Solubilities, Partition Coefficients, Density, and Surface Tension for Imidazoles + Octan-1-ol or + Water or + *n*-Decane[†]

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The solid−liquid equilibrium (SLE) has been measured from 270 K to the melting temperature of the solid for eight binary mixtures of imidazoles (1*H*-imidazole, 2-methyl-1*H*-imidazole, 1,2-dimethylimidazole, benzimidazole, and 2-methylbenzimidazole) with either octan-1-ol or water using a dynamic method. The melting temperature and enthalpy as well as the heat capacity change at the melting temperature were determined using differential scanning calorimetry (DSC). It was observed that the solubility of 1*H*-imidazole, 2-methyl-1*H*-imidazole, and 1,2-dimethylimidazole is much higher in water than in octan-1-ol. The solubility of benzimidazole and 2-methylbenzimidazole is much higher in octan-1-ol. Experimental solubility data were correlated using the Wilson, UNIQUAC ASM, and NRTL 1 models. The solid−solid first-order phase transition has been observed with 2-methyl-1*H*-imidazole, benzimidazole, and 2-methylbenzimidazole. The best description of the experimental solubility data was obtained by the NRTL 1 equation. The average root-mean-square deviation on the equilibrium temperatures obtained with solutions of five imidazoles in octan-1-ol is 2.1 K. The solubility data were used to calculate the octan-1-ol/water partition coefficients as a function of temperature. The surface tension of air/octan-1-ol or air/*n*-decane systems as well as the interfacial tension of octan-1-ol/water or *n*-decane/water were determined as a function of imidazole concentration at 298.15 K and 308.15 K.

Introduction

The use of imidazoles and their derivatives in chemical processes is becoming increasingly important. Derivatives of these strongly polar compounds are widely used in pharmacology. For instance, several ruthenium(III) complexes have been evaluated and used extensively in cancer therapy treatment.[1,2] 1*H*-Imidazole is used as an antimetabolite and as an inhibitor of histamine. The new family of nonvolatile ionic solvents is mainly based on imidazole-derived compounds. However, industrial applications of these new compounds is possible only when their fundamental physical properties are known. This is not the case with imidazoles.

We have begun systematic investigations of the thermodynamic properties and phase equilibria of simple imidazoles. The densities, surface tensions, octan-1-ol/water partition coefficients, and solid−liquid and liquid−liquid equilibria of many binary mixtures are under investigation. Recently, we reported the solubility of imidazoles in a series of *n*-alcohols.[3] In this paper we report the solubility of five imidazoles (1*H*-imidazole, 2-methyl-1*H*-imidazole, 1,2-dimethylimidazole, benzimidazole, and 2-methylbenzimidazole) in octan-1-ol and in water.

The octan-1-ol/water partition coefficients as a function of temperature were determined for 1*H*-imidazole, 2-methyl-1*H*-imidazole, 1,2-dimethylimidazole, benzimidazole, and 2-methylbenzimidazole from solubility data. The surface tension at the liquid/air and the liquid/liquid interface reflects interactions between molecular species present in the solution. In addition, the surface tension is an important parameter controlling the mass transfer between two phases. Surface tension data together with partition coefficient data enable the solute transfer modeling between the aqueous and organic phase. Unfortunately, only a limited body of experimental data is available in the literature. In this paper surface tension and interfacial data of imidazoles in octan-1-ol + water mixtures at 298.15 K and 308.15 K over a wide range of composition are reported.

Experimental Section

Herein are reported origins of the chemicals, Chemical Abstracts Service registry numbers, and the corresponding mass percent purities: octan-1-ol (111-87-5, Aldrich, >99%), *n*-decane (124-18-5, Fluka AG, >99%), 1*H*-imidazole (288-32-4, Koch-Light Laboratory, 99%), 2-methyl-1*H*-imidazole (693-98-1, Koch-Light Laboratory, 99%), 1,2-dimethylimidazole (1739-84-0, Koch-Light Laboratory, 98%), benzimidazole (51-17-2, Koch-Light Laboratory, 98%), and 2-methylbenzimidazole (615-15-6, Koch-Light Laboratory, 98%). All imidazoles were more than 98 mass % pure. Before use they were dried 24 h in a vacuum at the temperature 330 K. Their purity was checked by cryometry in benzene and DSC analysis. All imidazoles (except 1,2-dimethylimidazole) were used as purchased without further purification. Twice distilled and degassed water was used for solubility and surface tension measurements. 1,2-Dimethylimidazole

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[†] Presented at World Chemistry Congress, Brisbane, Australia, July 1−6, 2001.

10.1021/je0103014 CCC: $22.00

Table 1. Physical Constants of Pure Compounds: T_{m1}, Melting Point (This Work); T_{tr1}, Solid−Solid Transition Point; ΔH_{m1}, Molar Heat of Fusion (This Work); ΔH_{tr1}, Molar Heat of Solute−Solute Phase Transition; ΔCp_{m1}, Heat Capacity Change at the Melting Temperature; and $V^{298.15}$, Molar Volume

component	T_{m1} K	T_{tr1} K	ΔH_{m1} kJ·mol^{-1}	ΔH_{tr1} kJ·mol^{-1}	ΔCp_{m1} J·K·mol^{-1}	V_{m1}(298.15 K)^{a} cm^{3}·mol^{-1}
1*H*-imidazole	362.25^{b}		12.820^{c,d}		24.17^{e}	61.6^{f}
2-methyl-1*H*-imidazole	419.00	369.12	12.672^{g}	1.590^{f}	41.05^{e}	76.1^{f}
1,2-dimethylimidazole	311.50		7.930^{g}		12.00^{e}	96.1^{f}
benzimidazole	445.51	384.43	20.472	0.710	49.09	89.2
2-methylbenzimidazole	451.43	383.93	20.486	0.586	50.58	103.7

[a] Calculated by the group contribution method from ref 4. [b] Selected literature value from ref 5 is $T_{m1} = 362.67 \pm 0.05$ K. [c] Selected literature value from ref 5. [d] Other literature values: $\Delta H_{m1} = 11.184$ kJ·mol^{-1} from ref 3; $\Delta H_{m1} = 12.821$ kJ·mol^{-1} from ref 6; $\Delta H_{m1} = 12.50$ kJ·mol^{-1} from ref 7. [e] From ref 3. [f] Improved values compared with ref 3.

was used immediately after fractional distillation, under reduced pressure, because it is a very hygroscopic compound. Octan-1-ol and *n*-decane were fractionally distilled over different drying reagents and their mass fraction purity was better than 0.998 and 0.999, respectively, as was checked by GLC analysis. All products were stored over Union Carbide, 4-Å molecular sieves. Karl-Fisher analysis gave a water content of <0.02 mol %. Physical properties of pure imidazoles are reported in Table 1. The molar enthalpy of fusion was measured using the Pyris 1, differential scanning calorimeter of Perkin-Elmer. Fusion experiments were carried out at the scan rate of 2 K · min^{-1}. The instrument was calibrated against 99.9999 mol % purity indium sample.

Solid−liquid equilibrium (SLE) temperatures were determined using a dynamic method described in detail previously.[8] Samples placed in a thermostated, Pyrex glass cell were heated very slowly (at <2 K h^{-1} near the equilibrium temperature) with continuous stirring. The temperature of the crystal disappearance was detected visually and measured with an electronic thermometer P 500 (DOSTMANN electronic GmbH) with the probe totally immersed in the thermostating liquid. The thermometer was calibrated on the basis of ITS-90. The accuracy of temperature measurements was ±0.01. The error in the mole fraction did not exceed $\delta_{x1} = 0.0002$.

An Anton Paar DMA 602 vibrating-tube densitometer, thermostated at $T = (298.15 \pm 0.01)$ K or (308.15 ± 0.01) K was used to determine the density of pure liquids and that of solutions. The densitometer's calibration was performed at atmospheric pressure using twice distilled and degassed water, high-purity cyclohexane ($\rho^{298.15} = 0.77393$ g·cm^{-3}), and the dry air. The vibrating-tube temperature was measured with an Anton Paar DM 100-30 digital thermometer and was regulated to within ±0.01 K using a UT-2/77 thermostat. Mixtures were prepared by weighing, the error in mole fraction being estimated as $< 5 \times 10^{-5}$.

Surface tension and interfacial tension measurements were made by a Tensiometer KSV Sigma 70 System (Finland) using a Du-Noüy ring taking into account the Zuidema Waters correction. Measurements were performed using the ring method that is widely used[9] since studies of Harkins and Jordan[10] who improved the accuracy and established tables of correction factors based on the Freund and Freund[11] work.

The measurement procedure was as follows: mixtures of n_1 mol of imidazole and 25 cm^{3} of octan-1-ol and 25 cm^{3} of water were mixed in a thermostated tube for 2 to 6 h and then they were kept in the thermostat without mixing for the next 3 to 30 h for separations of the layers; after that the densities of octan-1-ol and water phases were measured; next, the samples to be measured were placed very carefully into the tensiometer vessel. When thermal equilibrium was attained, the sample was equilibrated for the period between 15 min and 3 h depending on the sample. The force acting on the balance was recorded with respect to time. The maximum value of the downward force was used to calculate the surface tension. All measurements were repeated three to five times. The reproducibility of measurements was about ±0.1%.

Solid−Liquid Equilibria

Tables 2 and 3 list the experimental, equilibrium temperature T, the mole fraction of the imidazole x_1, and the corresponding activity coefficient γ_1. The solid−liquid equilibria diagrams of imidazole(1) + octan-1-ol or water (2) are presented in Figures 1−3.

SLE phase diagrams of aqueous systems show mostly positive deviations from ideality. Thus, the solubility is lower than the ideal one and $\gamma_1 > 1$, for 1*H*-imidazole and 1,2-dimethylimidazole, benzimidazole and 2-methylbenzimidazole in water. For 2-methyl-1*H*-imidazole, benzimidazole, and 2-methylbenzimidazole the solubility in octan-1-ol is very close to the ideal solubility. The fact that the solubility of benzimidazole and 2-methylbenzimidazole in water is much smaller than observed with the other three imidazoles may be explained by higher melting temperature and higher enthalpy of melting of these compounds.

The addition of the benz- moiety to the imidazole ring increases the solubility of benzimidazole and 2-methylbenzimidazole in octan-1-ol compared with water.

1,2-Dimethylimidazole is highly hygroscopic, which means that it interacts strongly with water. Indeed, its solubility in water and octan-1-ol is much higher than that of other imidazoles. Both the melting temperature and the enthalpy of melting of this compound being low suggests that the formation of imidazole−imidazole hydrogen bonds is less probable for that imidazole. This facilitates the hydrogen bond formation between the imidazole and the hydroxyl group of alcohol or of water. This hydrogen bond can involve even two molecules of imidazole per one water molecule:

The solubility of a solid compound (1) in a liquid solvent (2) may be expressed as follows:

$$-\ln x_1 = \frac{\Delta H_{m1}}{R}\left(\frac{1}{T} - \frac{1}{T_{m1}}\right) + \frac{\Delta H_{tr1}}{R}\left(\frac{1}{T} - \frac{1}{T_{tr1}}\right) - \frac{\Delta Cp_{m1}}{R}\left(\ln\frac{T}{T_{m1}} + \frac{T_{m1}}{T} - 1\right) + \ln \gamma_1 \quad (1)$$

where x_1, γ_1, ΔH_{m1}, ΔCp_{m1}, T_{m1}, and T stand for mole fraction, activity coefficient, enthalpy of fusion, difference in solute heat capacity between the solid and the liquid at

Table 2. Experimental Solid−Liquid Equilibrium Temperatures, T (Two Crystallographic Phases α and β, Respectively) for {Imidazole(1) + an Octan-1-ol(2)} Systems; γ_1, Experimental Activity Coefficient of Solute

x_1	(T_α or T_β)/K	γ_1	x_1	(T_α or T_β)/K	γ_1	x_1	(T_α or T_β)/K	γ_1
				1*H*-Imidazole				
0.2991	275.05	1.00	0.5748	323.11	1.06	0.9683	357.21	1.00
0.3258	283.52	1.03	0.6859	334.10	1.03	1.0000	362.25	1.00
0.3791	293.62	1.04	0.7914	343.03	1.00			
0.4694	308.04	1.05	0.8708	349.42	1.00			
				2-Methyl-1*H*-imidazole				
0.2483	279.05(β)	0.88	0.3917	325.30(β)	0.99	0.7129	386.68(α)	1.05
0.2581	282.69(β)	0.89	0.4095	330.57(β)	1.01	0.7347	389.04(α)	1.05
0.2677	285.82(β)	0.89	0.4314	335.40(β)	1.01	0.7659	394.39(α)	1.05
0.2787	291.85(β)	0.92	0.4525	338.92(β)	1.01	0.7972	400.06(α)	1.05
0.2902	297.25(β)	0.95	0.4771	345.09(β)	1.02	0.8352	403.29(α)	1.05
0.3034	301.66(β)	0.96	0.5028	350.68(β)	1.03	0.8641	406.74(α)	1.01
0.3200	306.20(β)	0.96	0.5282	357.87(β)	1.07	0.8954	410.22(α)	1.03
0.3357	309.19(β)	0.95	0.5655	367.43(β)	1.11	0.9243	413.49(α)	1.03
0.3467	312.90(β)	0.96	0.5982	369.12(β)	1.06	0.9516	415.62(α)	1.02
0.3621	317.58(β)	0.98	0.6476	378.77(α)	1.08	0.9800	417.38(α)	1.01
0.3748	321.53(β)	0.99	0.6820	384.13(α)	1.08	1.0000	419.00(α)	1.00
				1,2-Dimethylimidazole				
0.5678	277.21	1.22	0.7204	290.60	1.13	0.9045	303.67	1.02
0.5812	278.24	1.20	0.7369	291.97	1.11	0.9190	304.37	1.01
0.5929	279.25	1.19	0.7545	293.33	1.10	0.9339	305.39	1.01
0.6059	280.27	1.18	0.7714	294.92	1.09	0.9559	306.25	0.99
0.6177	281.35	1.17	0.7888	296.39	1.09	0.9668	307.02	0.99
0.6336	282.51	1.16	0.8081	297.37	1.07	0.9830	307.95	0.98
0.6510	284.10	1.15	0.8300	298.88	1.07	0.9927	308.61	0.98
0.6670	285.82	1.14	0.8477	300.24	1.05	1.0000	311.50	1.00
0.6850	287.65	1.13	0.8680	301.31	1.04			
0.7013	288.88	1.13	0.8897	302.72	1.03			
				Benzimidazole				
0.0870	273.00(β)	0.74	0.1297	308.14(β)	0.98	0.1723	328.23(β)	1.05
0.0992	289.23(β)	0.90	0.1355	311.75(β)	1.00	0.1824	332.67(β)	1.07
0.1113	296.33(β)	0.91	0.1482	317.67(β)	1.02	0.1991	339.12(β)	1.09
0.1207	302.32(β)	0.94	0.1588	322.94(β)	1.04	0.2133	343.53(β)	1.10
				2-Methylbenzimidazole				
0.1407	289.49(β)	0.64	0.1724	308.87(β)	0.74	0.2176	328.43(β)	0.81
0.1472	294.43(β)	0.67	0.1818	313.07(β)	0.75	0.2314	333.38(β)	0.83
0.1549	299.32(β)	0.69	0.1927	317.52(β)	0.76	0.2484	339.52(β)	0.85
0.1635	303.68(β)	0.71	0.2044	322.64(β)	0.79			

the melting point, melting point of the solute (compound 1), and equilibrium temperature, respectively. $\Delta H_{\mathrm{tr}1}$ and $T_{\mathrm{tr}1}$ stand for enthalpy of transition and transition temperature of the solute, respectively, and is necessary if the solid−solid-phase transition is observed. The solubility, eq 1, with the solid−solid-phase transition term is used for temperatures below that of the phase transition.[12] This is the case of 2-methyl-1*H*-imidazole, benzimidazole, and 2-methylbenzimidazole. The existence of these transitions associated with small energetic effects was confirmed by DSC measurements.

In this study three methods are used to correlate the solute activity coefficients γ_1. They are based on the Wilson,[13] UNIQUAC ASM,[14] and NRTL 1[15] models describing the excess Gibbs energy. The exact mathematical formulation of these models was given previously.[16]

Model parameters were found by minimization of the objective function Ω using Marquardt's algorithm:[17]

$$\Omega = \sum_{i=1}^{n} [T_i^{\mathrm{exp}} - T_i^{\mathrm{cal}}(x_{1i},P_1,P_2)]^2 \tag{2}$$

where n is the number of experimental points and T_i^{exp} and T_i^{cal} denotes respectively experimental and calculated equilibrium temperature corresponding to the concentration x_{1i}. P_1 and P_2 are model parameters resulting from the minimization procedure. The root−mean−square deviation of temperature was defined as follows:

$$\sigma_{\mathrm{T}} = \left(\sum_{i=1}^{n} \frac{(T_i^{\mathrm{exp}} - T_i^{\mathrm{cal}})^2}{n-2}\right)^{1/2} \tag{3}$$

Parameters r_{i} and q_{i} of the UNIQUAC ASM and NRTL1 models were calculated with the following relationships:[18,19]

$$r_i = 0.029281 V_{\mathrm{m}} \tag{4}$$

$$q_i = \frac{(Z-2)r_i}{Z} + \frac{2(1-l_i)}{Z} \tag{5}$$

where V_{m} is the molar volume of pure component i at 298.15 K. The coordination number Z was assumed to be equal to 10 and the bulk factor l_i was assumed to be equal to 1. The calculations with UNIQUAC ASM and NRTL 1 models necessitate the use of association parameters. These parameters characterizing association at 323.15 K where respectively $K = 12.3$ and $-\Delta h_{\mathrm{h}} = 21.73$ kJ·mol^{-1} for alcohol [20] and $K = 1030$ and $-\Delta h_{\mathrm{h}} = 25.60$ kJ·mol^{-1} for water.[21] The temperature dependence of association constants was calculated from the van't Hoff relation assuming that the enthalpy of hydrogen-bond formation was temperature-independent. Values of model parameters obtain

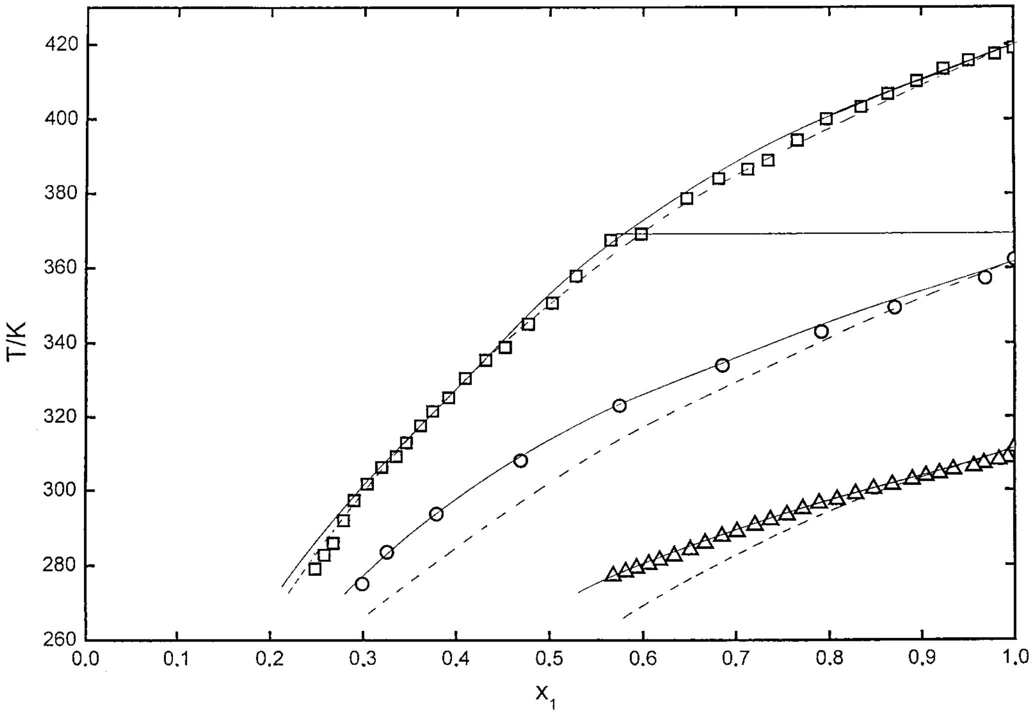

Figure 1. Solid–liquid equilibria diagram for ○, 1*H*-imidazole, or □, 2-methyl-1*H*-imidazole, or △, 1,2-dimethylimidazole(1) + octan-1-ol(2) mixtures. Solid lines, calculated by the NRTL 1 equation; dotted line, ideal solubility.

Table 3. Experimental Solid–Liquid Equilibrium Temperatures, *T* (Two Crystallographic Phases α and β, Respectively) for {Imidazole (1) + Water (2)} Systems; γ_1, Experimental Activity Coefficient of Solute

x_1	$(T_\alpha$ or $T_\beta)$/K	γ_1	x_1	$(T_\alpha$ or $T_\beta)$/K	γ_1	x_1	$(T_\alpha$ or $T_\beta)$/K	γ_1
				1*H*-Imidazole				
0.210	277.70	1.46	0.425	302.49	1.07	0.709	343.03	1.12
0.267	281.71	1.23	0.469	309.22	1.07	0.809	354.20	1.12
0.308	286.90	1.15	0.592	323.70	1.04	1.000	362.25	1.00
0.353	292.29	1.10	0.648	333.49	1.08			
				2-Methyl-1*H*-imidazole				
0.032	274.99(β)	6.46	0.142	306.86(β)	1.94	0.403	334.08(β)	1.07
0.043	281.54(β)	5.24	0.184	311.84(β)	1.90	0.487	343.86(β)	1.00
0.062	290.90(β)	4.10	0.268	320.50(β)	1.37	0.566	357.39(β)	1.00
0.098	299.93(β)	2.91	0.348	327.61(β)	1.15	1.000	419.00(α)	1.00
				1,2-Dimethylimidazole				
0.6295	275.22	1.07	0.7533	292.57	1.09	0.8802	304.94	1.06
0.6503	278.72	1.08	0.7774	294.58	1.08	0.9033	304.03	1.03
0.6728	282.32	1.09	0.7898	295.66	1.08	0.9450	306.80	1.00
0.6974	285.87	1.09	0.8181	300.25	1.09	1.0000	311.50	1.00
0.7198	288.66	1.09	0.8270	298.94	1.06			
0.7253	289.29	1.09	0.8586	301.59	1.05			
				Benzimidazole				
0.0003	274.27(β)	189	0.0017	326.39(β)	99	0.0050	350.67(β)	50
0.0005	287.83(β)	168	0.0025	333.95(β)	76	0.0069	359.88(β)	42
0.0007	304.60(β)	166	0.0035	341.55(β)	69	0.0086	363.34(β)	35
0.0011	317.56(β)	131	0.0040	345.25(β)	57			
				2-Methylbenzimidazole				
0.0005	296.64(β)	208	0.0021	341.17(β)	104	0.0048	363.04(β)	63
0.0007	308.15(β)	173	0.0028	349.53(β)	90	0.0056	366.43(β)	57
0.0011	321.17(β)	145	0.0035	354.71(β)	77			
0.0016	333.56(β)	122	0.0042	359.64(β)	69			

by fitting solubility curves are given in Table 4 together with corresponding standard deviations.

The best representation of solid–liquid equilibrium data for octan-1-ol was obtained using the NRTL 1 equation assuming association of an alcohol with the resulting standard deviation $\sigma_T = 2.12$ K. The results obtained with solubility data of imidazoles in octan-1-ol obtained with three models are similar. However, in the case of aqueous solutions results yielded by the Wilson model are much better.

Octan-1-ol/Water Partitioning

The partition coefficient, *P*, of organic compounds in the octan-1-ol/water system is used for the assessment of bioaccumulation potential and the distribution pattern of drugs and pollutants. The partition coefficient of imidazoles, which are of great pharmaceutical concern, strongly depends on a hydrogen bond formed by these molecules and is less than one for simple imidazoles, due to the high solubility in water. Generally, the hydrophobicity is favor-

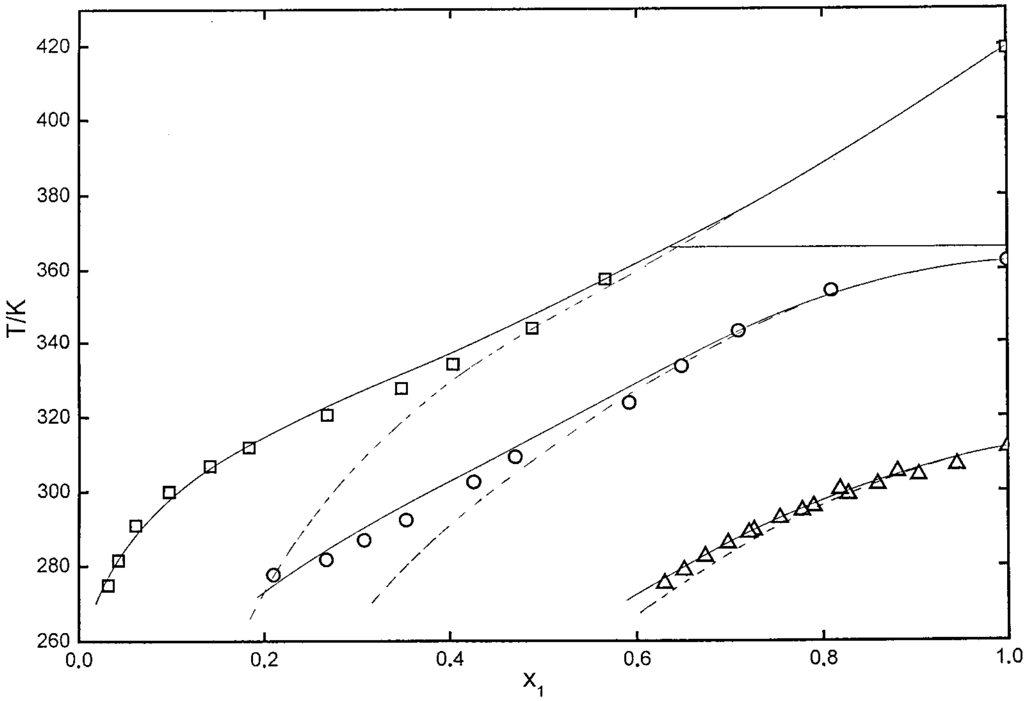

Figure 2. Solid−liquid equilibria diagram for ○, 1*H*-imidazole, or □, 2-methyl-1*H*-imidazole, or △, 1,2-dimethylimidazole(1) + water(2) mixtures. Solid lines, calculated by the Wilson equation; dotted line, ideal solubility.

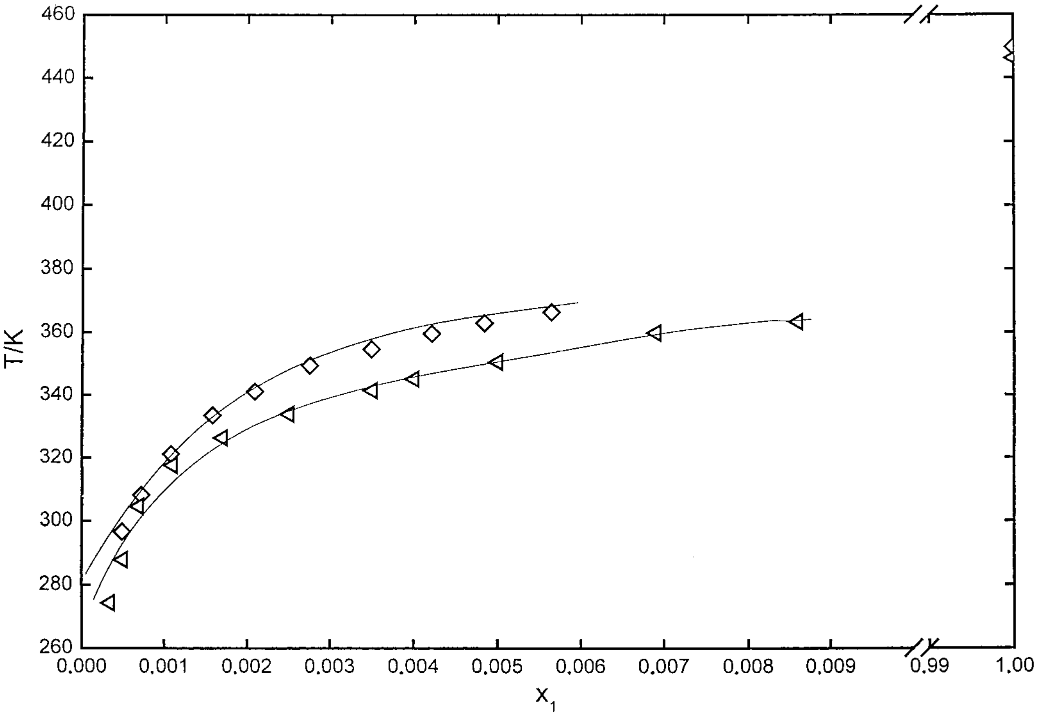

Figure 3. Solubility of △, benzimidazole, or ◇, 2-methylbenzimidazole(1) in water.

able for the bioaccumulation or the bioconcentration of organic compounds.[22] Therefore, the low value of the octan-1-ol/water partition coefficient is required for new insecticides to avoid bioaccumulation.

Due to the high solubility of imidazoles, we have used a simple, synthetic, visual method. The experimental results are reported in Table 5. It is evident from this table that the low aqueous solubility of octan-1-ol has a negligible influence on the aqueous solubility of imidazoles. On the other hand, the rather large amount of water present in the octan-1-ol phase ($x_w = 0.27$) changes considerably the imidazole solubility in the octan-1-ol phase. Corresponding values of the imidazole solubility are given in Table 5. It may be observed that the difference of the molar concentration of imidazoles in pure octan-1-ol (c_1^o) and in water-saturated octan-1-ol (c_1^{o*}) is about 10−25%. These important differences are in disagreement with values of the partition coefficient observed at infinite dilution conditions. Indeed, the water influence is negligible in this case. The solubility is changed with the composition of binary solvent (solute-free mole fraction) and agree well with the experimental value, obtained from the measured solubility in the mutually saturated solvents.

Table 4. Correlation of the Solubility Data, SLE, of {Imidazole(1) + an Octan-1-ol, or Water(2)} by Means of the Wilson, UNIQUAC ASM, and NRTL 1 Equations: Values of Parameters and Measures of Deviations

	parameters			deviations		
	Wilson $g_{12}-g_{11}$ $g_{12}-g_{22}$	UNIQUAC ASM Δu_{12} Δu_{21}	NRTL 1[a] Δg_{12} Δg_{21}	Wilson σ_T[b]	UNIQUAC ASM σ_T[b]	NRTL 1 σ_T[b]
solvent	J·mol^{-1}	J·mol^{-1}	J·mol^{-1}	K	K	K
			1*H*-Imidazole			
octan-1-ol	200.80	662.44	313.27	1.91	2.05	2.07
	2063.03	−730.89	−341.78			
water	977.86			4.67		
	1787.19					
			2-Methyl-1*H*-imidazole			
octan-1-ol	5047.70	−142.62	−80780.64	7.71	6.38	5.69
	132734	2798.68	5200.62			
water	3790.11			3.90		
	2680.07					
			1,2-Dimethylimidazole			
octan-1-ol	75.98	799.10	878.80	0.76	1.46	1.50
	3119.12	−930.46	−1095.22			
water	−6131.07	3568.14		0.69	2.95	
	10431.10	−4599.65				
			Benzimidazole			
octan-1-ol	−1299.87	−2722.26	−6037.12	4.16	1.04	1.00
	51844.46	4780.79	5185.43			
water	7731.62			3.31		
	5499.94					
			2-Methylbenzimidazole			
octan-1-ol	4719.77	−2088.62	−4834.40	0.35	0.35	0.35
	−3881.84	2036.44	2178.31			
water	7538.41			0.77		
	7080.12					

[a] Calculated with the third nonrandomness parameter α = 0.3. [b] According to eq 3 from the text.

Table 5. Solubilities in Pure Octan-1-ol, $c_1^{\rm o}$, and Water, $c_1^{\rm w}$, and Corrected Solubilities for the Solvent−Water Mutual Saturation, $(c_1^{\rm o})^*$, $(c_1^{\rm w})^*$; Experimental Partition Coefficient, log *P*, and Calculated from eq 7 at 298.15 K and 308. 15 K

substance	$(c_1^{\rm o})^a$ mol·dm^{-3}	$(c_1^{\rm w})^b$ mol·dm^{-3}	$(c_1^{\rm o})^*$ mol·dm^{-3}	$(c_1^{\rm w})^*$ mol·dm^{-3}	log *P*	(log *P**)[c]	log $P^{\rm lit}$
			298.15 K				
1*H*-imidazole	3.3920	11.1809	5.42	11.02	−0.308	−0.636	−0.3[d] −0.08[e]
2-methyl-1*H*-imidazole	2.1880	3.9050	2.60	3.85	−0.170	−0.014	
1,2-dimethylimidazole	7.6060	9.9880	8.21	9.92	−0.082	−0.273	
benzimidazole	0.6819	0.0303	0.51	0.03	1.228	1.530	1.2[f] 1.5[g]
2-methylbenzimidazole	1.0024	0.0282	0.77	0.027	1.455	1.633	1.43[h]
			308. 15 K				
1*H*-imidazole	4.1270	12.023	6.30	11.98	−0.279	−0.608	
2-methyl-1*H*-imidazole	2.4770	5.736	3.30	5.71	−0.238	−0.398	
1,2-dimethylimidazole	10.244	10.264	10.24	10.26	−0.0008	−0.220	
benzimidazole	0.8613	0.0423	0.70	0.042	1.220	1.450	
2-methylbenzimidazole	1.1465	0.0396	0.90	0.039	1.360	1.646	

[a] Was calculated using the density of octan-1-ol, 0.82260 (298.15 K) and 0.81552 (308.15 K). [b] Was calculated using the density of water, 0.99741 (298.15 K) and 0.99382 (308.15 K). The density of subcooled solute at 308.15 K was assumed to be 0.3% smaller than that in 298.15 K. [c] Calculated from eq 6 with corrected values of $c_1^{\rm w}$* and $\gamma_1^{\rm o}$* for mutual saturation. [d] From ref 23. [e] From ref 24. [f] From ref 25. [g] From ref 26. [h] From ref 27.

As is shown in Table 5, the solute partition coefficient, defined as $P = c_1^{\rm o*}/c_1^{\rm w*}$, of 1*H*-imidazole, 2-methyl-1*H*-imidazole, and 1,2-dimethylimidazole is <1. The bioconcentration of imidazoles can be increased by introducing in the molecule hydrophobic moieties. Indeed, the octan-1-ol/water partition coefficient, is used to evaluate the hydrophobicity of a products in environmental science and in pharmacology. The influence of temperature is shown in Figure 4, where the partition coefficient is presented as a function of the solute entropy of melting.

Miller et al.[28] proposed to calculate the partition coefficient from solubility data in the following way,

$$\log P = \log\left(\frac{1}{c_1^{\rm w}}\right) - \frac{\Delta H_{\rm m1}}{2.3R}\left(\frac{1}{T} - \frac{1}{T_{\rm m1}}\right) + \frac{\Delta Cp_{\rm m1}}{2.3R}\left[\left(\frac{T_{\rm m1}}{T} - 1\right) - \ln\left(\frac{T_{\rm m1}}{T}\right)\right] - \log \gamma_1^{\rm o} V_{\rm m}^{\rm o} \quad (6)$$

where $\gamma_1^{\rm o}$ is the solute mole fraction activity coefficient in

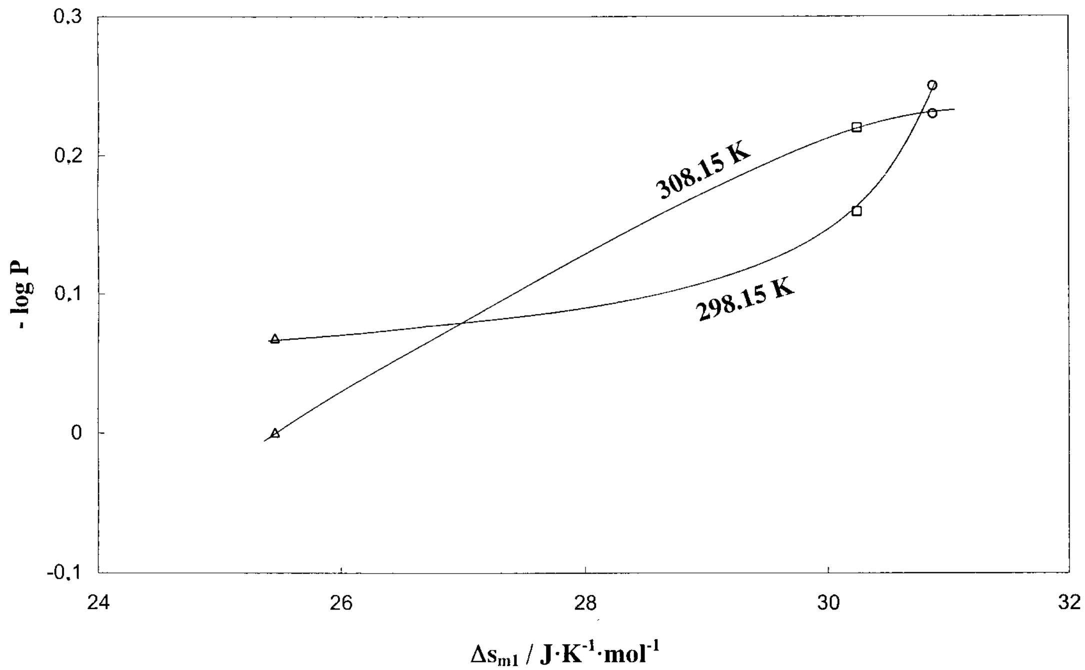

Figure 4. Log *P* as a function of the solute melting entropy for ○, 1*H*-imidazole, or □, 2-methyl-1*H*-imidazole, or ◇, 1,2-dimethylimidazole.

Table 6. Densities of Pure Substances, ρ; Surface Tension Air/Solvent, σ, at 298.15 K and 308.15 K

	298.15 K		308.15 K	
	ρ	σ^a	ρ	σ^a
substances	$\rho\cdot\mathrm{cm}^{-3}$	$\mathrm{mN\cdot m^{-1}}$	$\rho\cdot\mathrm{cm}^{-3}$	$\mathrm{mN\cdot m^{-1}}$
octan-1-ol	0.82260^b	26.73	0.81552^b	26.35
water	0.99741^c	71.94^d	0.99382^c	71.59
water*^{e}	0.99627	33.17	0.994113	32.36
n-decane	0.72576^f	23.39^g	0.71872	22.43

[a] Measured with the error ±0.3 ÷ 0.5 mN·m^{-1}. [b] Agrees with ref 29. [c] Density of water: $\rho^{297.11} = 0.99742$ g·cm^{-3}, $\rho^{299.09} = 0.99692$ g·cm^{-3}, $\rho^{307.79} = 0.99430$ g·cm^{-3}, $\rho^{310.0.39} = 0.99340$ g·cm^{-3} from ref 30. [d] $\sigma^{298.15}(\mathrm{H_2O}) = 72.04 \pm 0.6$ mN·m^{-1} from ref 31. [e] Water saturated with octan-1-ol. [f] Density of *n*-decane $\rho^{298.15} = 0.72625$ g·cm^{-3} from ref 32. [g] $\sigma^{298.15}(n\text{-decane}) = 23.6 \pm 0.5$ mN·m^{-1} from ref 31.

octan-1-ol (from Table 1) and $V_\mathrm{m}^\mathrm{o} = 0.1585$ dm^3·mol^{-1} is the molar volume of octan-1-ol at $T = 298.15$ K. As was stated above, the values of γ_1^o are strongly dependent on the water amount dissolved in octan-1-ol.

Surface Tension Measurements

The surface tension, σ, of imidazole solutions in octan-1-ol and in *n*-decane was measured as well as the surface tension of the same but water-saturated solutions. Results are reported in Table 6. Moreover, the interface tension, σ', at the interface (octan-1-ol or *n*-decane + water) was determined as a function of imidazole concentration. Measurements were performed at two temperatures, 298.15 K and 308.15 K, in the case of 1*H*-imidazole solutions. Densities of both phases, necessary for a precise determination of the surface tension, were measured as well. *n*-Decane represents solvent which does not dissolve imidazoles and water, which results in enhancing 10 times the interface tension, σ', between *n*-decane and octan-1-ol. The results are presented in Tables 7−10 and in Figure 5. As is shown in Figure 5b, The air/*n*-decane surface tension is not sensitive to the presence of the 1*H*-imidazole in the solution. It is a result of minimal solubilities of imidazoles in *n*-decane and water (with dissolved imidazoles) in *n*-decane; thus, aggregates of imidazoles are not present at the surface. In the case of octan-1-ol/water mixtures the increase of σ with concentration of imidazoles is observed with three imidazoles studied. Thus, the imidazole molecules are present at the surface.

In the concentration range covered by the experiment surface tension of three imidazoles on the octan-1-ol/water phase can be expressed with the linear relationship

$$\sigma = A + Bx_1 \tag{7}$$

Experimental data of 1*H*-imidazole, 2-methyl-1*H*-imidazole, and 2-methylbenzimidazole at 298.15 K and the corresponding correlation are presented in Figure 6. Parameters A and B of eq 7 are reported in Table 11. The influence of the temperature on the surface tension is more significant in the case of pure solvents than in the case of imidazole solutions. This effect is especially clear with the system 1*H*-imidazole + octan-1-ol/water. The interfacial tension, σ', in octan-1-ol/water mixtures shows a characteristic maximum for a certain concentration of imidazole (see Figure 7a,c). The influence of imidazole on the interfacial tension depends on the nature of imidazole substitutents and decreases in the following order:

1*H*-imidazole > 2-methyl-1*H*-imidazole >
2-methylbenzimidazole

The solubilities and the strength of specific interactions of imidazoles decreases in the same order. The opposite order was observed in the case of air/octan-1-ol surface tension.

Conclusions

Results presented in this paper indicate that physical and phase properties of imidazoles are controlled by the strength of specific interactions. The competition between

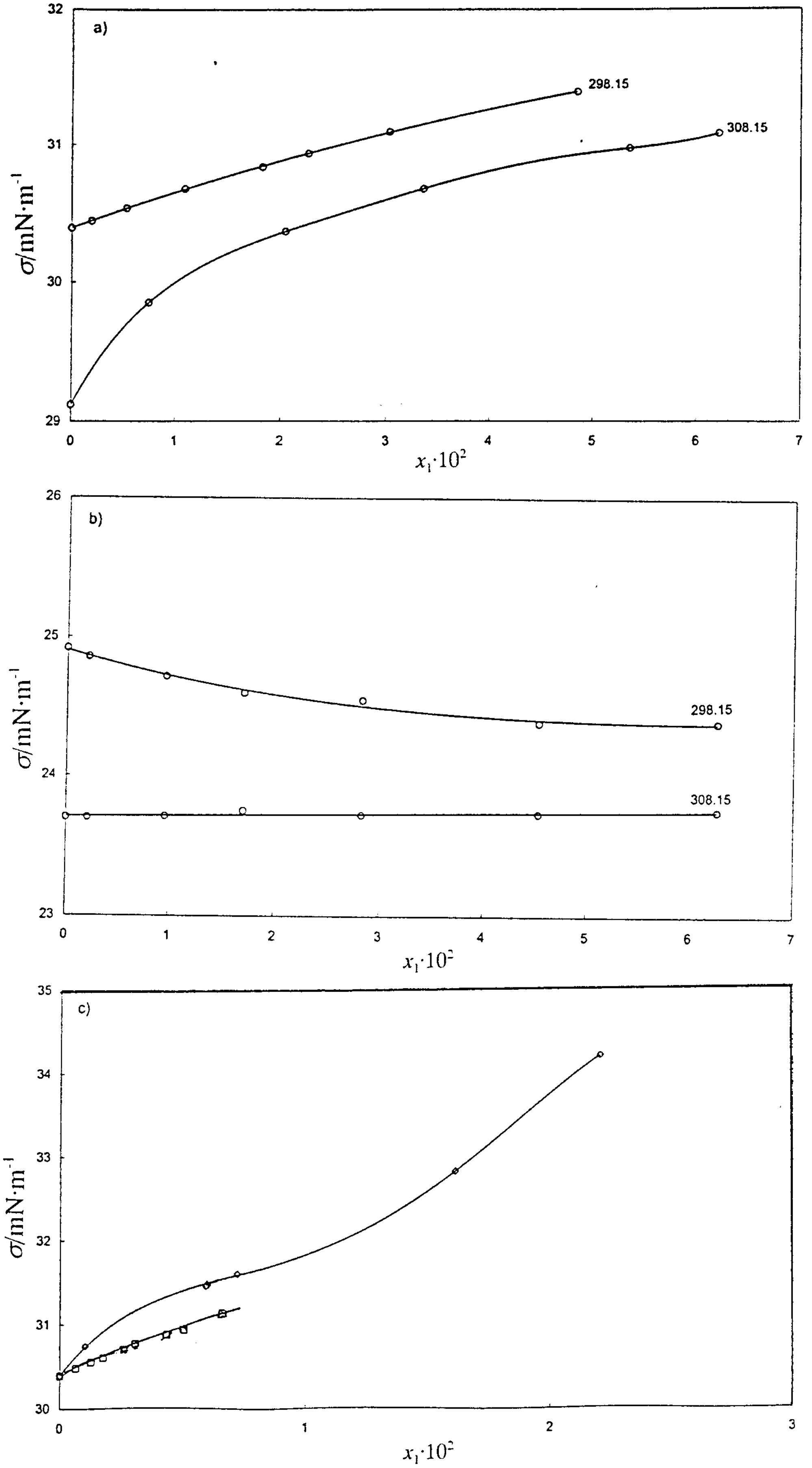

Figure 5. Surface tension, σ, as a function of summary imidazole mole fraction, x_1: (a) 1*H*-imidazole + octan-1-ol/water at 298.15 K and 308.15 K; (b) 1*H*-imidazole + *n*-decane/water at 298.15 K and 308.15 K; (c) □, 2-methyl-1*H*-imidazole; ◇, 2-methylbenzimidazole at 298.15 K. Solid lines, calculated by the polynomial of second to fifth degree.

Table 7. 1*H*-Imidazole Mole Fraction, x_1, in Binary Phases; Densities of Two Phases, Octan-1-ol, ρ^o, and Water, ρ^w; Surface Tension of Air/Octan-1-ol Mixture, σ; Interface Tension of Octan-1-ol/Water Mixture, σ', at 298.15 K and 308.15 K

$n_1 \times 10^2$ mol	$x_1 \times 10^2$	ρ^o $\rho\cdot cm^{-3}$	ρ^w $\rho\cdot cm^{-3}$	σ $mN\cdot m^{-1}$	σ' $mN\cdot m^{-1}$
		298.15 K			
0	0	0.82876	0.99627	30.39	0.80
0.3005	0.1946	0.82985	0.99787	30.44	1.25
0.8270	0.5337	0.83152	0.99872	30.53	1.55
1.704	1.093	0.83439	1.00037	30.67	1.99
2.870	1.828	0.83808	1.00237	30.83	2.26
3.571	2.264	0.84023	1.00359	30.93	2.38
4.823	3.034	0.84393	1.00557	31.09	2.51
7.853	4.848	0.85214	1.01052	31.39	2.21
		308.15 K			
0	0	0.822082	0.994113	29.12	1.53
1.164	0.7495	0.82590	0.99638	29.85	2.03
3.223	2.048	0.83454	0.99981	30.36	2.50
5.365	3.364	0.83914	1.00336	30.67	2.84
8.725	5.358	0.84749	1.008072	30.97	3.10
10.216	6.217	0.85117	1.01037	31.08	2.47

Table 8. 1*H*-Imidazole Mole Fraction, x_1, in Binary Phases; Densities of Two Phases, *n*-Decane, ρ^d, and Water, ρ^w; Surface Tension of Air/*n*-Decane Mixture, σ, and Interface Tension of *n*-Decane/Water Mixture, σ', at 298.15 K and 308.15 K

$n_1 \times 10^2$ mol	$x_1 \times 10^2$	ρ^d $\rho\cdot cm^{-3}$	ρ^w $\rho\cdot cm^{-3}$	σ $mN\cdot m^{-1}$	σ' $mN\cdot m^{-1}$
		298.15 K			
0	0	0.72578	0.99742	24.92	34.42
0.3205	0.2115	0.72578	0.99840	24.86	33.10
1.466	0.9607	0.72580	1.0021	24.72	27.80
2.625	1.706	0.72580	1.00545	24.60	25.15
4.395	2.825	0.72580	1.01027	24.55	23.20
7.180	4.535	0.72579	1.01715	24.39	21.60
10.106	6.265	0.72578	1.02317	24.39	20.30
		308.15 K			
0	0	0.71872	0.99386	23.70	28.52
0.3205	0.2115	0.71872	0.99548	23.70	25.90
1.466	0.9607	0.71872	0.99881	23.71	21.40
2.625	1.706	0.71872	1.00201	23.75	20.16
4.395	2.825	0.71872	1.00651	23.72	19.40
7.180	4.535	0.71872	1.01250	23.73	19.15
10.106	6.265	0.71872	1.01806	23.75	19.10

Table 9. 2-Methyl-1*H*-imidazole Mole Fraction, x_1, in Binary Phases; Densities of Two Phases, Octan-1-ol, ρ^o, and Water, ρ^w; Surface Tension of Air/Octan-1-ol Mixture, σ; Interface Tension of Octan-1-ol/Water Mixture, σ', at 298.15 K

$n_1 \times 10^2$ mol	$x_1 \times 10^2$	ρ^o $\rho\cdot cm^{-3}$	ρ^w $\rho\cdot cm^{-3}$	σ $mN\cdot m^{-1}$	σ' $mN\cdot m^{-1}$
0	0	0.82876	0.99627	30.39	0.80
0.1057	0.068	0.82929	0.99736	30.48	1.32
0.2035	0.132	0.82975	0.99738	30.55	1.64
0.2829	0.183	0.82995	0.99743	30.60	1.92
0.4120	0.267	0.83073	0.99760	30.69	2.15
0.4892	0.316	0.83089	0.99762	30.76	2.20
0.6865	0.443	0.83174	0.99762	30.87	2.29
0.7942	0.512	0.83213	0.99762	30.93	2.41
1.036	0.668	0.83296	0.99765	31.07	2.23

Table 10. 2-Methylbenzimidazole Mole Fraction, x_1, in Binary Phases; Densities of Two Phases, Octan-1-ol, ρ^o, and Water, ρ^w; Surface Tension of Air/Octan-1-ol Mixture, σ; Interface Tension of Octan-1-ol/Water Mixture, σ', at 298.15 K

$n_1 \times 10^2$ mol	$x_1 \times 10^2$	ρ^o $\rho\cdot cm^{-3}$	ρ^w $\rho\cdot cm^{-3}$	σ $mN\cdot m^{-1}$	σ' $mN\cdot m^{-1}$
0	0	0.82876	0.99627	30.39	0.80
0.1670	0.1082	0.83088	0.99733	30.74	1.05
0.9325	0.6014	0.84190	0.99735	31.46	1.51
1.130	0.7281	0.84455	0.99735	31.60	1.50
2.525	1.612	0.86121	0.99759	32.82	1.35
3.479	2.208	0.87286	0.99772	34.20	1.14

Table 11. Coefficients of Eq 7 and Average Quadratic Deviation for Imidazoles in Octan-1-ol at 298.15 K

substance	A	$B \times 10^2$	$R^2 \times 10^2$
1*H*-imidazole	30.39	21.99	98.71
2-methyl-1*H*-imidazole	30.39	109.74	99.34
2-methylbenzimidazole	30.39	165.83	98.85

autoassociation of imidazole molecules and the co-association with solvent molecules is an important factor determining phase behavior of imidazoles.

Results of partition coefficients reported in this paper indicate that simple imidazoles show a weak affinity toward bioaccumulation. This feature can be modified by increasing the imidazole hydrophobicity by suitable sub-

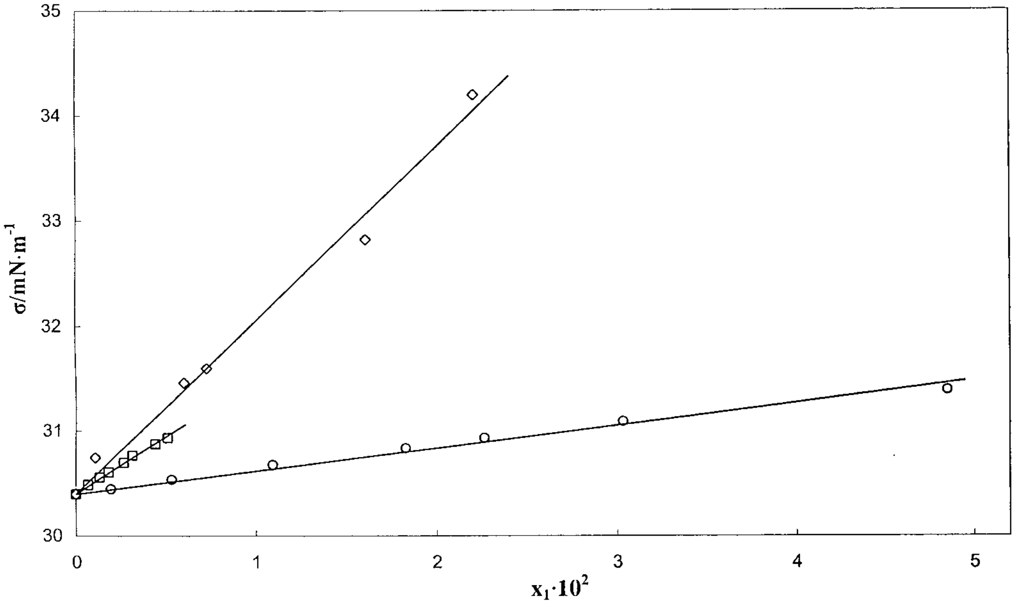

Figure 6. Surface tension, σ, as a function of the summary imidazole mole fraction, x_1: ○, 1*H*-imidazole, or □, 2-methyl-1*H*-imidazole, or ◇, 2-methylbenzimidazole in octan-1-ol at 298.15 K. Solid lines, calculated by eq 7.

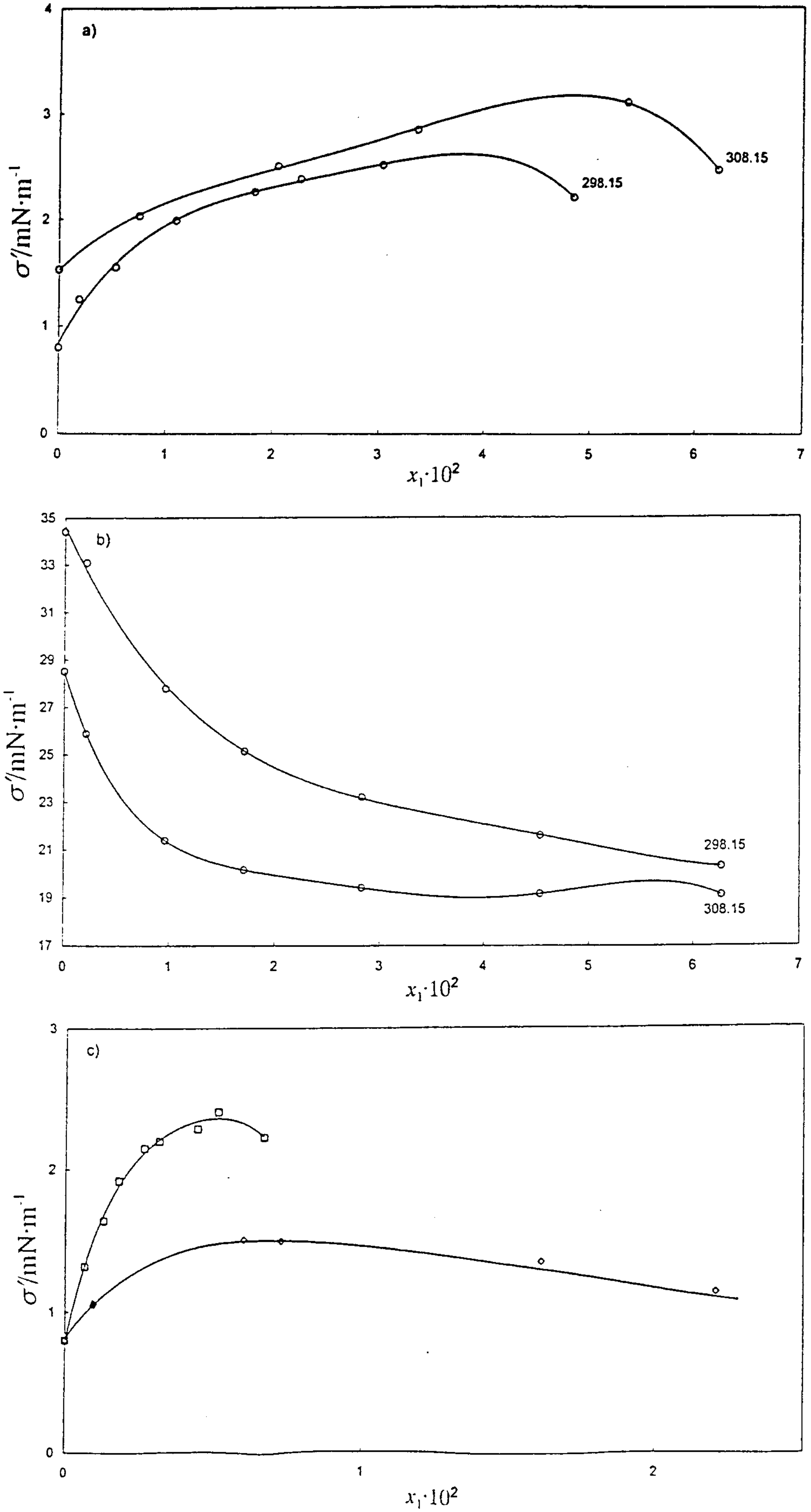

Figure 7. Interface tension, σ', as a function of summary imidazole mole fraction, x_1: (a) 1*H*-imidazole + octan-1-ol/water at 298.15 K and 308.15 K; (b) 1*H*-imidazole + *n*-decane/water at 298.15 K and 308.15 K; (c) □, 2-methyl-1*H*-imidazole, or ◇, 2-methylbenzimidazole at 298.15 K. Solid lines, calculated by the polynomial of second to fifth degree.

stitutents. Benzimidazoles show higher solubility in octan-1-ol than in water and positive values of the partition coefficients.

Our results, obtained with simple imidazoles, may be useful for predicting physical and phase properties of more complex compounds, synthesized on a base of imidazole.

Acknowledgment

The authors gratefully acknowledge Mrs T. Książczak for some DSC measurements.

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Received for review November 14, 2001. Accepted January 22, 2002.

JE0103014