Solubility of Biologically Active Chalcones in 1,4-Dioxane and *N*,*N*-Dimethyl Formamide from (298.15 to 318.15) K

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The solubilities of some chalcones in 1,4-dioxane and *N*,*N*-dimethyl formamide were measured by a gravimetrical method from (298.15 to 318.15) K under atmospheric pressure, and the solubility data were correlated against temperature.

Introduction

A literature survey shows that chalcones are associated with different biological activities like cardiovascular,[1] antispasmodic,[2] anthelmintics,[3] antiulcer,[4] anti-inflammatory,[5] antiviral,[6] antiallergic,[7] fungicidal,[8] bactericidal,[9] insecticidal,[10] antitumor,[11] antileishmanial,[12] herbicidal,[13] anticancer,[14] antitubercular,[15] anti HIV,[16] etc.

These biological properties prompted us to synthesize some new chalcones having furan. The solubility of these synthesized chalcones has been studied in 1,4-dioxane and DMF at different temperatures (298.15 K to 318.15 K). Further, enthalpy, Gibb's energy, and entropy of solution have also been evaluated.

Experimental Section

Materials. The synthesized chalcone derivatives were recrystallized in ethanol, and their purity was checked by elemental analysis, IR, NMR, and mass spectral data. Figure 1 shows the general structure of a synthesized chalcone derivative. The melting temperatures of all the synthesized compounds were determined by DSC (Universal V2.6D Instruments) and are given in Table 1 with substituted group R, molecular weight, and molecular formula.

The selected solvents DMF and 1,4-dioxane were purified by the reported method.[17] The purity was determined by gas chromatography with a SHIMADZU GC-MS (model No QP-2010) and was found to have a mole fraction purity greater than 0.9970.

Solubility Measurement. The solubilities were measured by a gravimetric method.[18] For each measurement, an excess mass of compound was added to a known mass 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, 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 weighted measuring vial (m_0). The vial was quickly and tightly closed and weighted (m_1) to determine the mass 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 mass of the constant residue solid ($m_2 - m_0$). All the masses were taken using an electronic balance (Mettler Toledo AB204-S, Switzerland) with an uncertainty of ± 0.0001 g. Thus, the concentration of the solid sample in the solution, mole fraction x, could be determined from eq 1.

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

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

Table 1. Physical Constants of Chalcones

Sr. No.	compound code	R	M.F.	MW (g·mol^{-1})	mp °C
1	AKFC-01	4-OCH_3-C_6H_4	$C_{20}H_{15}NO_5$	349.33	141
2	AKFC-02	4-NO_2-C_6H_4	$C_{19}H_{12}N_2O_6$	364.30	218
3	AKFC-03	3-NO_2-C_6H_4	$C_{19}H_{12}N_2O_6$	364.30	180
4	AKFC-04	4-NH_2-C_6H_4	$C_{19}H_{14}N_2O_4$	334.32	171
5	AKFC-05	4-Cl-C_6H_4	$C_{19}H_{12}NO_4Cl$	353.75	170
6	AKFC-06	4-Br-C_6H_4	$C_{19}H_{12}NO_4Br$	398.20	160
7	AKFC-07	-C_6H_5	$C_{19}H_{13}NO_4$	319.31	142
8	AKFC-08	4-OH-C_6H_4	$C_{19}H_{13}NO_5$	335.31	152
9	AKFC-09	2-furayl	$C_{14}H_{11}NO_5$	309.27	178
10	AKFC-10	3-coumarin	$C_{22}H_{13}NO_6$	387.34	172

Results and Discussion

The mole fraction solubilities x of chalcone derivatives in 1,4-dioxane and DMF at different temperatures (298.15 K to 318.15 K) are summarized in Tables 2 and 3. The variation of solubility with temperature is also shown in Figure 2. It is observed that solubility increases linearly with an increase in temperature. Comparison of solubility in the two solvents shows that overall solubility is greater in DMF than in 1,4-dioxane for all the chalcones. This is expected because the dielectric constant and dipole moment of DMF (36.71, 3.86) are greater than that of 1,4-dioxane (2.209, 0). Thus, these properties of solvent play an important role in the solubility.

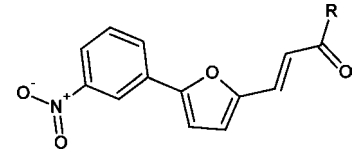

Figure 1. General structure of the chalcone derivative.

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Table 2. Observed Mole Fraction Solubilities (x), Calculated Mole Fraction Solubilities (x_{ci}), and Relative Deviation (RD) of Chalcones in Dioxane

T/K	10^2x	10^2x_{ci}	100 RD
	AKFC-1		
298.15	0.7316	0.7421	0.2703
303.15	0.7334	0.7454	0.3147
308.15	0.7367	0.7488	0.3142
313.15	0.7416	0.7522	0.3161
318.15	0.7441	0.7556	0.2955
	AKFC-2		
298.15	0.2292	0.2298	0.0247
303.15	0.2324	0.2340	0.2664
308.15	0.2388	0.2382	−0.0614
313.15	0.2411	0.2425	0.1595
318.15	0.2454	0.2469	0.0873
	AKFC-3		
298.15	0.5958	0.5952	−0.0385
303.15	0.6009	0.5981	−0.0772
308.15	0.6025	0.6011	−0.0289
313.15	0.6052	0.6041	−0.0505
318.15	0.6084	0.6072	−0.0562
	AKFC-4		
298.15	0.2450	0.2498	0.3044
303.15	0.2484	0.2421	0.1224
308.15	0.2502	0.2543	0.2569
313.15	0.2522	0.2566	0.2770
318.15	0.2549	0.2590	0.2488
	AKFC-5		
298.15	0.2712	0.2685	−0.1887
303.15	0.2721	0.2719	0.1027
308.15	0.2774	0.2753	−0.1485
313.15	0.2818	0.2788	−0.0899
318.15	0.2836	0.2823	−0.1002
	AKFC-6		
298.15	0.4887	0.4850	−0.1622
303.15	0.4913	0.4884	−0.0784
308.15	0.4951	0.4918	−0.1428
313.15	0.5007	0.4953	−0.1957
318.15	0.5013	0.4987	−0.1156
	AKFC-7		
298.15	0.5534	0.5611	0.2483
303.15	0.5604	0.5662	0.1959
308.15	0.5654	0.5713	0.1850
313.15	0.5712	0.5765	0.2024
318.15	0.5733	0.5817	0.2649
	AKFC-8		
298.15	0.5729	0.5688	−0.1560
303.15	0.5801	0.5734	−0.2381
308.15	0.5815	0.5780	−0.1357
313.15	0.5911	0.5827	−0.2602
318.15	0.5917	0.5873	−0.1618
	AKFC-9		
298.15	0.7052	0.7132	0.2103
303.15	0.7072	0.7153	0.2141
308.15	0.7096	0.7175	0.2052
313.15	0.7112	0.7196	0.2556
318.15	0.7138	0.7218	0.2079
	AKFC-10		
298.15	0.6171	0.6235	0.1831
303.15	0.6234	0.6263	0.1817
308.15	0.6220	0.6291	0.2066
313.15	0.6242	0.6319	0.2263
318.15	0.6285	0.6348	0.1775

Table 3. Observed Mole Fraction Solubilities (x), Calculated Mole Fraction Solubilities (x_{ci}), and Relative Deviation (RD) of Chalcones in DMF

T/K	10^2x	10^2x_{ci}	100 RD
	AKFC-1		
298.15	1.1151	1.1221	0.1221
303.15	1.1200	1.1277	0.1356
308.15	1.1276	1.1334	0.0959
313.15	1.1300	1.1390	0.1606
318.15	1.1377	1.1447	0.1205
	AKFC-2		
298.15	0.2374	0.2362	−0.1000
303.15	0.2400	0.2387	−0.1077
308.15	0.2436	0.2412	−0.1838
313.15	0.2450	0.2437	−0.1017
318.15	0.2478	0.2463	−0.1137
	AKFC-3		
298.15	0.6036	0.6013	−0.0890
303.15	0.6100	0.6056	−0.1593
308.15	0.6136	0.6098	−0.1383
313.15	0.6200	0.6141	−0.2042
318.15	0.6204	0.6184	−0.0781
	AKFC-4		
298.15	0.2638	0.2639	−0.0120
303.15	0.2639	0.2640	−0.0094
308.15	0.2641	0.2641	−0.0126
313.15	0.2641	0.2642	−0.0070
318.15	0.2643	0.2643	−0.0141
	AKFC-5		
298.15	0.4502	0.4495	−0.0425
303.15	0.4600	0.0456	−0.1644
308.15	0.4683	0.4632	−0.2186
313.15	0.4700	0.4702	−0.0066
318.15	0.4803	0.4773	−0.1318
	AKFC-6		
298.15	0.7045	0.7067	0.0446
303.15	0.7100	0.7120	0.0401
308.15	0.7136	0.7174	0.0896
313.15	0.7215	0.7228	0.0186
318.15	0.7255	0.72824	0.0599
	AKFC-7		
298.15	0.9833	0.9943	0.2247
303.15	0.9900	1.0028	0.2616
308.15	0.9981	1.0114	0.2705
313.15	1.0100	1.0200	0.1974
318.15	1.0148	1.0287	0.2791
	AKFC-8		
298.15	0.6649	0.6698	0.1320
303.15	0.6700	0.6762	0.1684
308.15	0.6754	0.6827	0.1978
313.15	0.6800	0.6892	0.2528
318.15	0.6916	0.6958	0.1050
	AKFC-9		
298.15	0.9403	0.9457	0.1067
303.15	0.9452	0.9500	0.0914
308.15	0.9500	0.9543	0.0794
313.15	0.9500	0.9586	0.1760
318.15	0.9589	0.9629	0.0733
	AKFC-10		
298.15	0.6957	0.6929	−0.0981
303.15	0.7000	0.6998	−0.0212
308.15	0.7101	0.7069	−0.1077
313.15	0.7200	0.7140	−0.1869
318.15	0.7214	0.7211	−0.0231

As shown in Figure 2, the mole fraction solubility x of chalcones was correlated as a function of temperature. Theoretically, solubilities (x_{ci}) were also evaluated using A and B parameters using eq 2. The temperature dependence of chalcone solubility in solvents is described by the modified Apelblat equation[19,20]

$$\ln x = A + B(T/\mathrm{K}) \qquad (2)$$

where x is the mole fraction solubility of chalcones; T is the absolute temperature; and A and B are the parameters. The

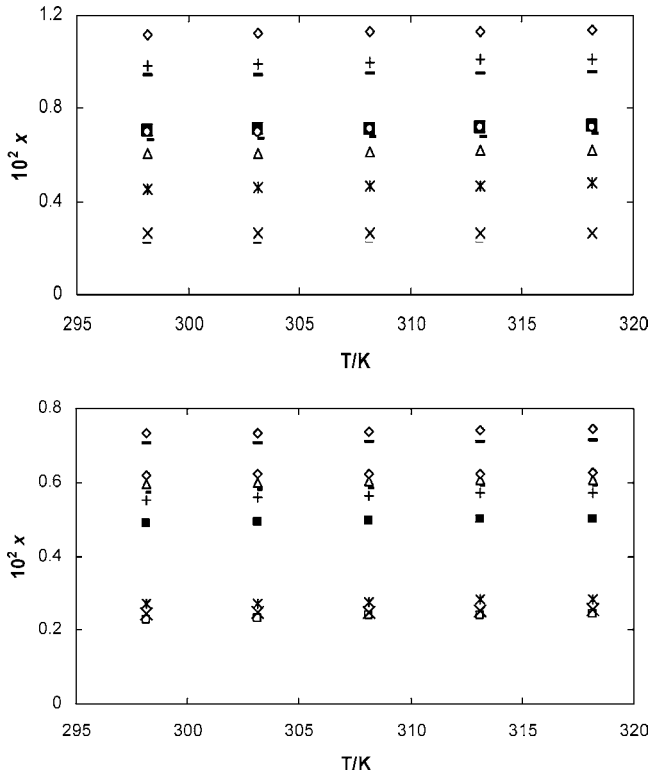

Figure 2. Variation of mole fraction solubilities (x) with temperature (T) for chalcones in DMF and doxane. ×, AKFC-1; □, AKFC-2; △, AKFC-3; solid heart symbol, AKFC-4; *, AKFC-5; ■, AKFC-6; ◆, AKFC-7; −, AKFC-8; —, AKFC-9; ◇, AKFC-10.

Table 4. Constants *A* and *B* of Equation 2, Relative Average Deviations (ARD), and Root Mean Square Deviation (rmsd) of Chalcones in Dioxane

compounds	*A*	*B*	10^8 rmsd	100 ARD
AKFC-1	−5.1726	0.0009	5.4756	0.3021
AKFC-2	−7.1500	0.0036	0.2074	0.0953
AKFC-3	−5.4231	0.001	0.0049	−0.0503
AKFC-4	−6.5298	0.0018	0.0653	0.2419
AKFC-5	−6.6663	0.0025	0.0151	−0.0849
AKFC-6	−5.7471	0.0014	0.0445	−0.1389
AKFC-7	−5.7205	0.0018	1.9829	0.2193
AKFC-8	−5.6472	0.0016	1.1491	−0.1904
AKFC-9	−5.1229	0.0006	2.8099	0.2186
AKFC-10	−5.3468	0.0009	1.8492	0.1950

Table 5. Constants *A* and *B* of Equation 2, Relative Average Deviations (ARD), and Root Mean Square Deviation (rmsd) of Chalcones in DMF

compounds	*A*	*B*	10^8 rmsd	100 ARD
AKFC-1	−4.7889	0.0010	2.2066	0.1269
AKFC-2	−6.6754	0.0021	0.0994	−0.1214
AKFC-3	−5.5320	0.0014	0.6057	−0.1338
AKFC-4	−5.9652	0.0009	0.0053	−0.0110
AKFC-5	−6.3000	0.0030	0.3764	−0.1128
AKFC-6	−5.4004	0.0015	0.0263	0.0505
AKFC-7	−5.1185	0.0017	6.0959	0.2467
AKFC-8	−5.5732	0.0019	1.7756	0.1712
AKFC-9	−4.9301	0.0009	1.3055	0.1054
AKFC-10	−5.5692	0.0020	0.4262	−0.0874

values of these parameters are given in Tables 4 and 5. These values were calculated, and solubilities x_{ci} are also reported in Tables 2 and 3. The experimental solubility values were compared with calculated solubility (x_{ci}).

Further, relative average deviations (ARD) and root-mean-square deviations (rmsd), calculated by eqs 3 and 4, are listed in Tables 4 and 5.

$$\mathrm{ARD} = \frac{1}{N}\sum_{i}^{N}\frac{x_i - x_{ci}}{x_i} \tag{3}$$

$$\mathrm{rmsd} = \left[\sum_{i=1}^{N}\frac{(x_{ci} - x_i)^2}{N-1}\right]^{1/2} \tag{4}$$

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

The relative deviations (RD) between the experimental and calculated values of solubilities are also calculated by eq 5 and are given in Tables 2 and 3.

$$\text{Relative Deviation} = \left(\frac{x - x_{ci}}{x}\right) \tag{5}$$

The heat of solution (ΔH_{sol}) was calculated by the modified van't Hoff equation[21,22]

$$\frac{\partial \ln x}{\partial(1/T - 1/T_{hm})_P} = -\frac{\Delta H_{sol}}{R} \tag{6}$$

where T is the experimental temperature and R is the gas constant. T_{hm} is the mean harmonic temperature which is given as

$$T_{hm} = \frac{n}{\sum_{i}^{n}(1/T)} \tag{7}$$

where n is the number of experimental temperatures.[23] In the present case, the T_{hm} value obtained is only 308 K. The slope of the plot of ln x versus $(1/T - 1/308)$ gives the value of ΔH_{sol}.

The Gibbs energy change for the solubility process was then evaluated from the following relation[21]

$$\Delta G_{sol} = -RT \cdot \text{intercept} \tag{8}$$

Using these evaluated ΔH_{sol} and ΔG_{sol} values, the entropy of solution ΔS_{sol} was obtained from the equation[21,22]

$$\Delta S_{sol} = \frac{\Delta H_{sol} - \Delta G_{sol}}{T_{hm}} \tag{9}$$

All these thermodynamic parameters are given in Tables 6 and 7.

It is evident from Tables 6 and 7 that for all the compounds ΔH_{sol} and ΔG_{sol} values in both the solvents are positive, whereas ΔS_{sol} values are negative. When stronger bonds are broken and weaker bonds are formed, energy is consumed. So, ΔH_{sol} becomes positive.[22] This indicates endothermic dissolution of compounds where the enthalpy term contributes to an unfavorable positive value of ΔG_{sol}. Thus, the positive value of ΔG_{sol}

Table 6. Thermodynamic Parameter Gibb's Free Energy (ΔG_{sol}), Heat of Solution (ΔH_{sol}), and Entropy of Solution (ΔS_{sol}) of the Dissolution of Chalcones in Dioxane

compounds	ΔG / kJ·mol^{-1}	ΔH / kJ·mol^{-1}	$-\Delta S$ / J·mol^{-1}·K^{-1}
AKFC-1	3.0045	0.1601	9.2356
AKFC-2	3.6973	0.6745	9.8146
AKFC-3	3.1288	0.1900	9.5421
AKFC-4	3.6665	0.3310	10.8291
AKFC-5	3.6028	0.4730	10.1622
AKFC-6	3.2484	0.2683	9.6762
AKFC-7	3.1687	0.3552	9.1351
AKFC-8	3.1494	0.3078	9.2262
AKFC-9	3.0282	0.1063	9.4871
AKFC-10	3.1082	0.1382	9.6433

Table 7. Thermodynamic Parameters Gibb's Free Energy (ΔG_{sol}), Heat of Solution (ΔH_{sol}), and Entropy of Solution (ΔS_{sol}) of Dissolution of Chalcones in DMF

	ΔG	ΔH	$-\Delta S$
compounds	kJ·mol^{-1}	kJ·mol^{-1}	J·mol^{-1}·K^{-1}
AKFC-1	2.7451	0.1847	8.3132
AKFC-2	3.6842	0.4007	10.6612
AKFC-3	3.1182	0.2689	9.2513
AKFC-4	3.6330	0.1734	11.7399
AKFC-5	3.6028	0.5698	9.8476
AKFC-6	3.0239	0.2810	8.9061
AKFC-7	2.8190	0.3133	8.1356
AKFC-8	3.0567	0.3517	8.7829
AKFC-9	2.8498	0.1664	8.7126
AKFC-10	3.0287	0.4342	8.4238

indicates that the dissolution process is not spontaneous.[22,23] The negative value of entropy indicates increased order due to the solvation process.

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