Calculation of Aqueous Solubility of Organic Compounds

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The aqueous solubility of 14 organic solutes has been calculated from their octanol/water partition eoefficient and from their solute activity coefficient in octanol at infinite dilution. The solute activity coefficients were calculated from the Flory-Huggins and Hildebrand-Scatchard (FH-HS) equations and were found to be in good agreement with the activity coefficients determined from GC specific retention volume measurements. The calculated solubilities were in good agreement with the experimental solubilities.

Key words: activity coefficients, gas chromatography, octanol/water partition eoefficients, solubility parameters.

1. Introduction

The octanol/water partition coefficient, $K_{o/w}$, and the aqueous solubility, C^s, of organie compounds have been used widely to assess and prediet the fate of toxic substances in the marine environment. Both of these quantities have been successfully correlated with environmental partitioning phenomenon such as bioconcentration and sorption. These two quantities are thermodynamically related via eq (1) [1].[1]

$$K_{o/w} = \frac{\gamma_\phi^w}{\gamma_\phi^o} \tag{1}$$

where γ_ϕ^w and γ_ϕ^o are the activity coefficients at infinite dilution based on volume fraction for the solute in water and in n-octanol, respectively. The quantity, γ_ϕ^w, is generally defined as the reciprocal of the volume fraction of the solute in water, i.e. $\frac{1}{\phi}$, and is expressed as the reciprocal of the solute concentration in water (C^s) times the molar volume of the solute (V), $1/C^sV$.

Hansch, Quinlan, and Lawrence [2] have developed a method for estimating $K_{o/w}$ based on the additivity principle of thermodynamic properties. On this basis group contributions to $\log K_{o/w}$ or Π values are defined by eq (2).

$$\Pi_x = \log K_{o/w}(x) - \log K_{o/w}(h) \tag{2}$$

where $K_{o/w}(x)$ is the partition coefficient of a derivative and $K_{o/w}(h)$ is that of the parent molecule. Despite evidenee that

Π values are often not additive, usually for steric reasons but sometimes through electronic and hydrogen bonding effects, there are many series of compounds in which Π appears to be invariant.

Equations (1) and (2) suggest that the aqueous solubility, C^s, may be calculated from the molecular structure of the solute provided γ_ϕ^o can be estimated with some degree of accuracy. There are methods [3] available for calculating γ_ϕ^o from the solute physical properties. Because of the simplicity of the calculations, the Flory-Huggins and Hildebrand-Scatchard (FH-HS) method was chosen to evaluate γ_ϕ^o.

According to solution theories [4], the solute activity coefficient (γ_x) based on mole fraction consists of an athermal term and a thermal term. At infinite dilution, in terms of the Flory-Huggins equation for the athermal term and the Hildebrand-Scatchard equation for the thermal term, this may be expressed [5] as

$$ln\gamma_x^\infty = ln\frac{1}{r} + \left(1 - \frac{1}{r}\right) + \frac{V}{RT}(\delta' - \delta)^2 \tag{3}$$

where r is the ratio of the molar volume of the solvent V' to that of the solute V, $\left(\frac{V'}{V}\right)$, and the δ and δ' are, respectively, the solute and solvent solubility parameters. These are defined [6] as

$$\delta = \left(\frac{\Delta E_v}{V}\right)^{1/2} = \left(\frac{\Delta H_v - RT}{V}\right)^{1/2} \tag{4}$$

where ΔE_v and ΔH_v are, respectively, the molar energy and enthalpy of vaporization. At infinite dilution the volume fraction activity coefficient (γ_ϕ^∞) may be expressed in terms of

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[1]Figures in brackets indicate literature references at the eud of this paper.

mole fraction activity coefficient (γ_x^∞) by the following equation [5, 7].

$$\gamma_\phi^\infty = \gamma_x^\infty \left(\frac{V'}{V}\right) \qquad (5)$$

Now combining eq (3) and (5), the solute activity coefficient γ_ϕ^∞ may be expressed as

$$ln\gamma_\phi^\infty = \left(1 - \frac{1}{r}\right) + \frac{V}{RT}(\delta' - \delta)^2 \qquad (6)$$

In this paper we are concerned with estimating the solute activity coefficients in water, γ_ϕ^w, using eq 1, from the estimated values of γ_ϕ^o and the experimental values of $K_{o/w}$. Activity coefficients, γ_ϕ^∞, in octanol for a number of solutes have also been calculated from the Flory-Huggins and Hildebrand-Scatchard equations and compared with the experimental values obtained by the gas chromatographic (GC) method.

2. Experimental Procedure

The stationary phase, n-octanol, used in this study was obtained from the Aldrich Chemical Company. The purity was checked by GC and was found to be 99 + mole %. The stationary phase was coated onto the support material, Chromosorb W-HP, 100/120 mesh, and the weight percent of coating was determined by an ashing method [8]. A stainless steel column (1/8 in OD) was then packed with a known amount of the coated support and was connected to a Hewlett-Packard 5830A[2] gas chromatograph equipped with a flame ionization detector (FID) for the determination of the solute retention time. The temperature of the column was controlled by circulating water through a copper tubing jacket around the column and by a Haake Model FK temperature regulator which regulated the water temperature to 25.0 ± 0.05 °C.

The column inlet pressure, measured with a precalibrated pressure gauge (range 0–15 PSI), was kept constant during a run by regulating with a precision valve. In order to measure the carrier gas flow rate the column was disconnected from the FID, just before and after the experiment, and a soap bubble flowmeter was connected to the column outlet. The carrier gas was presaturated with n-octanol in order to reduce bleeding of the stationary phase.

Since the retention times decreased as the experiment progressed due to column loss of the n-octanol, toluene was used as a reference retention time standard and injected with each

solute. The measured retention times were then corrected for bleeding using the reference solute retention time.

The solute specific retention volumes (V_g^o) were calculated by using the following equation [9].

$$V_g^o = \frac{t_R \cdot F}{w} \cdot \frac{P_a - P_w}{P_a} \cdot \frac{273.2}{T_a} \cdot \frac{3}{2} \cdot \frac{(P_i/P_a)^2 - 1}{(P_i/P_a)^3 - 1} \qquad (7)$$

where t_R is the retention time (min), F is the carrier gas flow rate (ml/min), P_i and P_a are the column inlet and atmospheric pressure (in Torr), P_w is the saturated water vapor pressure (in Torr) at room temperature T_a(°K), and W is the weight (in gram) of stationary phase packed in the column. The reported specific retention volumes listed in column 1 of table 1 are an average of 6 measurements.

3. Results and discussion

The solute activity coefficients at infinite dilution (γ_x^∞) were determined from the following equation [8].

$$ln\gamma_x^\infty = ln \frac{273.2R}{P^oV_g^o M'} - \frac{P^oB}{RT} \qquad (8)$$

where M' is the molecular weight of stationary phase, n-octanol, (g/mole), P^o and B are, respectively, the vapor pressure (in Torr) and the gas phase second virial coefficient (ml/mole) of the pure solute at temperature T(°K), and R is the gas constant. The second virial coefficients were calculated from the McGlashan and Potter equation [10] using the constants tabulated by Dreisbach [11, 12, 13] and Timmermans [14]. These sources were also used for Antoine constants to calculate values of P^o and for constants for the law of rectilinear diamcters to compute values of molar volumes. The solute mole fraction and volume fraction activity coefficients listed in table 1 were calculated using equations 8 and 5. It is estimated that the probable uncertainty in the activity coefficients listed in table 1 is about 2 %.

The solute solubility parameters, δ, listed in table 1 were calculated from their molar enthalpies of vaporization listed in the Dreisbach compilations [11, 12, 13]; whereas the solvent solubility parameter, δ' was treated as an adjustable parameter. In order to fit the experimental data of the systems studied, two different solubility parameters (δ') were used, one for aromatic solutes (δ' = 6.71) and another for aliphatic solutes (δ' = 9.57). The solute activity coefficients calculated using equation 6 are listed in column 5 of table 1. The agreement between the two sets of data (calculated and experimental activity coefficients) is in general good. The average deviation is 8.7%; however, in a few systems it is as high as 18%. These results suggest that the activity coefficient of a system may be calculated from the knowledge of their

Solute	V_g^0 (ml/g)	γ_x^∞	γ_ϕ (expt)	δ^a (cal/cm³)$^{1/2}$	γ_ϕ (calc)	$\dfrac{\gamma_\phi^\infty(\text{expt}) - \gamma_\phi^\infty(\text{calc})}{\gamma_\phi^\infty(\text{expt})} \times 100$
n-Pentane	100.6	2.62	3.59	7.17	4.04	− 12.5
n-Hexane	312.5	2.81	3.39	7.33	3.61	− 6.5
n-Heptane	943.0	3.06	3.29	7.47	3.21	2.4
n-Octane	2793.	3.36	3.25	7.55	2.99	8.0
1-Hexene	280.5	2.54	3.19	7.38	3.40	6.6
1-Heptene	—	—	—	7.53	3.01	—
1-Octene	2518.	3.00	3.01	7.61	2.79	7.3
1-Nonene	7589.	3.24	2.95	7.73	2.45	16.9
Benzene	669.9	2.07	3.67	9.20	3.94	− 7.4
Toluene	2120.	2.18	3.23	8.91	3.32	− 2.8
Ethylbenzene	5542.	2.49	3.20	8.79	3.07	4.1
o-Xylene	8317.	2.38	3.12	8.99	3.67	− 17.6
m-Xylene	6763.	2.34	3.00	8.82	3.15	− 5.0
n-Propylbenzene	13854.	2.76	3.12	8.64	2.71	13.1
Isopropylbenzene	10623.	2.66	3.00	8.61	2.64	12.0

^{a} 1 calorie = 4.184 Joules

physical properties using the Flory-Huggins and the Hildebrand-Scatchard equations.

The quantity γ_ϕ^0 in eq 1 is defined as the activity coefficient of a solute measured in octanol saturated with water. However, Purnell [15] has shown that γ_ϕ^0 for a solute in a binary mixture may be expressed as

$$\frac{1}{\gamma_\phi^0} = \frac{\phi_w}{\gamma_\gamma^{w'}} + \frac{\phi_o}{\gamma_\phi^\infty} \qquad (9)$$

where γ_ϕ^∞ and $\gamma_\phi^{w'}$ are the solute activity coefficients at infinite dilution in pure octanol and in pure water, respectively, and ϕ_o and ϕ_w are their volume fractions. It has been reported [16] that at equilibrium the volume fraction of water in octanol is 0.0414. The value of γ_ϕ^w for the solutes used in this study vary between 380 and 63,000 while those of γ_ϕ^∞ vary between 3.00 and 3.60. Thus the errors involved in assuming $\gamma_\phi^0 = \gamma_\phi^\infty$ and $\gamma_\phi^{w'} = \gamma_\phi^w$ are minimal.

The solute activity coefficients in water, γ_ϕ^w, listed in column 3 of table 2, were calculated using the experimental log $K_{o/w}$ and calculated log γ_ϕ^∞ from the Flory-Huggins and Hildebrand-Scatchard equation. Considering that the average standard deviation in the experimental log $K_{o/w}$ is 0.04 and log γ_ϕ^w is 0.03, the agreement between the experimental log γ_ϕ^w (listed in the last column) and the calculated log γ_ϕ^w is very encouraging.

In summary this study suggests that the solute activity coefficient γ_ϕ^∞, may be calculated accurately using the Flory-Huggins and Hildebrand-Scatchard equations, and the solubility of organic compounds in water may be predicted successfully from the knowledge of their octanol/water partition

TABLE 2. *Activity Coefficients and Octanol/Water Partition Coefficients at 25.0 °C.*

Solute	log γ_ϕ^0 calculated	log $K_{o/w}$(17) Experimental	log γ_ϕ^w calculated	Experimental (17)
n-Pentane	0.61	3.62	4.23	4.19
n-Hexane	0.56	4.11	4.67	4.73
n-Heptane	0.51	4.66	5.17	5.27
n-Octane	0.48	5.18	5.66	5.80
1-Hexene	0.53	3.39	3.90	3.99
1-Heptene	0.48	3.99	4.47	4.58
1-Octene	0.45	4.57	5.02	5.24
1-Nonene	0.39	5.15	5.54	5.82
Benzene	0.60	2.13[2]	2.73	2.59[2]
Toluene	0.52	2.65	3.17	3.17
Ethylbenzene	0.49	3.13	3.62	3.69
o-Xylene	0.56	3.13	3.69	3.60
m-Xylene	0.50	3.20	3.70	3.73
n-Propylbenzene	0.43	3.69	4.12	4.22
Isopropylbenzene	0.42	3.90	4.32	4.09

coefficients and the solute activity coefficient calculated from the FH-HS equation.

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