | 0.0086 | -1.217 |
| 318.15 | 0.0096 | 0.0096 | -0.339 | 0.0096 | -0.468 | 0.0089 | 0.0090 | -0.924 | 0.0091 | -1.605 |
| 323.15 | 0.0103 | 0.0104 | -0.520 | 0.0104 | -0.630 | 0.0096 | 0.0096 | 0.358 | 0.0096 | 0.201 |
| 328.15 | 0.0111 | 0.0111 | 0.006 | 0.0112 | -0.076 | 0.0102 | 0.0102 | -0.007 | 0.0101 | 0.643 |
| | ***KC-5*** | | | | | | | ***KC-10*** | | |
| 298.15 | 0.0079 | 0.0080 | -0.688 | 0.0079 | 0.241 | 0.0059 | 0.0059 | -0.394 | 0.0059 | -0.278 |
| 303.15 | 0.0086 | 0.0086 | 0.454 | 0.0086 | 0.119 | 0.0073 | 0.0072 | 1.076 | 0.0072 | 1.119 |
| 308.15 | 0.0093 | 0.0092 | 1.223 | 0.0093 | 0.182 | 0.0087 | 0.0088 | -1.070 | 0.0088 | -1.067 |
| 313.15 | 0.0099 | 0.0099 | -0.367 | 0.0101 | -1.625 | 0.0106 | 0.0106 | 0.136 | 0.0106 | 0.129 |
| 318.15 | 0.0106 | 0.0107 | -1.026 | 0.0108 | -2.001 | 0.0126 | 0.0127 | -0.973 | 0.0127 | -0.964 |
| 323.15 | 0.0116 | 0.0116 | -0.374 | 0.0117 | -0.597 | 0.0153 | 0.0152 | 0.849 | 0.0150 | 0.900 |
| 328.15 | 0.0127 | 0.0126 | 0.629 | 0.0125 | 1.562 | 0.0180 | 0.0180 | -0.229 | 0.0180 | -0.111 |
| | ***DMSO*** | | | | | | | | | |
| | ***KC-1*** | | | | | | | ***KC-6*** | | |
| 298.15 | 0.0036 | 0.0037 | -1.710 | 0.0036 | -0.405 | 0.0029 | 0.0029 | -0.289 | 0.0030 | -1.987 |
| 303.15 | 0.0042 | 0.0042 | -0.473 | 0.0042 | 0.778 | 0.0037 | 0.0037 | 0.462 | 0.0037 | 0.478 |
| 308.15 | 0.0047 | 0.0049 | -3.165 | 0.0048 | -1.898 | 0.0046 | 0.0046 | -0.542 | 0.0046 | 0.435 |
| 313.15 | 0.0055 | 0.0056 | -1.067 | 0.0055 | 0.175 | 0.0057 | 0.0057 | 0.075 | 0.0057 | 1.313 |
| 318.15 | 0.0062 | 0.0063 | -1.726 | 0.0063 | -0.457 | 0.0069 | 0.0069 | -0.491 | 0.0069 | 0.381 |
| 323.15 | 0.0071 | 0.0072 | -1.459 | 0.0071 | -0.157 | 0.0084 | 0.0084 | 0.459 | 0.0084 | 0.350 |
| 328.15 | 0.0080 | 0.0082 | -1.527 | 0.0081 | -0.172 | 0.0099 | 0.0100 | -0.272 | 0.0101 | -1.951 |
| | ***KC-2*** | | | | | | | ***KC-7*** | | |
| 298.15 | 0.0042 | 0.0042 | 0.400 | 0.0042 | 1.194 | 0.0029 | 0.0029 | 0.393 | 0.0029 | 2.148 |
| 303.15 | 0.0048 | 0.0048 | -0.429 | 0.0048 | -0.637 | 0.0035 | 0.0035 | -0.443 | 0.0035 | -0.660 |
| 308.15 | 0.0054 | 0.0055 | -1.178 | 0.0055 | -1.965 | 0.0042 | 0.0043 | -1.212 | 0.0043 | -2.578 |
| 313.15 | 0.0063 | 0.0063 | 0.662 | 0.0063 | -0.267 | 0.0052 | 0.0052 | 0.696 | 0.0053 | -0.958 |
| 318.15 | 0.0071 | 0.0071 | -0.302 | 0.0072 | -1.007 | 0.0063 | 0.0063 | -0.252 | 0.0064 | -1.462 |
| 323.15 | 0.0082 | 0.0081 | 1.030 | 0.0081 | 0.923 | 0.0077 | 0.0076 | 0.912 | 0.0076 | 0.883 |
| 328.15 | 0.0092 | 0.0092 | -0.847 | 0.0092 | -0.019 | 0.0092 | 0.0093 | -0.801 | 0.0091 | 1.008 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | ***KC-3*** | | | | | | | ***KC-8*** | | |
| 298.15 | 0.0032 | 0.0033 | -0.715 | 0.0033 | -0.759 | 0.0019 | 0.0019 | -1.083 | 0.0020 | -2.584 |
| 303.15 | 0.0038 | 0.0038 | -0.252 | 0.0038 | -0.342 | 0.0027 | 0.0026 | 2.535 | 0.0026 | 2.619 |
| 308.15 | 0.0045 | 0.0044 | 0.891 | 0.0044 | 0.776 | 0.0035 | 0.0036 | -2.653 | 0.0035 | -1.664 |
| 313.15 | 0.0051 | 0.0051 | 0.136 | 0.0051 | 0.014 | 0.0048 | 0.0047 | 1.748 | 0.0047 | 2.936 |
| 318.15 | 0.0058 | 0.0059 | -0.275 | 0.0059 | -0.385 | 0.0060 | 0.0062 | -2.446 | 0.0061 | -1.559 |
| 323.15 | 0.0067 | 0.0067 | 0.113 | 0.0067 | 0.031 | 0.0081 | 0.0080 | 1.657 | 0.0080 | 1.623 |
| 328.15 | 0.0076 | 0.0076 | -0.589 | 0.0076 | -0.625 | 0.0101 | 0.0101 | -0.500 | 0.0101 | -1.982 |
| | ***KC-4*** | | | | | | | ***KC-9*** | | |
| 298.15 | 0.0037 | 0.0037 | 0.412 | 0.0037 | 0.252 | 0.0025 | 0.0025 | -0.471 | 0.0025 | -2.034 |
| 303.15 | 0.0042 | 0.0042 | -0.205 | 0.0042 | -0.400 | 0.0032 | 0.0031 | 2.024 | 0.0031 | 1.980 |
| 308.15 | 0.0047 | 0.0047 | -0.505 | 0.0048 | -0.719 | 0.0038 | 0.0039 | -3.316 | 0.0039 | -2.490 |
| 313.15 | 0.0053 | 0.0053 | -0.337 | 0.0053 | -0.552 | 0.0048 | 0.0047 | 1.278 | 0.0047 | 2.298 |
| 318.15 | 0.0059 | 0.0059 | -0.085 | 0.0060 | -0.286 | 0.0057 | 0.0057 | -0.378 | 0.0057 | 0.325 |
| 323.15 | 0.0066 | 0.0066 | -0.405 | 0.0066 | -0.579 | 0.0069 | 0.0068 | 1.048 | 0.0068 | 0.879 |
| 328.15 | 0.0074 | 0.0074 | 0.463 | 0.0074 | 0.332 | 0.0080 | 0.0081 | -0.741 | 0.0082 | -2.314 |
| | ***KC-5*** | | | | | | | ***KC-10*** | | |
| 298.15 | 0.0032 | 0.0032 | -0.612 | 0.0032 | -0.612 | 0.0053 | 0.0053 | -0.167 | 0.0054 | -0.242 |
| 303.15 | 0.0038 | 0.0038 | 0.466 | 0.0038 | 0.412 | 0.0061 | 0.0061 | 0.545 | 0.0061 | 0.430 |
| 308.15 | 0.0044 | 0.0044 | -0.089 | 0.0045 | -0.172 | 0.0069 | 0.0069 | -0.063 | 0.0069 | -0.201 |
| 313.15 | 0.0052 | 0.0052 | 0.063 | 0.0052 | -0.028 | 0.0077 | 0.0077 | -0.252 | 0.0077 | -0.395 |
| 318.15 | 0.0060 | 0.0060 | -0.218 | 0.0061 | -0.295 | 0.0085 | 0.0087 | -1.486 | 0.0087 | -1.620 |
| 323.15 | 0.0070 | 0.0070 | -0.096 | 0.0070 | -0.141 | 0.0097 | 0.0097 | 0.175 | 0.0097 | 0.070 |
| 328.15 | 0.0081 | 0.0081 | -0.183 | 0.0081 | -0.177 | 0.0109 | 0.0108 | 0.608 | 0.0108 | 0.545 |
| | ***THF*** | | | | | | | | | |
| | ***KC-1*** | | | | | | | ***KC-6*** | | |
| 298.15 | 0.0036 | 0.0036 | -0.285 | 0.0036 | -0.471 | 0.0036 | 0.0037 | -0.670 | 0.0037 | -0.777 |
| 303.15 | 0.0041 | 0.0041 | -0.081 | 0.0041 | -0.300 | 0.0042 | 0.0042 | -0.165 | 0.0042 | -0.313 |
| 308.15 | 0.0046 | 0.0046 | 0.355 | 0.0046 | 0.120 | 0.0048 | 0.0048 | 0.068 | 0.0048 | -0.103 |
| 313.15 | 0.0052 | 0.0052 | 0.176 | 0.0052 | -0.061 | 0.0055 | 0.0055 | 0.603 | 0.0055 | 0.428 |
| 318.15 | 0.0057 | 0.0058 | -1.127 | 0.00582 | -1.353 | 0.0062 | 0.0062 | 0.416 | 0.0062 | 0.251 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 323.15 | 0.0065 | 0.0065 | 0.377 | 0.0065 | 0.181 | 0.0070 | 0.0070 | 0.084 | 0.0070 | -0.056 |
| 328.15 | 0.0072 | 0.0072 | -0.080 | 0.0072 | -0.237 | 0.0078 | 0.0079 | -0.995 | 0.0079 | -1.097 |
| | ***KC-2*** | | | | | | | ***KC-7*** | | |
| 298.15 | 0.0042 | 0.0042 | 0.071 | 0.0042 | 0.786 | 0.0027 | 0.0028 | -1.396 | 0.0028 | -1.405 |
| 303.15 | 0.0045 | 0.0045 | -0.575 | 0.0045 | -0.821 | 0.0033 | 0.0033 | 1.021 | 0.0033 | 0.960 |
| 308.15 | 0.0049 | 0.0049 | 0.296 | 0.0049 | -0.491 | 0.0039 | 0.0038 | 0.712 | 0.0038 | 0.622 |
| 313.15 | 0.0052 | 0.0052 | -0.210 | 0.0053 | -1.153 | 0.0045 | 0.0045 | 0.093 | 0.0045 | -0.005 |
| 318.15 | 0.0056 | 0.0056 | 0.248 | 0.0056 | -0.469 | 0.0052 | 0.0052 | -1.211 | 0.0052 | -1.298 |
| 323.15 | 0.0060 | 0.0060 | -0.559 | 0.0060 | -0.710 | 0.0061 | 0.0061 | 0.464 | 0.0061 | 0.409 |
| 328.15 | 0.0065 | 0.0065 | 0.089 | 0.0065 | 0.826 | 0.0070 | 0.0070 | -0.389 | 0.0070 | -0.395 |
| | ***KC-3*** | | | | | | | ***KC-8*** | | |
| 298.15 | 0.0045 | 0.0045 | -1.132 | 0.0045 | -1.379 | 0.0025 | 0.0025 | -0.875 | 0.0025 | -1.025 |
| 303.15 | 0.0051 | 0.0050 | 0.993 | 0.0051 | 0.724 | 0.0030 | 0.0030 | 0.668 | 0.0030 | 0.472 |
| 308.15 | 0.0056 | 0.0056 | -0.746 | 0.0056 | -1.034 | 0.0035 | 0.0035 | -0.248 | 0.0035 | -0.472 |
| 313.15 | 0.0063 | 0.0062 | 1.054 | 0.0063 | 0.769 | 0.0041 | 0.0041 | 0.615 | 0.0041 | 0.387 |
| 318.15 | 0.0069 | 0.0069 | -0.125 | 0.0069 | -0.401 | 0.0047 | 0.0047 | -0.802 | 0.0047 | -1.019 |
| 323.15 | 0.0076 | 0.0076 | 0.004 | 0.0077 | -0.248 | 0.0055 | 0.0055 | 0.562 | 0.0055 | 0.380 |
| 328.15 | 0.0083 | 0.0084 | -0.710 | 0.0084 | -0.930 | 0.0063 | 0.0063 | -0.627 | 0.0063 | -0.761 |
| | ***KC-4*** | | | | | | | ***KC-9*** | | |
| 298.15 | 0.0028 | 0.0029 | -0.780 | 0.0029 | -1.230 | 0.0022 | 0.0022 | -0.907 | 0.0022 | -2.247 |
| 303.15 | 0.0033 | 0.0033 | 1.132 | 0.0033 | 0.654 | 0.0027 | 0.0027 | 1.346 | 0.0027 | 1.367 |
| 308.15 | 0.0037 | 0.0037 | -1.164 | 0.0037 | -1.675 | 0.0032 | 0.0032 | -0.611 | 0.0032 | 0.170 |
| 313.15 | 0.0042 | 0.0042 | 0.213 | 0.0042 | -0.295 | 0.0038 | 0.0038 | -0.057 | 0.0038 | 0.928 |
| 318.15 | 0.0047 | 0.0047 | 0.495 | 0.0048 | -0.001 | 0.0044 | 0.0045 | -0.725 | 0.0044 | -0.034 |
| 323.15 | 0.0053 | 0.0053 | -0.074 | 0.0053 | -0.548 | 0.0052 | 0.0052 | -0.086 | 0.0052 | -0.178 |
| 328.15 | 0.0059 | 0.0059 | -0.528 | 0.0060 | -0.966 | 0.0060 | 0.0060 | 0.124 | 0.0061 | -1.208 |
| | ***KC-5*** | | | | | | | ***KC-10*** | | |
| 298.15 | 0.0038 | 0.0038 | 0.055 | 0.0038 | -0.172 | 0.0028 | 0.0028 | 0.478 | 0.0029 | -1.136 |
| 303.15 | 0.0042 | 0.0042 | 0.169 | 0.0042 | -0.088 | 0.0033 | 0.0033 | -1.229 | 0.0033 | -1.308 |
| 308.15 | 0.0046 | 0.0046 | -0.084 | 0.0047 | -0.357 | 0.0039 | 0.0039 | -0.244 | 0.0039 | 0.542 |
| 313.15 | 0.0051 | 0.0051 | -0.366 | 0.0051 | -0.643 | 0.0046 | 0.0045 | 1.156 | 0.0045 | 2.168 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 318.15 | 0.0056 | 0.0056 | -1.156 | 0.0057 | -1.425 | 0.0052 | 0.0052 | -0.286 | 0.0052 | 0.402 |
| 323.15 | 0.0062 | 0.0062 | 0.401 | 0.0062 | 0.157 | 0.0059 | 0.0059 | -0.602 | 0.0059 | -0.803 |
| 328.15 | 0.0068 | 0.0068 | 0.305 | 0.0068 | 0.094 | 0.0067 | 0.0067 | 0.104 | 0.0068 | -1.510 |
| | ***1,4-Dioxane*** | | | | | | | | | |
| | ***KC-1*** | | | | | | | ***KC-6*** | | |
| 298.15 | 0.0035 | 0.0035 | -0.176 | 0.0035 | -0.321 | 0.0033 | 0.0034 | -0.745 | 0.0034 | -1.833 |
| 303.15 | 0.0040 | 0.0040 | -0.409 | 0.0040 | -0.591 | 0.0041 | 0.0041 | 0.548 | 0.0041 | 0.491 |
| 308.15 | 0.0046 | 0.0046 | 0.189 | 0.0046 | -0.011 | 0.0049 | 0.0049 | 0.568 | 0.0049 | 1.083 |
| 313.15 | 0.0052 | 0.0052 | 0.371 | 0.0052 | 0.170 | 0.0058 | 0.0058 | -0.026 | 0.0058 | 0.653 |
| 318.15 | 0.0058 | 0.0059 | -0.534 | 0.0059 | -0.723 | 0.0067 | 0.0068 | -1.809 | 0.0068 | -1.346 |
| 323.15 | 0.0066 | 0.0066 | 0.270 | 0.0066 | 0.111 | 0.0080 | 0.0080 | 0.557 | 0.0080 | 0.425 |
| 328.15 | 0.0074 | 0.0074 | -0.384 | 0.0074 | -0.501 | 0.0092 | 0.0092 | 0.068 | 0.0093 | -1.000 |
| | ***KC-2*** | | | | | | | ***KC-7*** | | |
| 298.15 | 0.0025 | 0.0025 | -0.914 | 0.0026 | -2.147 | 0.0032 | 0.0032 | -0.690 | 0.0032 | -0.889 |
| 303.15 | 0.0031 | 0.0030 | 2.004 | 0.0030 | 1.902 | 0.0037 | 0.0037 | 0.757 | 0.0037 | 0.522 |
| 308.15 | 0.0036 | 0.0036 | -1.786 | 0.0036 | -1.255 | 0.0042 | 0.0042 | -0.291 | 0.0042 | -0.550 |
| 313.15 | 0.0043 | 0.0043 | 0.681 | 0.0042 | 1.372 | 0.0048 | 0.0048 | -0.067 | 0.0048 | -0.327 |
| 318.15 | 0.0050 | 0.0050 | -0.817 | 0.0050 | -0.365 | 0.0054 | 0.0055 | -0.307 | 0.0055 | -0.554 |
| 323.15 | 0.0058 | 0.0058 | 0.302 | 0.0058 | 0.104 | 0.0062 | 0.0062 | 0.268 | 0.0062 | 0.053 |
| 328.15 | 0.0066 | 0.0066 | -0.052 | 0.0067 | -1.280 | 0.0070 | 0.0070 | -0.349 | 0.0070 | -0.521 |
| | ***KC-3*** | | | | | | | ***KC-8*** | | |
| 298.15 | 0.0020 | 0.0020 | -0.473 | 0.0020 | -1.794 | 0.0026 | 0.0026 | -0.142 | 0.0026 | -0.327 |
| 303.15 | 0.0026 | 0.0025 | 2.291 | 0.0026 | 2.165 | 0.0030 | 0.0030 | 0.249 | 0.0030 | 0.022 |
| 308.15 | 0.0031 | 0.0032 | -4.016 | 0.0032 | -3.458 | 0.0034 | 0.0035 | -1.320 | 0.0035 | -1.573 |
| 313.15 | 0.0040 | 0.0039 | 1.755 | 0.0039 | 2.465 | 0.0040 | 0.0040 | -0.130 | 0.0040 | -0.384 |
| 318.15 | 0.0048 | 0.0048 | -0.675 | 0.0048 | -0.208 | 0.0047 | 0.0046 | 1.279 | 0.0046 | 1.043 |
| 323.15 | 0.0059 | 0.0058 | 1.445 | 0.0058 | 1.231 | 0.0053 | 0.0053 | 0.595 | 0.0053 | 0.389 |
| 328.15 | 0.0069 | 0.0070 | -0.954 | 0.0071 | -2.269 | 0.0059 | 0.0060 | -1.253 | 0.0060 | -1.415 |
| | ***KC-4*** | | | | | | | ***KC-9*** | | |
| 298.15 | 0.0025 | 0.0025 | 0.399 | 0.0025 | 0.264 | 0.0022 | 0.0022 | -1.186 | 0.0022 | -1.262 |
| 303.15 | 0.0028 | 0.0028 | -0.346 | 0.0028 | -0.510 | 0.0025 | 0.0025 | 0.906 | 0.0025 | 0.799 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 308.15 | 0.0031 | 0.0031 | -0.442 | 0.0031 | -0.623 | 0.0028 | 0.0028 | -0.164 | 0.0028 | -0.291 |
| 313.15 | 0.0034 | 0.0034 | -0.194 | 0.0034 | -0.378 | 0.0032 | 0.0032 | 1.250 | 0.0032 | 1.122 |
| 318.15 | 0.0037 | 0.0037 | -0.527 | 0.0037 | -0.705 | 0.0035 | 0.0035 | -1.722 | 0.0036 | -1.843 |
| 323.15 | 0.0041 | 0.0041 | 0.412 | 0.0041 | 0.253 | 0.0040 | 0.0040 | 0.683 | 0.0040 | 0.588 |
| 328.15 | 0.0045 | 0.0045 | -0.033 | 0.0045 | -0.166 | 0.0044 | 0.0044 | -0.538 | 0.0044 | -0.599 |
| | ***KC-5*** | | | | | | | ***KC-10*** | | |
| 298.15 | 0.0027 | 0.0027 | -0.425 | 0.0027 | -0.675 | 0.0032 | 0.0032 | -0.323 | 0.0032 | -0.468 |
| 303.15 | 0.0030 | 0.0030 | -0.152 | 0.0030 | -0.430 | 0.0037 | 0.0037 | 0.895 | 0.0037 | 0.709 |
| 308.15 | 0.0034 | 0.0034 | -0.218 | 0.0034 | -0.510 | 0.0042 | 0.0042 | -0.657 | 0.0042 | -0.870 |
| 313.15 | 0.0038 | 0.0038 | 1.250 | 0.0038 | 0.962 | 0.0048 | 0.0048 | -0.714 | 0.0049 | -0.932 |
| 318.15 | 0.0041 | 0.0042 | -0.578 | 0.0042 | -0.859 | 0.0055 | 0.0055 | -0.199 | 0.0055 | -0.403 |
| 323.15 | 0.0046 | 0.0046 | -0.541 | 0.0046 | -0.798 | 0.0063 | 0.0063 | 0.483 | 0.0063 | 0.310 |
| 328.15 | 0.0051 | 0.0051 | -0.054 | 0.0051 | -0.274 | 0.0071 | 0.0071 | -0.160 | 0.0071 | -0.289 |
| | ***Ethyl acetate*** | | | | | | | | | |
| | ***KC-1*** | | | | | | | ***KC-6*** | | |
| 298.15 | 0.0026 | 0.0026 | 0.678 | 0.0026 | 0.728 | 0.0037 | 0.0037 | -0.450 | 0.0037 | -0.568 |
| 303.15 | 0.0028 | 0.0028 | 0.256 | 0.0028 | 0.287 | 0.0042 | 0.0042 | 0.357 | 0.0042 | 0.207 |
| 308.15 | 0.0030 | 0.0030 | -1.061 | 0.0030 | -1.039 | 0.0047 | 0.0047 | -0.648 | 0.0047 | -0.816 |
| 313.15 | 0.0032 | 0.0032 | -1.066 | 0.0032 | -1.046 | 0.0053 | 0.0053 | 0.331 | 0.0053 | 0.162 |
| 318.15 | 0.0035 | 0.0035 | -0.031 | 0.0035 | -0.007 | 0.0059 | 0.0059 | 0.096 | 0.0059 | -0.061 |
| 323.15 | 0.0037 | 0.0037 | -0.331 | 0.0037 | -0.296 | 0.0066 | 0.0066 | 0.365 | 0.0066 | 0.234 |
| 328.15 | 0.0040 | 0.0040 | 0.815 | 0.0040 | 0.868 | 0.0073 | 0.0073 | -0.712 | 0.0073 | -0.807 |
| | ***KC-2*** | | | | | | | ***KC-7*** | | |
| 298.15 | 0.0029 | 0.0029 | -1.088 | 0.0029 | -1.104 | 0.0023 | 0.0023 | 0.069 | 0.0023 | -0.003 |
| 303.15 | 0.0032 | 0.0032 | 1.101 | 0.0032 | 1.070 | 0.0024 | 0.0024 | -1.434 | 0.0024 | -1.522 |
| 308.15 | 0.0034 | 0.0034 | -0.030 | 0.0034 | -0.069 | 0.0026 | 0.0026 | 1.093 | 0.0026 | 1.000 |
| 313.15 | 0.0037 | 0.0037 | -0.441 | 0.0037 | -0.479 | 0.0028 | 0.0028 | -0.082 | 0.0028 | -0.177 |
| 318.15 | 0.0040 | 0.0040 | 0.436 | 0.0040 | 0.406 | 0.0030 | 0.0030 | 0.189 | 0.0030 | 0.100 |
| 323.15 | 0.0043 | 0.0043 | -0.515 | 0.0043 | -0.528 | 0.0032 | 0.0032 | 0.046 | 0.0032 | -0.033 |
| 328.15 | 0.0046 | 0.0046 | -0.175 | 0.0047 | -0.165 | 0.0034 | 0.0034 | -0.630 | 0.0034 | -0.694 |
| | ***KC-3*** | | | | | | | ***KC-8*** | | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 298.15 | 0.0027 | 0.0027 | 0.327 | 0.0027 | 0.224 | 0.0019 | 0.0019 | 0.440 | 0.0019 | 0.215 |
| 303.15 | 0.0029 | 0.0029 | -0.407 | 0.0029 | -0.530 | 0.0022 | 0.0022 | -1.355 | 0.0022 | -1.620 |
| 308.15 | 0.0032 | 0.0032 | -0.265 | 0.0032 | -0.398 | 0.0026 | 0.0026 | 0.250 | 0.0026 | -0.030 |
| 313.15 | 0.0034 | 0.0034 | -0.711 | 0.0034 | -0.845 | 0.0029 | 0.0029 | -0.325 | 0.0029 | -0.608 |
| 318.15 | 0.0037 | 0.0037 | 0.363 | 0.0037 | 0.238 | 0.0033 | 0.0033 | 1.386 | 0.0033 | 1.120 |
| 323.15 | 0.0040 | 0.0040 | 0.304 | 0.0040 | 0.195 | 0.0037 | 0.0037 | -0.985 | 0.0038 | -1.229 |
| 328.15 | 0.0043 | 0.0043 | -0.329 | 0.0043 | -0.416 | 0.0042 | 0.0042 | -0.174 | 0.0042 | -0.374 |
| | ***KC-4*** | | | | | | | ***KC-9*** | | |
| 298.15 | 0.0032 | 0.0032 | -0.220 | 0.0032 | -0.352 | 0.0025 | 0.0025 | 0.469 | 0.0025 | 0.328 |
| 303.15 | 0.0035 | 0.0034 | 2.090 | 0.0034 | 1.946 | 0.0028 | 0.0028 | -0.522 | 0.0028 | -0.696 |
| 308.15 | 0.0037 | 0.0037 | -0.645 | 0.0037 | -0.800 | 0.0031 | 0.0031 | -0.570 | 0.0032 | -0.761 |
| 313.15 | 0.0039 | 0.0040 | -1.736 | 0.0040 | -1.892 | 0.0035 | 0.0035 | 0.149 | 0.0035 | -0.044 |
| 318.15 | 0.0042 | 0.0043 | -2.509 | 0.0043 | -2.658 | 0.0039 | 0.0039 | -0.530 | 0.0039 | -0.715 |
| 323.15 | 0.0046 | 0.0046 | 1.004 | 0.0046 | 0.877 | 0.0043 | 0.0043 | 0.379 | 0.0043 | 0.218 |
| 328.15 | 0.0049 | 0.0049 | 1.239 | 0.0049 | 1.134 | 0.0047 | 0.0047 | -0.102 | 0.0047 | -0.231 |
| | ***KC-5*** | | | | | | | ***KC-10*** | | |
| 298.15 | 0.0041 | 0.0041 | -0.596 | 0.0041 | -0.620 | 0.0031 | 0.0030 | 0.510 | 0.0030 | 1.464 |
| 303.15 | 0.0046 | 0.0046 | -0.297 | 0.0046 | -0.355 | 0.0033 | 0.0033 | -0.816 | 0.0033 | -1.017 |
| 308.15 | 0.0052 | 0.0052 | 0.513 | 0.0052 | 0.436 | 0.0036 | 0.0037 | -0.378 | 0.0037 | -1.241 |
| 313.15 | 0.0058 | 0.0058 | 0.084 | 0.0058 | 0.003 | 0.0040 | 0.0040 | -0.390 | 0.0041 | -1.438 |
| 318.15 | 0.0065 | 0.0065 | 0.322 | 0.0065 | 0.251 | 0.0045 | 0.0044 | 0.695 | 0.0045 | -0.078 |
| 323.15 | 0.0072 | 0.0072 | 0.263 | 0.0072 | 0.214 | 0.0049 | 0.0049 | 0.524 | 0.0049 | 0.429 |
| 328.15 | 0.0079 | 0.0080 | -0.942 | 0.0080 | -0.956 | 0.0053 | 0.0054 | -0.726 | 0.0053 | 0.254 |

*($x_i$)* = Experimental mole fraction solubility with an uncertainty of ± 0.00001
*($x^a_{ci}$) and ($x^b_{ci}$)* = Calculated mole fraction solubility
[a]=Values obtained by Apelblat equation (eq. 2)
[b]=Values obtained by Buchowski-Ksiazczak equation (eq. 3)
[η] =Standard uncertainty $u_r$ ($T$) = ±0.1K, $u_r(P)$= ±0.05MPa and $u_r(x)$ = ±0.0103

**Table 5: Parameters of Modified Apelblat Equation for Studied Compounds in Studied Solvents**

| | | | ***DMF*** | | |
|---|---|---|---|---|---|
| **Parameters** | **KC-1** | **KC-2** | **KC-3** | **KC-4** | **KC-5** |
| *A* | 182.8 | -90.71 | -0.33 | -2.49 | -128.03 |
| *B* | -13667.3 | 2355.16 | -3224.55 | 1429.91 | 4441.75 |
| *C* | -24.98 | 13.70 | 1.01 | 0.41 | 19.01 |
| $10^5$ *RMSD*[a] | 18.41 | 3.75 | 14.6 | 3.47 | 8.065 |
| *100 ARD*[a] | -1.11 | 0.004 | -0.06 | -0.12 | -0.02 |
| ***Parameters*** | ***KC-6*** | ***KC-7*** | ***KC-8*** | ***KC-9*** | ***KC-10*** |
| *A* | -128.03 | 182.09 | -2.50 | -90.17 | -0.24 |
| *B* | 4441.75 | -12092.9 | -1526.5 | 3030.32 | -3297.82 |
| *C* | 19.01 | -25.74 | 0.45 | 13.18 | 1.08 |
| $10^5$ *RMSD*[a] | 8.077 | 7.93 | 3.32 | 4.39 | 8.38 |
| *100 ARD*[a] | -0.045 | -0.062 | -0.089 | -0.093 | -0.086 |
| | ***DMSO*** | | | | |
| ***Parameters*** | ***KC-1*** | ***KC-2*** | ***KC-3*** | ***KC-4*** | ***KC-5*** |
| *A* | -1.64 | -99.48 | -1.31 | -2.16 | -1.11 |
| *B* | -2396.78 | 2205.62 | -2535.67 | -2037.22 | -2765.38 |
| *C* | 0.71 | 15.20 | 0.72 | 0.60 | 0.82 |
| $10^5$ *RMSD*[a] | 9.79 | 5.37 | 2.55 | 2.11 | 1.39 |
| *100 ARD*[a] | -1.5895 | -0.095 | -0.099 | -0.094 | -0.096 |
| ***Parameters*** | ***KC-6*** | ***KC-7*** | ***KC-8*** | ***KC-9*** | ***KC-10*** |
| *A* | 179.11 | -195.80 | 169.82 | 158.79 | -1.93 |
| *B* | -11970.1 | 5604.60 | -12748.5 | -10862.8 | -2087.3 |
| *C* | -25.42 | 30.04 | -23.40 | -22.53 | 0.65 |
| $10^5$ *RMSD*[a] | 2.496 | 4.62 | 9.48 | 6.85 | 6.10 |
| *100 ARD*[a] | -0.085 | -0.101 | -0.106 | -0.079 | -0.091 |
| | ***THF*** | | | | |
| ***Parameters*** | ***KC-1*** | ***KC-2*** | ***KC-3*** | ***KC-4*** | ***KC-5*** |
| *A* | -2.026 | -98.71 | -2.02 | -1.87 | -2.53 |
| *B* | -2054.1 | 3135.14 | -1848.08 | -2195 | -1743.17 |
| *C* | 0.58 | 14.52 | 0.50 | 0.59 | 0.49 |
| $10^5$ *RMSD*[a] | 2.75 | 1.84 | 4.60 | 2.76 | 3.06 |
| *100 ARD*[a] | -0.0951 | -0.091 | -0.094 | -0.101 | -0.097 |

| ***Parameters*** | ***KC-6*** | ***KC-7*** | ***KC-8*** | ***KC-9*** | ***KC-10*** |
|---|---|---|---|---|---|
| *A* | -1.52 | -1.075 | -1.21 | 140.82 | 158.53 |
| *B* | -2292.40 | -2788.26 | -2733.34 | -9586.29 | -10002.9 |
| *C* | 0.63 | 0.80 | 0.77 | -20.15 | -22.97 |
| *$10^5$ RMSD[a]* | 3.48 | 3.55 | 2.80 | 2.14 | 3.23 |
| *100 ARD[a]* | -0.094 | -0.101 | -0.101 | -0.131 | -0.089 |
| | ***1,4-Dioxane*** | | | | |
| ***Parameters*** | ***KC-1*** | ***KC-2*** | ***KC-3*** | ***KC-4*** | ***KC-5*** |
| *A* | -1.78 | 117.25 | 126.51 | -2.75 | -2.22 |
| *B* | -2223.37 | -8378.39 | -9581.14 | -1695.87 | -1956.36 |
| *C* | 0.63 | -16.70 | -17.65 | 0.43 | 0.50 |
| *$10^5$ RMSD[a]* | 2.01 | 4.01 | 7.20 | 1.25 | 2.47 |
| *100 ARD[a]* | -0.0963 | -0.083 | -0.090 | -0.104 | -0.103 |
| ***Parameters*** | ***KC-6*** | ***KC-7*** | ***KC-8*** | ***KC-9*** | ***KC-10*** |
| *A* | 108.16 | -1.66253 | -1.45705 | -2.01667 | -1.68465 |
| *B* | -8045.33 | -2345.42 | -2549.05 | -2144.43 | -2407.68 |
| *C* | -15.25 | 0.66 | 0.71 | 0.54 | 0.70 |
| *$10^5$ RMSD[a]* | 5.16 | 1.92 | 4.18 | 3.32 | 2.68 |
| *100 ARD[a]* | -0.120 | -0.097 | -0.103 | -0.110 | -0.097 |
| | ***Ethyl acetate*** | | | | |
| ***Parameters*** | ***KC-1*** | ***KC-2*** | ***KC-3*** | ***KC-4*** | ***KC-5*** |
| *A* | -3.18 | -2.85 | -3.02 | -3.11 | -1.88 |
| *B* | -1306.09 | -1428.19 | -1435.75 | -1299.06 | -1998.12 |
| *C* | 0.28 | 0.32 | 0.34 | 0.30 | 0.54 |
| *$10^5$ RMSD[a]* | 2.31 | 2.19 | 1.41 | 6.24 | 3.61 |
| *100 ARD[a]* | -0.1057 | -0.102 | -0.102 | -0.111 | -0.093 |
| ***Parameters*** | ***KC-6*** | ***KC-7*** | ***KC-8*** | ***KC-9*** | ***KC-10*** |
| *A* | -1.957 | -3.174 | -1.924 | -2.478 | -117.68 |
| *B* | -2038.44 | -1264.71 | -2336.05 | -1900.23 | 3609.08 |
| *C* | 0.56 | 0.23 | 0.62 | 0.50 | 17.51 |
| *$10^5$ RMSD[a]* | 2.68 | 1.90 | 2.57 | 1.42 | 2.75 |
| *100 ARD[a]* | -0.094 | -0.107 | -0.109 | -0.104 | -0.083 |

a= value calculated by modified Apelblat equation

**Table 6: Parameters of Buchowski Equation for Studied Compounds in Studied Solvents**

| Solvents | λ | h | 100ARD[b] | $10^5$RMSD[b] |
|---|---|---|---|---|
| | ***DMF*** | | | |
| *KC-1* | 19.40 | 301.85 | -0.2243 | 19.86 |
| *KC-2* | 0.15 | 13344.90 | -0.2505 | 7.89 |
| *KC-3* | 0.75 | 4719.92 | -0.2255 | 14.58 |
| *KC-4* | 0.073 | 21256.17 | -0.2317 | 3.88 |
| *KC-5* | 0.061 | 24745.08 | -0.3026 | 12.89 |
| *KC-6* | 0.0760 | 19740.40 | -0.131 | 12.65 |
| *KC-7* | 2.0317 | 1991.44 | -0.056 | 19.11 |
| *KC-8* | 0.0566 | 29473.99 | -0.331 | 4.32 |
| *KC-9* | 0.0361 | 30164.37 | -0.290 | 7.38 |
| *KC-10* | 1.7699 | 2054.41 | -0.039 | 8.43 |
| | ***DMSO*** | | | |
| *KC-1* | 0.15 | 17638.20 | -0.3052 | 3.87 |
| *KC-2* | 0.17 | 14725.79 | -0.2539 | 6.10 |
| *KC-3* | 0.18 | 15594.51 | -0.1844 | 2.60 |
| *KC-4* | 0.11 | 20500.67 | -0.2789 | 2.60 |
| *KC-5* | 0.19 | 15595.17 | -0.1450 | 1.37 |
| *KC-6* | 1.278 | 3148.96 | -0.140 | 8.34 |
| *KC-7* | 0.655 | 5786.33 | -0.231 | 7.59 |
| *KC-8* | 2.284 | 2378.47 | -0.087 | 11.75 |
| *KC-9* | 0.718 | 5317.11 | -0.194 | 9.70 |
| *KC-10* | 0.194 | 11790.06 | -0.202 | 5.93 |
| | ***THF*** | | | |
| *KC-1* | 0.087 | 25773.66 | -0.3032 | 3.15 |
| *KC-2* | 0.033 | 43064.91 | -0.2903 | 4.15 |
| *KC-3* | 0.082 | 24451.60 | -0.3570 | 5.06 |
| *KC-4* | 0.11 | 22459.10 | -0.5801 | 3.72 |

| | | | | |
|---|---|---|---|---|
| *KC-5* | 0.05 | 38175.94 | -0.3476 | 3.34 |
| *KC-6* | 0.157 | 15830.15 | -0.238 | 3.61 |
| *KC-7* | 0.216 | 14077.73 | -0.159 | 3.57 |
| *KC-8* | 0.121 | 24520.95 | -0.291 | 3.017 |
| *KC-9* | 0.286 | 11493.13 | -0.172 | 3.85 |
| *KC-10* | 0.239 | 11801.05 | -0.235 | 6.12 |
| | ***1,4-Dioxane*** | | | |
| *KC-1* | 0.11 | 22152.61 | -0.2665 | 2.38 |
| *KC-2* | 0.26 | 12288.87 | -0.2383 | 5.27 |
| *KC-3* | 0.72 | 5631.47 | -0.2670 | 8.88 |
| *KC-4* | 0.04 | 44893.17 | -0.2664 | 1.53 |
| *KC-5* | 0.047 | 44749.72 | -0.3690 | 2.65 |
| *KC-6* | 0.479 | 6842.14 | -0.218 | 6.12 |
| *KC-7* | 0.125 | 20522.09 | -0.324 | 2.44 |
| *KC-8* | 0.095 | 29324.47 | -0.321 | 4.32 |
| *KC-9* | 0.067 | 34711.02 | -0.212 | 3.36 |
| *KC-10* | 0.196 | 13430.77 | -0.278 | 2.81 |
| | ***Ethyl acetate*** | | | |
| *KC-1* | 0.019 | 74400.35 | -0.0722 | 2.34 |
| *KC-2* | 0.027 | 56429.91 | -0.1241 | 2.19 |
| *KC-3* | 0.025 | 62060.91 | -0.2186 | 1.56 |
| *KC-4* | 0.026 | 53095.14 | -0.2494 | 6.32 |
| *KC-5* | 0.078 | 27879.27 | -1.1468 | 3.30 |
| *KC-6* | 0.1046 | 21156.40 | -0.236 | 2.86 |
| *KC-7* | 0.0154 | 86719.30 | -0.190 | 1.94 |
| *KC-8* | 0.0521 | 48564.65 | -0.361 | 2.76 |
| *KC-9* | 0.0526 | 39123.29 | -0.272 | 1.68 |
| *KC-10* | 0.0561 | 33257.43 | -0.233 | 3.61 |

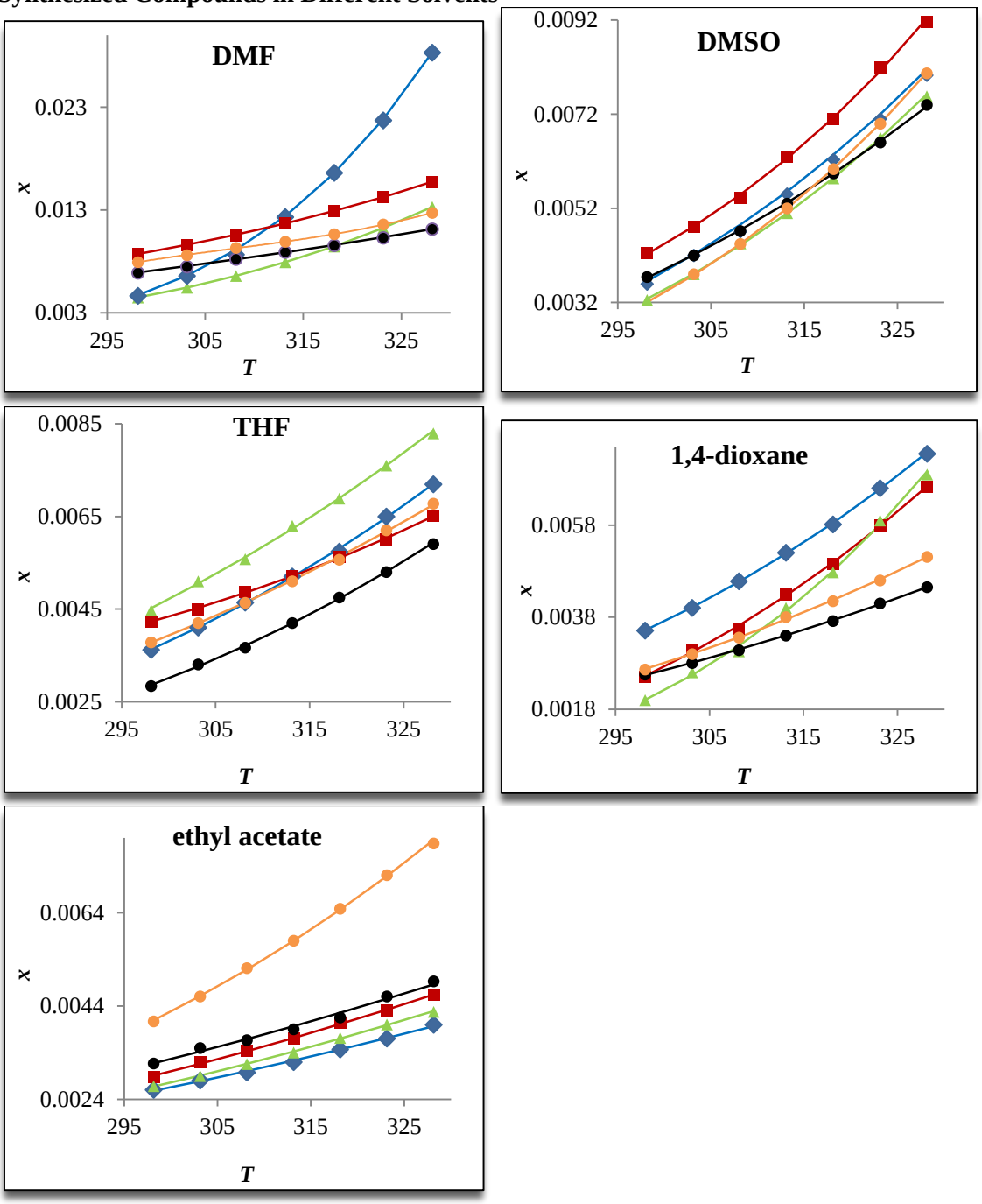
b=value calculated by Buchowski-Ksiazczak equation

**Table 7: Thermodynamic Parameters of Dissolution of Synthesized Compounds in Studied Solvents**

| **Thermodynamic Parameters** | | | | | |
|---|---|---|---|---|---|
| | ***DMF*** | | | | |
| | ***KC-1*** | ***KC-2*** | ***KC-3*** | ***KC-4*** | ***KC-5*** |
| $\Delta G_{sol}$ / *kJ.mol*$^{-1}$ | 11.52 | 11.57 | 12.61 | 12.30 | 11.98 |
| $\Delta H_{sol}$ / *kJ.mol*$^{-1}$ | 48.70 | 16.03 | 29.43 | 12.94 | 12.48 |
| $\Delta S_{sol}$ / *J.mol*$^{-1}$.*K*$^{-1}$ | 118.83 | 14.26 | 53.73 | 2.028 | 1.59 |
| | ***KC-6*** | ***KC-7*** | ***KC-8*** | ***KC-9*** | ***KC-10*** |
| $\Delta G_{sol}$ / *kJ.mol*$^{-1}$ | 11.98 | 11.60 | 12.44 | 12.39 | 11.86 |
| $\Delta H_{sol}$ / *kJ.mol*$^{-1}$ | 12.48 | 33.64 | 13.86 | 9.05 | 30.23 |
| $\Delta S_{sol}$ / *J.mol*$^{-1}$.*K*$^{-1}$ | 1.59 | 70.45 | 4.55 | -10.65 | 58.72 |
| | ***DMSO*** | | | | |
| | ***KC-1*** | ***KC-2*** | ***KC-3*** | ***KC-4*** | ***KC-5*** |
| $\Delta G_{sol}$ / *kJ.mol*$^{-1}$ | 13.57 | 13.20 | 13.76 | 13.64 | 13.71 |
| $\Delta H_{sol}$ / *kJ.mol*$^{-1}$ | 21.77 | 21.18 | 22.95 | 18.48 | 25.19 |
| $\Delta S_{sol}$ / *J.mol*$^{-1}$.*K*$^{-1}$ | 26.21 | 25.50 | 29.38 | 15.48 | 36.71 |
| | ***KC-6*** | ***KC-7*** | ***KC-8*** | ***KC-9*** | ***KC-10*** |
| $\Delta G_{sol}$ / *kJ.mol*$^{-1}$ | 13.51 | 13.69 | 14.01 | 13.98 | 12.67 |
| $\Delta H_{sol}$ / *kJ.mol*$^{-1}$ | 33.45 | 31.49 | 45.16 | 31.75 | 19.04 |
| $\Delta S_{sol}$ / *J.mol*$^{-1}$.*K*$^{-1}$ | 63.73 | 56.88 | 99.58 | 56.80 | 20.36 |
| | ***THF*** | | | | |
| | ***KC-1*** | ***KC-2*** | ***KC-3*** | ***KC-4*** | ***KC-5*** |
| $\Delta G_{sol}$ / *kJ.mol*$^{-1}$ | 13.70 | 13.67 | 13.23 | 14.26 | 13.74 |
| $\Delta H_{sol}$ / *kJ.mol*$^{-1}$ | 18.58 | 11.68 | 16.65 | 19.79 | 15.76 |

| | | | | | |
|---|---|---|---|---|---|
| $\Delta S_{sol}$ / *J.mol*$^{-1}$.*K*$^{-1}$ | 15.57 | -6.38 | 10.93 | 17.67 | 4.48 |
| | ***KC-6*** | ***KC-7*** | ***KC-8*** | ***KC-9*** | ***KC-10*** |
| $\Delta G_{sol}$ / *kJ.mol*$^{-1}$ | 13.57 | 14.08 | 14.34 | 14.55 | 14.08 |
| $\Delta H_{sol}$ / *kJ.mol*$^{-1}$ | 20.71 | 25.25 | 24.73 | 27.33 | 23.46 |
| $\Delta S_{sol}$ / *J.mol*$^{-1}$.*K*$^{-1}$ | 22.80 | 35.69 | 33.20 | 40.85 | 29.98 |
| | ***1,4-Dioxane*** | | | | |
| | ***KC-1*** | ***KC-2*** | ***KC-3*** | ***KC-4*** | ***KC-5*** |
| $\Delta G_{sol}$ / *kJ.mol*$^{-1}$ | 13.71 | 14.24 | 14.47 | 14.80 | 14.55 |
| $\Delta H_{sol}$ / *kJ.mol*$^{-1}$ | 20.11 | 26.26 | 33.76 | 15.23 | 17.56 |
| $\Delta S_{sol}$ / *J.mol*$^{-1}$.*K*$^{-1}$ | 20.47 | 38.41 | 61.69 | 1.37 | 9.63 |
| | ***KC-6*** | ***KC-7*** | ***KC-8*** | ***KC-9*** | ***KC-10*** |
| $\Delta G_{sol}$ / *kJ.mol*$^{-1}$ | 13.44 | 13.91 | 14.38 | 14.99 | 13.89 |
| $\Delta H_{sol}$ / *kJ.mol*$^{-1}$ | 27.25 | 21.22 | 23.03 | 19.23 | 21.84 |
| $\Delta S_{sol}$ / *J.mol*$^{-1}$.*K*$^{-1}$ | 44.14 | 23.37 | 27.65 | 13.54 | 25.41 |
| | ***Ethyl acetate*** | | | | |
| | ***KC-1*** | ***KC-2*** | ***KC-3*** | ***KC-4*** | ***KC-5*** |
| $\Delta G_{sol}$ / *kJ.mol*$^{-1}$ | 14.56 | 14.57 | 14.78 | 14.39 | 13.41 |
| $\Delta H_{sol}$ / *kJ.mol*$^{-1}$ | 11.59 | 12.69 | 12.80 | 11.57 | 18.01 |
| $\Delta S_{sol}$ / *J.mol*$^{-1}$.*K*$^{-1}$ | -9.51 | -6.00 | -6.31 | -9.02 | 14.71 |
| | ***KC-6*** | ***KC-7*** | ***KC-8*** | ***KC-9*** | ***KC-10*** |
| $\Delta G_{sol}$ / *kJ.mol*$^{-1}$ | 13.66 | 15.30 | 15.21 | 14.73 | 14.34 |
| $\Delta H_{sol}$ / *kJ.mol*$^{-1}$ | 18.40 | 11.12 | 21.02 | 17.10 | 15.51 |
| $\Delta S_{sol}$ / *J.mol*$^{-1}$.*K*$^{-1}$ | 13.66 | 15.30 | 15.21 | 14.73 | 14.34 |

**Figure 2: The Variation of Experimental Mole Fraction Solubilities ($x_i$) with Temperature for the Synthesized Compounds in Different Solvents**




**KC-1: (■); KC-2: (■); KC-3: (▲); KC-4: (●); KC-5: (●);** Corresponding lines (—) are for calculated mole fraction solubilities $x_{ci}{}^{a}$ by Apelblat equation.

The solubility of compounds calculated by Apelblat equation ($x^{a}{}_{ci}$) and Buchowski-Ksiazczak λh equation ($x^{b}{}_{ci}$) are also given in Table 4.

It is observed from the Table 4 and that solubility of compound increases nonlinearly with increasing temperature. Further, it is shown from the Table 4 that the values obtained by modified Apelblat equation

and Buchowski-Ksiazczak λh equation shows good agreement with each other and also with experimental solubility data.

The relative deviations (RD), root-mean-square deviations (RMSD) and relative average deviations (ARD) between the experimental and calculated solubility are evaluated for both modified Apelblat and λh equations by equations 4, 5 and 6 respectively.

$$RD = \left(x_i - x_{ci}^{a/b}\right) \Big/ x_i \tag{4}$$

$$RMSD = \left[\sum_{i=1}^{N} (x_{ci} - x_i)^2 \Big/ N-1\right]^{1/2} \tag{5}$$

$$ARD = \frac{1}{N}\sum_{i}^{N} (x_i - x_{ci}) \Big/ x_i \tag{6}$$

Where, *N* is the number of experimental points. All these evaluated values are given Tables 4, 5 and 6. It is evident from these Tables that the results evaluated by modified Apelblat equation and λh equations are in good agreement with experimental solubility.

***Thermodynamic Parameters of Solution***

The correlation between temperature and solubility can be described by thermodynamic analysis. The dissolution of compound in a solvent is associated with changes in thermodynamic functions such as enthalpy ($\Delta H_{sol}$), Gibb's energy ($\Delta G_{sol}$) and entropy of solution ($\Delta S_{sol}$). The changes that occur in the solute during dissolution process can be explained by these thermodynamic functions.

The enthalpies of solution ($\Delta H_{sol}$) was calculated by modified Van't Hoff equation i.e., from the slope of the plot of *lnx* versus ($1/T - 1/T_{hm}$). Figure 4 shows plot of $lnx_i$ versus ($1/T - 1/T_{hm}$). From the slope of plot of $lnx_i$ versus ($1/T - 1/T_{hm}$) the enthalpy of solution ($\Delta H_{sol}$) determined.

$$\left(\partial \ln x_i \Big/ \partial\left(\frac{1}{T} - \frac{1}{T_{hm}}\right)\right)_p = -\Delta H_{sol} \Big/ R \tag{7}$$

Where, *T* is the experimental temperature, $T_m$ is mean harmonic temperature (Krug *et al.*, 1976) which is calculated by equation (8) and *R* is universal gas constant (8.314 *J/ mol K*).

$$T_{hm} = n \Big/ \Sigma_{i=1}^{n}\left(\frac{1}{T}\right) \tag{8}$$

Where, *n* is the number of experimental temperatures studied. The $T_{hm}$ value calculated by this equation is found to be 312.83 K.

The change in Gibb's free energy during solubility process can be calculated by intercept of the plot of $lnx_i$ versus ($1/T - 1/T_{hm}$) by following equation:

$$\Delta G_{sol} = -R \times T_{hm} \times Intercept \tag{9}$$

Finally, the entropy of solution ($\Delta S_{sol}$) was obtained from these evaluated $\Delta H$ and $\Delta G$ values at $T_{hm}$ (Bustamante *et al.*, 1998; Meng *et al.*, 2013).

$$\Delta S = (\Delta H - \Delta G) \Big/ T_{hm} \tag{10}$$

All the thermodynamic parameters are given in Table 7.

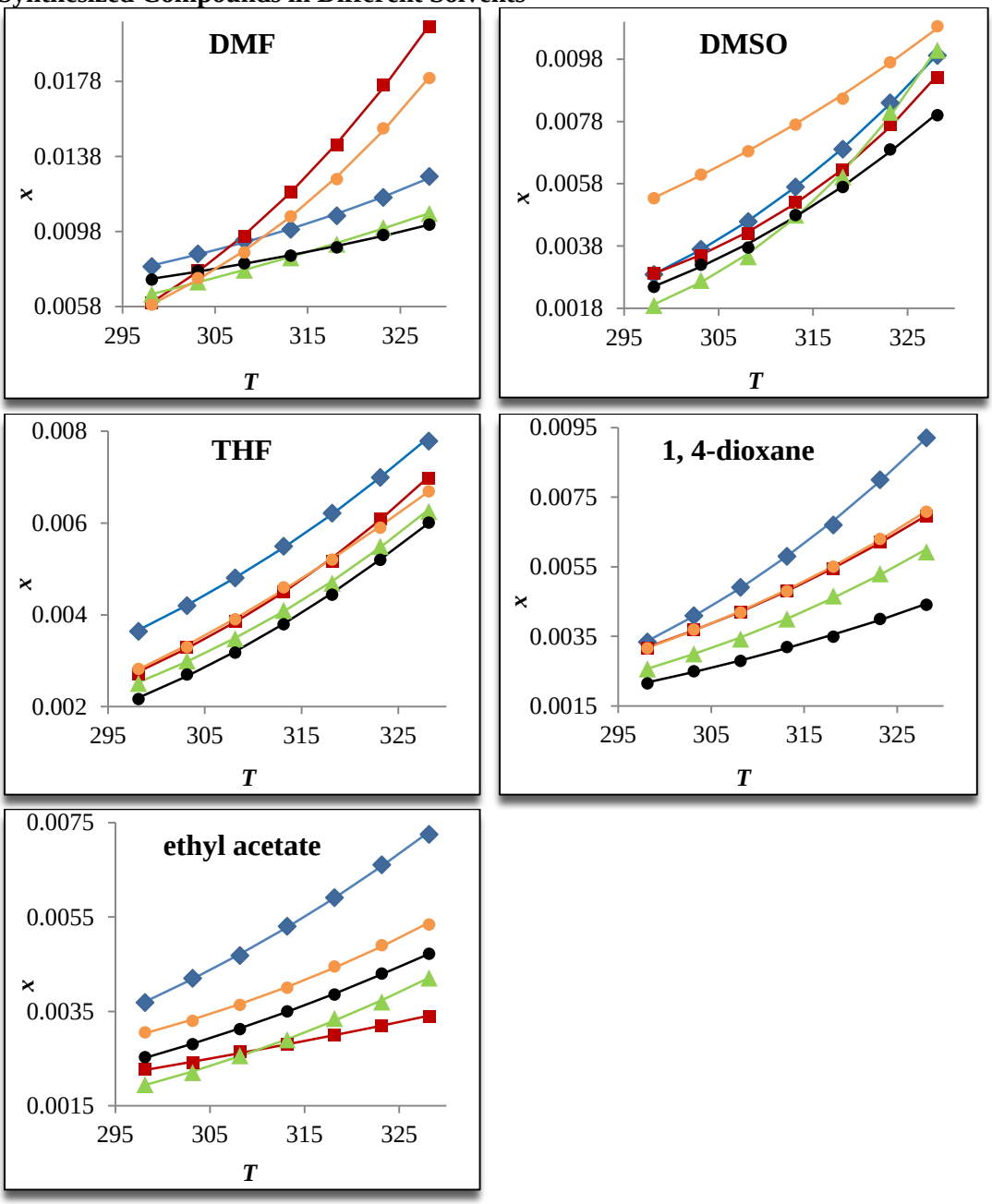
Table 7 shows that for the studied compounds, values of $\Delta H_{sol}$ and $\Delta G_{sol}$ are positive. However, $\Delta S_{sol}$ values are both positive and negative in the studied solvents.

Comparison of solubility data with Gibb's energy values shows that these two are inversely related. The positive $\Delta G_{sol}$ indicates that the dissolution process is spontaneous whereas positive enthalpy of

dissolution ($\Delta H_{sol}$) indicates endothermic dissolution process. This may be due to the powerful interaction between compounds and solvent molecules than those between the solvent-solvent and compound-compound molecules.

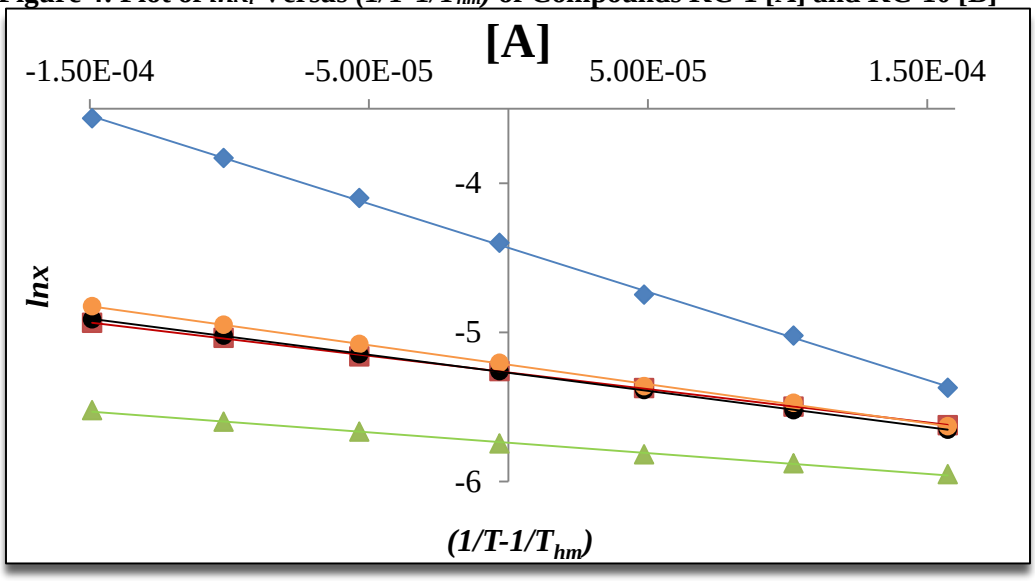
Thus, the newly formed bond energy between compound and solvent molecule is not powerful enough to compensate the energy needed for breaking the original association bond in various solvents. The positive entropy of dissolution suggests that the entropy of solubilization is more favorable (Martin, 1993), whereas negative entropy is due to more order in solutions (El-Bindary *et al.*, 2003).

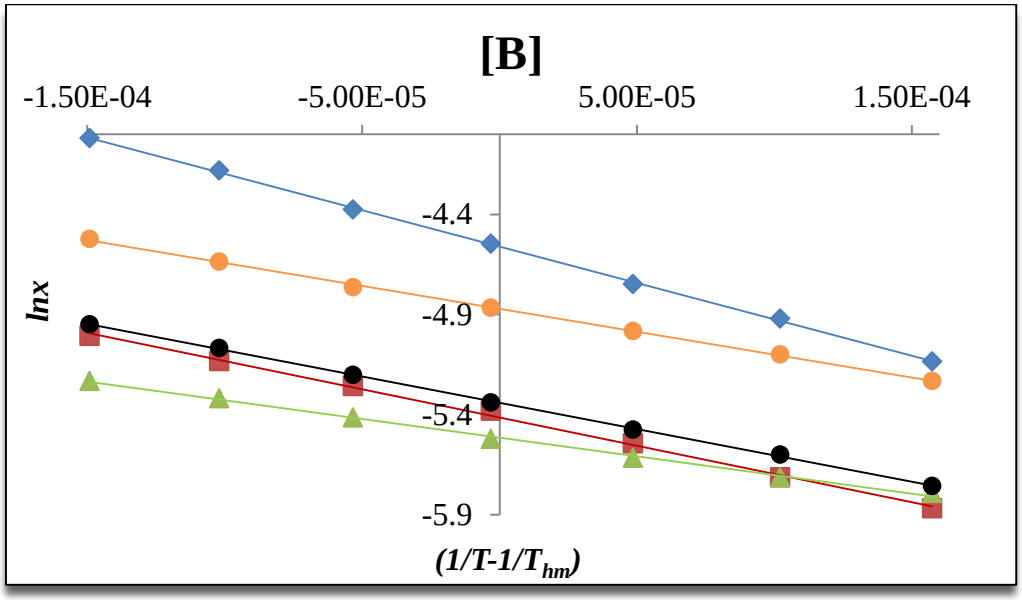
**Figure 3: The Variation of Experimental Mole Fraction Solubilities ($x_i$), with Temperature for Synthesized Compounds in Different Solvents**




**KC-6: (■); KC-7: (■); KC-8: (▲); KC-9: (●); KC-10: (●);** Corresponding lines (—) are for calculated mole fraction solubilities $x_{ci}{}^{a}$ by Apelblat equation

**Figure 4: Plot of $lnx_i$ Versus $(1/T-1/T_{hm})$ of Compounds KC-1 [A] and KC-10 [B]**




**[DMF, (■); THF, (■); ethyl acetate, (▲); 1, 4-dioxane, (●); DMSO, (●);]**

***Conclusion***

The solubility of studied compounds in solvents is a function of temperature. Solubility of studied compounds increases non linearly with increase in temperature. Solubility is found to be maximum in DMF. The solubility of the synthesized compounds are different in studied solvents. The solubility data calculated by modified Apelblat and λh equations are in good agreement with experimental values. The positive $\Delta H_{sol}$ and $\Delta G_{sol}$ suggest endothermic and spontaneous dissolution of compounds in all the studied solvents.

***Nomenclature***

| | |
|---|---|
| $x_i$ | *Experimental mole fractions solubility.* |
| $x^a_{ci}$ | *Calculated solubility by modified Apelblat equation.* |
| $x^b_{ci}$ | *Calculated solubility by Buchowsli equation.* |

| | |
|---|---|
| $M_1$ | *Molecular weight of solvents* |
| $M_2$ | *Molecular weight of synthesized compounds (KC-1 to KC-5)* |
| $m_1$ | *weights of solvents* |
| $m_2$ | *weights of synthesized compounds (KC-1 to KC-5)* |
| *A, B and C* | *parameters of modified Apelblat equation* |
| *λ and h* | *parameters of Buchowsli equation* |
| *N* | *Number of experimental points* |
| *n* | *Number of experimental temperatures studied.* |
| *T* | *Temperature in Kelvin* |
| $T_m$ | *Melting temperature* |
| $T_{hm}$ | *Mean harmonic temperature.* |
| $\Delta H$ | *Enthalpy change* ($kJ \cdot mol^{-1}$) |
| $\Delta G$ | *Gibb's energy change* ($kJ \cdot mol^{-1}$) |
| $\Delta S$ | *Entropy change* ($J \cdot K^{-1}.mol^{-1}$) |
| *R* | *Universal gas constant* ($8.314\ J.mol^{-1} \cdot K^{-1}$) |

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