Research Article

Measurement and Correlation for Solubility of Some Pyrimidine Derivatives in Different Solvents

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Some new pyrimidine derivatives have been synthesized and their characterization was done by IR, NMR, and mass spectral data. The solubility of these synthesized compounds has been studied in methanol, *N,N* dimethylformamide (DMF), and carbon tetrachloride (CCl_4) by gravimetric method from 298.15 to 328.15 K under atmospheric pressure and the solubility data were correlated against temperature. The solubility is found to increase with temperature and order of solubility is $\text{DMF} > \text{methanol} > \text{CCl}_4$. The experimental solubility data is correlated with the modified Apelblat equation. Some thermodynamic parameters such as dissolution enthalpy, Gibbs energy of dissolution, and entropy of mixing have also been calculated.

1. Introduction

The pyrimidine ring is an important structure in numerous natural products and bioactive compounds [1]. Further, the pyrimidine nucleus is present as a building block in materials science [2, 3]. Literature survey reveals that as pharmacologically active compounds, substituted pyrimidine scaffolds have become increasingly important with antimicrobial [4, 5], antimalarial [6], anticancer [7], and antimycotic activities [1].

So, it will be interesting to study their solubility in different solvents due to their various applications, which may help their uses in other fields also. Thus, in the present paper, solubility of some pyrimidine derivatives in methanol, DMF, and CCl_4 from 298.15 to 328.15 K has been studied at atmospheric pressure. Some thermodynamic parameters such as dissolution enthalpy, Gibbs energy of dissolution, and entropy of mixing have also been calculated.

2. Experimental

2.1. Materials. The choice of solvent depends upon solubility and relative permeability. 2,4-Dichloropyrimidine (DCP) (CAS no.: 3934-20-1) and 4-((1*H*-1,2,4-triazol-1-yl)methyl)aniline (TMA) (CAS no.: 119192-10-8) used in

the synthesis were purchased from Sigma-Aldrich. *N,N*-diisopropylethylamine (DIPEA) (CAS no.: 7087-68-5), the solvents methanol, dimethylformamide (DMF), and carbon tetrachloride (CCl_4) used in the present work were of AR grade supplied by Spectrochem Pvt. Ltd. (Mumbai, India) and were purified according to the standard procedure [8]. The purity of solvents was checked by GC-MS (SHIMADZU-Model no.-QP-2010) and found to be greater than 99.0%.

2.2. Synthesis. A mixture of 2,4-dichloropyrimidine (DCP) (1.0 equi.), 4-((1*H*-1,2,4-triazol-1-yl)methyl)aniline (TMA), and *N,N*-diisopropylethylamine (DIPEA) (1.2 equi.) in *n*-Butanol was refluxed for 3 h. The completion of reaction was confirmed by analytical thin layer chromatography (TLC). After completion of reaction, reaction mass was cooled and the resulting solid was filtered, washed with cold water, and dried in vacuo to give crude product.

This resulting product was refluxed for 3 h with ethanolic solution of different aromatic amines (1.1 equi.) in presence of glacial acetic acid (2-3 drops). After completion of reaction, the reaction mass was cooled and the resulting solid was filtered, washed with cold ethanol, and dried in vacuo to give crude product. The obtained crude product was purified by trituration with diethyl ether and purity of all these synthesized compounds was checked by TLC (performed on

FIGURE 1: The reaction scheme of pyrimidine derivatives.

aluminum coated TLC plates Gel 60 F254 (E. Merck)). The reaction scheme is given in Figure 1.

2.3. Spectroscopy Study. Spectroscopic study of all the synthesized compounds was done by IR, ^1H NMR, and mass spectroscopy. IR spectra were recorded on KBr discs, using FT-IR (Shimadzu Spectrophotometer Model no.-8400). ^1H -NMR spectra were taken on a Bruker AVANCE II 400. In all the cases, NMR spectra were obtained in $\text{DMSO}-d_6$ using TMS as an internal standard. The NMR signals are reported in δppm . Mass spectra were determined using direct inlet probe on a GCMS-QP-2010 mass spectrometer. Melting points of compounds were measured by Differential Scanning Calorimeter (Shimadzu-DSC-60).

2.4. Solubility Measurements. The solubility was measured by a gravimetric method [9]. For each measurement, an excess mole of compound was added to a known mole of solvent. Then, the equilibrium cell was heated to a constant temperature with continuous stirring. After at least 3 h (the temperature of the water bath approached constant value, and then the actual value of the temperature was recorded), the stirring was stopped and the solution was kept still for 2 h. A portion of this solution was filtered and by a preheated injector, 2 mL of this clear solution was taken in another weighed measuring vial (m_0). The vial was quickly and tightly closed and weighed (m_1) to determine the mole of the sample ($m_1 - m_0$). Then, the vial was covered with a piece of filter paper to prevent dust contamination. After the solvent in the vial had completely evaporated at room temperature, the vial was dried and reweighed (m_2) to determine the mole of the constant residue solid ($m_2 - m_0$). All the moles were taken using an electronic balance (Mettler Toledo AB204-S, Switzerland) with an uncertainty of $\pm 0.0001\text{ g}$. Thus, the concentration of the solid sample in the solution, mole fraction x , could be determined from

$$x = \frac{(m_2 - m_0)/M_1}{(m_2 - m_0)/M_1 + (m_1 - m_2)/M_2}, \quad (1)$$

where M_1 is the molar mole of compound and M_2 is the molar mole of the solvent.

At each temperature, the measurement was repeated three times and an average value is given in Table 3.

TABLE 1: Physical properties of synthesized pyrimidine derivatives.

Sr. no.	Code	R	M.F	M.P.
1	BKD-1	4-Cl	$\text{C}_{19}\text{H}_{16}\text{ClN}_7$	130.31
2	BKD-2	4- CH_3	$\text{C}_{20}\text{H}_{19}\text{N}_7$	160.64
3	BKD-3	4-F	$\text{C}_{19}\text{H}_{16}\text{FN}_7$	197.35
4	BKD-4	3- CF_3	$\text{C}_{20}\text{H}_{16}\text{F}_3\text{N}_7$	205.87
5	BKD-5	3-Cl, 4-F	$\text{C}_{19}\text{H}_{15}\text{ClFN}_7$	225.82

3. Results and Discussion

The physical properties of all the synthesized compounds are given in Table 1. For compound BKD-5, IR and ^1H NMR spectra are shown in Figures 2 and 3, respectively.

3.1. IR Spectra. The IR spectrum of BKD-5 is depicted in Figure 2. The IR data of BKD-5 clearly shows a $-\text{NH}$ (secondary) stretching band at 3396 and 3196 cm^{-1} . The IR stretching bands at 3090 – 2987 cm^{-1} and 1651 – 1494 cm^{-1} confirmed the presence of aromatic $\text{C}-\text{H}$ and $\text{C}=\text{C}$ in basic skeleton. The absorption band at 758 cm^{-1} and 1062 – 972 indicates presence of $\text{C}-\text{Cl}$ and $\text{C}-\text{F}$ stretching present in synthesized compounds and IR stretching band at 1379 cm^{-1} indicates presence of triazole ring in synthesized compound. The bending vibration $-\text{CH}_2$ was observed at 1462 cm^{-1} , respectively. The $\text{C}-\text{H}$ symmetric stretching and asymmetric stretching absorption are observed at 2833 cm^{-1} and 2850 cm^{-1} , respectively. All the IR group frequencies were suggestive of the fact that pyrimidine derivative is prepared successfully.

3.2. ^1H -NMR Spectra. The proton NMR spectrum of BKD-5 is depicted in Figure 3. The peak due to residual DMSO was observed at about $3.505\delta\text{ppm}$. It can be seen from the chemical structure of compound BKD-5 that proton of the phenyl ring attached to the carbons appeared as an appropriate multiplicity in the aromatic region at 6.463 – $8.698\delta\text{ppm}$. The protons, which were present in methylene ($-\text{CH}_2$) (attached to phenyl ring and triazole ring), appeared as a singlet at $5.421\delta\text{ppm}$. The other two characteristic $-\text{NH}$ groups appeared as a singlet at $10.527\delta\text{ppm}$ and $10.8\delta\text{ppm}$.

FIGURE 2: IR spectrum of compound BKD-5.

FIGURE 3: ^1H NMR spectrum of compound BKD-5.

TABLE 2: Dielectric constant and dipole moment of solvents.

Sr. no.	Solvent	Dielectric constant	Dipole moment
1	Methanol	32.70	1.7
2	DMF	36.71	3.86
3	CCl_4	2.238	0

3.3. Solubility Measurements. The solubility of the compounds in methanol, DMF, and CCl_4 is summarized in Table 3 at temperatures ranging from 298.15 to 328.15 K. It is observed that for all the compounds, solubility is found to increase with temperature and order of solubility is $\text{DMF} > \text{methanol} > \text{CCl}_4$. These solubility results are correlated with the dielectric constant and dipole moment of solvents which are given in Table 2. It is observed from Table 2 that both dielectric constant and dipole moment are higher for DMF

FIGURE 4: Variation of mole fraction solubilities (x_i) with temperature for pyrimidine derivatives, (a) in methanol, (b) in DMF, and (c) in CCl_4 . BKD-1 ($\diamond$), BKD-2 (Δ), BKD-3 (+), BKD-4 (O), and BKD-5 ($\square$). Dotted lines: x_{ci} .

and lower for CCl_4 . This is in accordance with the solubility trend in the three solvents. Thus, in present study, these properties affect the solubility. The variation of solubility in studied solvent with temperature is also shown in Figure 4.

The temperature dependence of solubility of compounds in solvents is described by the modified Apelblat equation [10, 11]. Consider

$$\ln x_{ci} = A + \frac{B}{T} + C \ln(T), \quad (2)$$

where x_{ci} is the mole fraction solubility of compound, T is the absolute temperature, and A , B , and C are constants

TABLE 3: Observed mole fraction solubilities (x_i), calculated mole fraction solubilities (x_{ci}), and relative deviation (RD) of pyrimidine derivatives in studied solvents.

T/K	$10^3 \cdot x_i$	$10^3 \cdot x_{ci}$ Methanol	100 RD	$10^3 \cdot x_i$	$10^3 \cdot x_{ci}$ DMF	100 RD
BKD-1						
298.15	0.7424	0.7032	5.2714	1.2858	1.3644	-6.1101
308.15	0.9546	0.9179	3.8396	2.1772	2.2143	-1.7032
318.15	1.2917	1.2125	6.1314	3.1280	3.3990	-8.6658
328.15	1.6961	1.6178	4.6146	4.7797	4.9642	-3.8605
BKD-2						
298.15	7.2089	7.2173	-0.1160	6.4013	6.6624	-4.0791
308.15	7.5441	7.5349	0.1224	9.1663	9.6171	-4.9179
318.15	7.8357	7.8549	-0.2447	12.4275	12.8846	-3.6788
328.15	8.1781	8.1773	0.0096	15.4508	16.1567	-4.5692
BKD-3						
298.15	1.8396	1.8414	-0.0994	2.9352	3.0049	-2.3744
308.15	2.0265	2.0266	-0.0060	4.5676	4.7638	-4.2964
318.15	2.2303	2.2336	-0.1457	6.8753	6.9688	-1.3609
328.15	2.4631	2.4642	-0.0462	9.1798	9.4912	-3.3916
BKD-4						
298.15	2.1697	2.1656	0.1879	4.7890	4.8779	-1.8557
308.15	2.4994	2.5239	-0.9774	6.6104	6.8106	-3.0278
318.15	2.9719	2.9472	0.8294	8.8903	9.0000	-1.2333
328.15	3.4326	3.4465	-0.4054	11.0513	11.3250	-2.4764
BKD-5						
298.15	1.8804	1.9788	-5.2320	4.3717	4.3519	0.4518
308.15	2.0425	2.1480	-5.1682	7.1020	7.3718	-3.7998
318.15	2.1859	2.3010	-5.2636	11.9189	11.5947	2.7203
328.15	2.3156	2.4359	-5.1961	16.7816	17.0697	-1.7170
T/K	$10^3 \cdot x_i$	$10^3 \cdot x_{ci}$	100 RD	$10^3 \cdot x_i$	$10^3 \cdot x_{ci}$	100 RD
CCl ₄						
BKD-1			BKD-2			
298.15	0.2086	0.2063	1.0639	0.3117	0.3199	-2.6167
308.15	0.5074	0.5129	-1.0775	0.6170	0.7129	-15.5464
318.15	1.0532	1.0611	-0.7491	1.3231	1.4269	-7.8428
328.15	1.8654	1.8655	-0.0074	2.6507	2.5944	2.1236
BKD-3			BKD-4			
298.15	0.4526	0.4792	-5.8771	0.7293	0.7230	0.8634
308.15	0.7606	0.7935	-4.3353	1.0161	1.0104	0.5649
318.15	1.1252	1.2016	-6.7924	1.4272	1.4121	1.0633
328.15	1.5984	1.6805	-5.1353	1.9872	1.9724	0.7442
BKD-5						
298.15	0.5563	0.5807	-4.3813			
308.15	0.7813	0.8526	-9.1205			
318.15	1.0849	1.2004	-10.6449			
328.15	1.5232	1.6278	-6.8658			

determined by least square analysis and values of these constants are given in Table 4. The calculated solubilities x_{ci} are also reported in Table 3. The experimental solubility (x_i) of synthesized compounds in the studied solvents was compared with calculated solubility (x_{ci}) and relative deviations (RD) between the experimental and calculated value are

calculated by the following equation:

$$RD = \left(\frac{x_i - x_{ci}}{x_i} \right) \quad (3)$$

and the values are given in Table 3.

TABLE 4: Constants A , B , and C of (2), ARD and RMSD of pyrimidine derivatives in studied solvents.

Parameters	BKD-1	BKD-2	BKD-3	BKD-4	BKD-5
Methanol					
A	-188.055	-11.7269	-52.2145	-77.6811	49.6358
B	6084.210	-29.1148	1325.46	2035.83	-3161.55
C	28.150	1.2097	7.2786	11.3586	-7.9434
10^5 RMSD	3.5676	0.6605	0.1126	1.0857	6.3598
100 ARD	4.964265	-0.05721	-0.07432	-0.09137	-5.21496
DMF					
A	174.3	345.3	346.99	229.015	280.85
B	-11941.99	-18676.27	-19519.51	-13181.27	-17033.54
C	-24.72	-50.49	-50.43	-33.37	-40.22
10^5 RMSD	9.7924	28.56	11.145	10.602	14.764
100 ARD	-5.08489	-4.31126	-2.85585	-2.1483	-0.58617
CCl_4					
A	850.32	392.96	387.99	-136.24	121.48
B	-45868.6	-24351.6	-21792.9	3214.51	-8815.27
C	-123.73	-56.047	-56.61	20.75	-17.44
10^5 RMSD	0.2844	4.3974	3.4608	0.6593	4.9956
100 ARD	-0.19255	-5.97058	-5.53503	0.808956	-7.75314

The relative average deviations (ARD) and root-mean-square deviations (RMSD) calculated by (4) are listed in Table 4. Consider

$$\text{ARD} = \frac{1}{N} \sum_i^N \frac{x_i - x_{ci}}{x_i} \quad (4)$$

$$\text{RMSD} = \left[\sum_{i=1}^N \frac{(x_{ci} - x_i)^2}{N-1} \right]^{1/2},$$

where N is the number of experimental points and x_{ci} is the solubility calculated by (2).

According to the Krug et al. [12] approach, the following modified Van't Hoff expression was used to determine the enthalpy of solution (ΔH_{sol}):

$$\left(\frac{\partial \ln x}{\partial (1/T - 1/T_{\text{hm}})} \right)_P = -\frac{\Delta H_{\text{sol}}}{R}, \quad (5)$$

where $\Delta H_{\text{sol}}/R$ is the apparent standard enthalpy energy charge for the solution process and T_{hm} is the harmonic mean of the experimental temperatures, which is evaluated by the following equation:

$$T_{\text{hm}} = \frac{n}{\sum_1^n (1/T)}, \quad (6)$$

where n is the number of experimental temperatures [13]. In the present case, the T_{hm} value obtained is 312.7505 K. The value of ΔH_{sol} was obtained from the slope of the plot of $\ln x_i$ versus $(1/T - 1/312.7505)$ as shown in Figure 5 for methanol, DMF, and CCl_4 .

FIGURE 5: Van't Hoff plot for pyrimidine derivatives solubility in (a) in methanol, (b) in DMF, and (c) in CCl_4 . BKD-1 ($\diamond$), BKD-2 ($\square$), BKD-3 (Δ), BKD-4 ($\circ$), and BKD-5 ($+$).

The apparent standard Gibbs energy change for the solution process (ΔG_{sol}), considering the approach proposed by Krug et al., is calculated at T_{hm} by the following equation:

$$\Delta G_{\text{sol}} = -RT \cdot \text{Intercept} \quad (7)$$

in which the intercept was from the plot of $\ln x$ versus $(1/T - 1/T_{\text{hm}})$.

Finally, using these evaluated ΔH_{sol} and ΔG_{sol} values, the entropies of solutions ΔS_{sol} were obtained from equation [12, 14]

$$\Delta S_{\text{sol}} = \frac{\Delta H_{\text{sol}} - \Delta G_{\text{sol}}}{T_{\text{hm}}}. \quad (8)$$

All these thermodynamic parameters are given in Table 5.

TABLE 5: Thermodynamic parameters of dissolution of pyrimidine derivatives in studied solvents.

Parameters	BKD-1	BKD-2	BKD-3	BKD-4	BKD-5
Methanol					
$\Delta G_{\text{sol}}/\text{kJ}\cdot\text{mol}^{-1}$	17.6736	12.6578	15.9965	15.3516	16.0303
$\Delta H_{\text{sol}}/\text{kJ}\cdot\text{mol}^{-1}$	22.5891	3.3855	7.8958	12.5874	5.6410
$\Delta S_{\text{sol}}/\text{J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$	15.7171	-29.6478	-25.9014	-8.8385	-33.2189
DMF					
$\Delta G_{\text{sol}}/\text{kJ}\cdot\text{mol}^{-1}$	15.5336	11.8960	13.5783	12.7332	12.2834
$\Delta H_{\text{sol}}/\text{kJ}\cdot\text{mol}^{-1}$	35.0186	23.4372	31.2108	22.8552	37.0804
$\Delta S_{\text{sol}}/\text{J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$	62.3018	36.9023	56.3787	32.3644	79.2870
CCl_4					
$\Delta G_{\text{sol}}/\text{kJ}\cdot\text{mol}^{-1}$	18.9815	18.2170	18.2716	17.4786	18.1754
$\Delta H_{\text{sol}}/\text{kJ}\cdot\text{mol}^{-1}$	59.5282	58.3892	34.0375	27.2034	27.2283
$\Delta S_{\text{sol}}/\text{J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$	129.6456	128.4480	50.4103	31.0944	28.9460

It is evident from Table 5 that for all the compounds ΔH_{sol} and ΔG_{sol} values are positive. Further, ΔS_{sol} values are also positive for all compounds in DMF and CCl_4 whereas it is negative in methanol excepting BKD-1. When stronger bonds are broken and weaker bonds are formed, energy is consumed. So, ΔH_{sol} becomes positive [12] which indicates endothermic dissolution of compounds [15]. The positive value of ΔG_{sol} indicates that the dissolution process is not spontaneous [12, 15]. The positive entropy change indicates that the entropy of solubilization is unfavorable for solute in solution [15], whereas negative entropy is due to more order in solutions [16]. This depends on the functional groups present in the compound as well as on the solvent. The negative entropy in methanol may be due to the fact that there may be hydrogen bonding between solute and solvent molecules which may give more ordered structure in solution, whereas in DMF and CCl_4 , due to larger structure (in comparison to methanol), the structure may be disrupted, thus giving positive entropy.

Appendix

Spectral Data

BKD-1: IR (cm^{-1} , KBr). 3375, 3225 (–NH (sec.) str.), 3095, 3036 (Ar–H str.), 2883 (–CH₂ asym. str.), 2833 (–CH₂ sym. str.), 1654–1489 (C=C str. Phenyl nucleus), 1456 (–CH₂ bending vib.), 1371 (triazole ring str.), 1273 (C–N str.), 1242–1010 (C–H in plane bending, phenyl ring), 827 (C–H oop phenyl ring), 759 (C–Cl str.), 705–675 (C–H oop triazole ring), 626 (in plane pyrimidine ring bending), 422 (Out of plane pyrimidine ring bending). ¹H NMR ($\text{DMSO}-d_6$) δ (ppm): 5.458 (s, 2H), 6.559–6.575 (d, 1H, $J = 6.4$), 7.308–7.329 (d, 2H, $J = 8.4$), 7.396–7.418 (d, 2H, $J = 8.8$), 7.518–7.538 (d, 2H, $J = 8$), 7.583–7.601 (d, 2H, $J = 7.2$) 8.019–8.037 (d, 1H, $J = 7.2$), 8.095 (s, 1H), 8.820 (s, 1H), 10.984 (s, 1H), 11.282 (s, 1H). MS: (m/z) = 377.

BKD-2: IR (cm^{-1} , KBr). 3394, 3217 (–NH (sec.) str.), 3088 (Ar–H str.), 3041 (–CH₂ asym. str.), 2897 (–CH₃ sym. str.), 2837

(–CH₂ sym str.), 1647–1516 (C=C str. Phenyl nucleus), 1460 (–CH₂ bending vib.), 1352 (–CH₃ asy bending) 1274 (C–N str.), 1240–972 (C–H in plane bending, phenyl ring), 868–813 (C–H oop phenyl ring), 813 (C–Cl str.), 758 (C–H oop triazole ring). ¹H NMR ($\text{DMSO}-d_6$) δ (ppm): 2.331 (s, 3H), 5.425 (s, 2H), 6.432–6.449 (d, 1H, $J = 6.8$), 7.161–7.181 (d, 2H, $J = 8$), 7.249–7.270 (d, 2H, $J = 8.4$), 7.342–7.363 (d, 2H, $J = 8.4$), 7.592–7.612 (d, 2H, $J = 8$), 7.930–7.947 (d, 1H, $J = 6.8$), 8.016 (s, 1H), 8.693 (s, 1H), 10.418 (s, 1H), 10.873 (s, 1H). MS: (m/z) = 357.

BKD-3: IR (cm^{-1} , KBr). 3391, 3213 (–NH (sec.) str.), 3059 (Ar–H str.), 2893 (–CH₂ asym. str.), 1654–1506 (C=C str. Phenyl nucleus), 1462 (–CH₂ bending vib.), 1388 (triazole ring str.), 1273 (C–N str.), 1219–1136 (C–H in plane bending, phenyl ring), 1018 (C–F str.), 835–768 (C–H oop phenyl ring), 767 (C–H oop triazole ring). ¹H NMR ($\text{DMSO}-d_6$) δ (ppm): 5.36 (s, 2H), 6.2–6.214 (d, 1H, $J = 5.6$), 7.114–7.212 (m, 4H), 7.22–7.247 (m, 1H), 7.605–7.627 (d, 2H, $J = 8.8$), 7.721–7.765 (m, 1H), 7.963–7.981 (d, 2H, $J = 4$), 8.635 (s, 1H), 8.699 (s, 1H), 9.432 (s, 1H). MS: (m/z) = 361.

BKD-4: IR (cm^{-1} , KBr). 3311, 3203 (–NH (sec.) str.), 3107–3041 (Ar–H str.), 2951 (–CH₂ asym. str.), 2883 (–CH₂ sym str.), 1637–1491 (C=C str. Phenyl nucleus), 1456–1419 (–CH₂ bending vib.), 1334 (triazole ring str.), 1271 (C–N str.), 1230–1157 (C–H in plane bending, phenyl ring), 1107–1014 (C–F str.), 966–848 (C–H oop phenyl ring), 794–650 (C–H oop triazole ring). ¹H NMR ($\text{DMSO}-d_6$) δ (ppm): 5.377 (s, 2H), 6.279–6.293 (d, 1H, $J = 5.6$), 7.222–7.257 (t, 3H, $J = 8$), 7.434–7.474 (t, 1H, $J = 8$), 7.686–7.707 (d, 2H, $J = 8.4$), 7.996–8.012 (d, 2H, $J = 6.4$), 8.068–8.083 (d, 1H, $J = 6$), 8.175 (s, 1H), 8.654 (s, 1H), 9.521 (s, 2H). MS: (m/z) = 411.

BKD-5: IR (cm^{-1} , KBr). 3396, 3196 (–NH (sec.) str.), 3090–2987 (Ar–H str.), 2850 (–CH₂ asym. str.), 2833 (–CH₂ sym str.), 1651–1494 (C=C str. Phenyl nucleus), 1462 (–CH₂ bending vib.), 1379 (triazole ring str.), 1265 (C–N str.), 1205, 1139 (C–H in plane bending, phenyl ring), 1060–972 (C–F str.), 879–819 (C–H oop phenyl ring), 758 (C–Cl str.), 680–509 (C–H oop triazole ring). ¹H NMR ($\text{DMSO}-d_6$) δ (ppm): 5.421 (s, 2H), 6.463–6.480 (d, 1H, $J = 6.8$), 7.286–7.307 (d, 2H, $J = 8.4$), 7.333–7.353 (d, 2H, $J = 8$), 7.405–7.422 (d, 2H, $J = 6.8$), 7.903–7.920 (d, 1H, $J = 6.8$), 8.004–8.021 (d, 2H, $J = 6.8$), 8.685–8.698 (d, 1H, $J = 5.2$), 10.52 (s, 1H), 10.8 (s, 1H). MS: (m/z) = 395.

Nomenclature

- C: Concentration ($\text{mol}\cdot\text{L}^{-1}$)
- T: Absolute temperature (K)
- x_i : Experimental solubility (x_i)
- x_{ci} : Calculated mole fraction solubility (x_{ci})
- ΔH_{sol} : Enthalpy of solution
- G_{sol} : Gibbs energies of dissolution ($\text{kJ}\cdot\text{mol}^{-1}$)
- ΔS_{sol} : Entropy of solutions ($\text{kJ}\cdot\text{mol}^{-1}$)
- R: Universal gas constant ($\text{J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$)
- T_{hm} : Harmonic temperature (K).

Abbreviations

DCP: 2,4-Dichloropyrimidine
TMA: 4-((1*H*-1,2,4-Triazol-1-yl)methyl)aniline
DIPEA: *N,N*-Diisopropylethylamine
DMF: *N,N*-Dimethylformamide
CCl₄: Carbon tetrachloride
AR: Analytical reagent
AAD: Absolute average deviations
rmsd: Root-mean-square deviations
RD: Relative deviations.

Conflict of Interests

The authors of this paper do not have a direct financial relation with the commercial identity that might lead to a conflict of interests for any of the authors.

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