J. Chem. Eng. Data **1982**, *27*, 451–454 **451**

Aqueous Solubility and Octanol/Water Partition Coefficient of Organic Compounds at 25.0 °C

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Aqueous solubilities (C_s^w) and octanol/water partition coefficients ($K_{o/w}$) of 62 organic solutes, falling into 7 general chemical classes, have been systematically determined by using the modified generator column method. From thermodynamics an equation is derived relating $K_{o/w}$ to the volume-fraction-based solute activity coefficient in water (γ_s^w), the latter being determinable from C_s^w. For each class of compound, excellent linear correlations are found between log $K_{o/w}$ and log γ_s^w, with slopes close to the theoretical value of unity.

Introduction

The octanol/water partition coefficient, $K_{o/w}$, is an important property to model the fate and transport of organic chemicals in the environment. The ability of organic compounds to bioconcentrate in the marine environment was found to be dependent upon the concentration distribution of molecules between lipid and aqueous phases, which, in turn can be correlated to $K_{o/w}$. For example, bioconcentration factors for organic compounds in trout muscles from water containing low levels of these compounds have been successfully correlated with their $K_{o/w}$ values. $K_{o/w}$ is also a measure of the hydrophobicity of organic compounds, which has been demonstrated to be an important parameter in bioaccumulation and biotransport (*1*).

Aqueous solubility, C_s^w, is another property which affects the fate and transport of organic chemicals in the environment. Aqueous solubility can affect adsorption and desorption in soils and volatility of aquatic systems. It can also affect possible transformations by hydrolysis, photolysis, oxidation, reduction, and biodegradation in water (*2*). Other specialized transport pathways, such as washout from the atmosphere by rain, are also influenced by the extent of water solubility.

Because of the environmental importance of $K_{o/w}$ and C_s^w, it is desirable to be able to estimate $K_{o/w}$ from C_s^w (or a directly related quantity), and vice versa. Hansch et al. (*3*, *4*) first proposed a linear free energy relationship between the logarithms of $K_{o/w}$ and C_s^w. Recently MacKay and co-workers (*5*) derived a similar expression from more rigorous thermodynamic considerations. Here we extend the thermodynamic derivation and obtain a simple relationship between $K_{o/w}$ and C_s^w by employing solute activity coefficients based on volume fraction. In order to test this expression, we have systematically measured aqueous solubilities and octanol/water partition coefficients of a number of compounds of different classes using the modified May–Wasik–Freeman method (*6*, *7*).

Thermodynamic Background

The octanol/water partition coefficient, $K_{o/w}$, is defined as the ratio of the molar concentration of solute in octanol saturated with water, C_s^o, to its concentration in water saturated with octanol, C_s^w, under equilibrium conditions:

$$K_{o/w} = C_s^o / C_s^w \qquad (1)$$

Furthermore, the chemical potential of the solute in water, μ_s^w, and in octanol, μ_s^o, may be expressed by the following equations:

$$\mu_s^w = \mu_s^* + RT \ln \gamma_s^w \phi_s^w \qquad (2)$$

$$\mu_s^o = \mu_s^* + RT \ln \gamma_s^o \phi_s^o \qquad (3)$$

where μ_s^* is the chemical potential of the pure liquid solute, R is the gas constant, T is the temperature of the system in Kelvin, ϕ_s^w and ϕ_s^o are respectively the volume fractions of solute in water and in octanol, and γ_s^w and γ_s^o are the solute activity coefficients on a volume fraction basis ($\gamma_s \rightarrow 1$ as $\phi_s \rightarrow 1$) in water and octanol, respectively.

Under equilibrium conditions $\mu_s^w = \mu_s^o$; hence

$$\gamma_s^w \phi_s^w = \gamma_s^o \phi_s^o \qquad (4)$$

Recognizing that $C_s^l V_s^l = \phi_s^l$, where V_s^l is the partial molar volume of the solute, and combining eq 1 and 4, we obtain

$$\log K_{o/w} = \log \gamma_s^w - \log \gamma_s^o \qquad (5)$$

where we have assumed that $V_s^w \approx V_s^o \approx V_s^*$ the last being the molar volume of the pure liquid solute. Activity coefficients of the solute in the aqueous phase in equilibrium with essentially pure solute may be expressed as

$$\gamma_s^w \phi_s^w = \gamma_s^s \phi_s^s \qquad (6)$$

where γ_s^s and ϕ_s^s are respectively the solute activity coefficient and the volume fraction in the solute. We note that, under experimental conditions, γ_s^s approaches unity as ϕ_s^s approaches unity; hence

$$\gamma_s^w = (\phi_s^w)^{-1} = (C_s^w V_s^*)^{-1} \qquad (7)$$

Therefore, according to eq 5, if the variation in γ_s^o is very small with respect to the variation in γ_s^w, linear regression analysis of log $K_{o/w}$ as a function of log γ_s^w should yield a slope of unity. Finally, we note that substitution of eq 7 into eq 5 yields an expression similar to that derived by MacKay et al. (*5*) for liquid solutes.

Experimental Section

The solutes used in this study were obtained from several sources. Their purity was checked by high-temperature gas chromatography and found to be at least 99%. The 1-octanol was purified as described elsewhere (*6*) and had at least 99% purity. Baker-analyzed[12] HPLC grade methanol and water were used to prepare the mobile phase for liquid chromatography.

The details of the generator column have been discussed elsewhere (*6*, *7*). It consists of a 20-cm section of 6-mm o.d. Pyrex tubing joined to a short section of 9-mm o.d. Pyrex tubing. The 6-mm o.d. section of the column was packed with 100–120 mesh Chromosorb W-HP (solid support) which was held in place by two plugs of silanized glass wool. The column was thermostated at 25.0 ± 0.1 °C by pumping water from a constant-temperature bath through a jacket enclosing column.

For solubility measurements, the column was coated with a liquid solute by pulling approximately 2 mL of the liquid through the clean, dry support with gentle suction. For $K_{o/w}$ measure-

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Table I. Aqueous Solubilities and Octanol/Water Partition Coefficients of Aromatic Hydrocarbons[a]

	aqueous concn, mol/L			log $K_{o/w}$	
solute	this study	lit.	log γ_s^w	this study	lit. ref *3*
toluene	6.28×10^{-3} (a)	5.80×10^{-3} (*10*)	3.17	2.65 (a)	2.69
ethylbenzene	1.76×10^{-3} (a)	1.52×10^{-3} (*10*)	3.66	3.13 (a)	3.15
o-xylene	2.08×10^{-3} (a)	1.61×10^{-3} (*10*)	3.60	3.13 (a)	3.12
m-xylene	1.51×10^{-3} (a)	1.38×10^{-3} (*10*)	3.73	3.20 (a)	3.20
p-xylene	2.02×10^{-3} (a, b)	1.47×10^{-3} (*10*)	3.60	3.18 (a, b)	3.15
n-propylbenzene	4.34×10^{-4} (a, b)	4.99×10^{-4} (*8*)	4.22	3.69 (a, b)	3.68
n-butylbenzene	1.03×10^{-4} (a, b)	8.79×10^{-5} (*10*)	4.79	4.28 (a, b)	4.26
n-pentylbenzene	2.59×10^{-5} (a)		5.35	4.90 (a)	
n-hexylbenzene	6.27×10^{-6} (a)		5.92	5.52 (a)	
1,2,3-trimethylbenzene	5.45×10^{-4} (a)	4.01×10^{-4} (*10*)	4.13	3.55 (a)	
1-ethyl-2-methylbenzene	6.21×10^{-4} (a)		4.07	3.53 (a)	
chlorobenzene	2.62×10^{-3} (a)	2.84×10^{-3} (*4*)	3.56	2.98 (a)	2.84
iodobenzene	9.84×10^{-4} (a)		3.96	3.28 (a)	3.25
o-fluorobenzyl chloride	2.88×10^{-3} (a)		3.47	2.67 (a)	
m-fluorobenzyl chloride	2.86×10^{-3} (a)		3.46	2.77 (a)	
m-cresol	2.59×10^{-2} (a)		2.52	1.96 (a)	
nitrobenzene	3.11×10^{-2} (a)		2.50	1.85 (a)	

[a] a = HPLC method of analysis; b = GC method of analysis.

Table II. Aqueous Solubilities and Octanol/Water Partition Coefficients of Unsaturated Hydrocarbons[a]

	aqueous concn, mol/L			log $K_{o/w}$	
solute	this study	ref *8*	log γ_s^w	this study	ref *4*
1-hexene	8.28×10^{-4} (b)	5.89×10^{-4}	3.98	3.39 (b)	2.70*
1-heptene	1.85×10^{-4} (b)		4.58	3.99 (b)	
1-octene	3.65×10^{-5} (b)	2.40×10^{-5}	5.24	4.57 (b)	3.70*
1-nonene	8.85×10^{-6} (b)		5.81	5.15 (b)	
1-pentyne	1.54×10^{-2} (b)		2.81	2.12 (b)	
1-hexyne	8.37×10^{-3} (b)		3.01	2.73 (b)	

[a] b = GC method of analysis. An asterisk indicates that the literature data are calculated values according to Hansch et al. (*4*).

ments, approximately 2 mL of 1-octanol containing about 1% (by weight) of solute was poured into the clean, dry generator column until the solid support was saturated, as evidenced by the appearance of 1-octanol at the base of the column.

For the aqueous solubility and the $K_{o/w}$ determinations, the aqueous phase of the solute was generated by pumping water into the inlet of the coated generator column either by using a minipump or by means of a water reservoir using compressed air at 5 psi. Analysis of the aqueous phase from the pure solute coated column yielded the aqueous solubility, whereas analysis of the aqueous phase from the 1% (by weight) in octanol coated column was used in the determination of $K_{o/w}$. The $K_{o/w}$

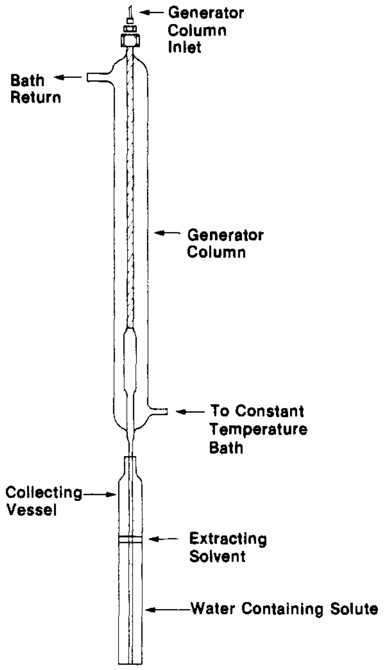

Figure 1. Generator column and collecting vessel used for analysis of the aqueous phase by the GC–solvent extraction method.

Table III. Aqueous Solubilities and Octanol/Water Partition Coefficients of Halogenated Hydrocarbons[a]

	aqueous concn, mol/L			log $K_{o/w}$	
solute	this study	ref *4*	log γ_s^w	this study	ref *4*
1-chlorobutane	9.43×10^{-3} (b)	7.19×10^{-3}	3.00	2.55 (b)	2.39
1-chloroheptane	1.01×10^{-4} (b)		4.81	4.15 (b)	
1-bromobutane	6.34×10^{-3} (b)	4.13×10^{-3}	3.16	2.75 (b)	2.60*
1-bromopentane	8.38×10^{-4} (b)		3.98	3.37 (b)	
1-bromohexane	1.56×10^{-4} (b)		4.65	3.80 (b)	
1-bromoheptane	3.71×10^{-5} (b)		5.23	4.36 (b)	
1-bromooctane	8.65×10^{-6} (b)		5.82	4.89 (b)	
bromochloromethane	0.129 (b)		2.06	1.41 (b)	
1-bromo-3-chloropropane	1.42×10^{-2} (b)		2.82	2.18 (b)	
1-iodoheptane	1.55×10^{-5} (b)		5.60	4.70 (b)	
trichloroethylene	1.04×10^{-2} (a)	0.80×10^{-2}	3.03	2.53 (a)	
4-bromo-1-butene	5.66×10^{-3} (a)		3.24	2.53 (a)	
allyl bromide	3.17×10^{-2} (a)		2.56	1.79 (a)	

[a] a = HPLC method of analysis; b = GC method of analysis. An asterisk indicates that the literature data are calculated values according to Hansch et al. (*4*).

Table IV. Aqueous Solubilities and Octanol/Water Partition Coefficients of Normal Hydrocarbons[a]

	aqueous concn, mol/L			$\log K_{o/w}$	
solute	this study	ref *8*	$\log \gamma_s^w$	this study	lit.
n-pentane	5.65×10^{-4} (b)	5.39×10^{-4}	4.19	3.62 (b)	3.23 (*3*)
n-hexane	1.43×10^{-4} (b)	1.13×10^{-4}	4.73	4.11 (b)	3.00 (*4*)*
n-heptane	3.57×10^{-5} (b)	3.05×10^{-5}	5.28	4.66 (b)	3.50 (*4*)*
n-octane	9.66×10^{-6} (b)	5.97×10^{-6}	5.80	5.18 (b)	4.00 (*4*)*

[a] See footnote to Table III.

Table V. Aqueous Solubilities and Octanol/Water Partition Coefficients of Aldehydes and Ketones[a]

	aqueous concn, mol/L			$\log K_{o/w}$	
solute	this study	lit.	$\log \gamma_s^w$	this study	ref *4*
2-butanone	1.89 (b)		0.77	0.69 (b)	0.29
3-pentanone	0.53 (b)	0.48 (*4*)	1.25	0.99 (b)	0.79*
2-heptanone	3.57×10^{-2} (a)	3.79×10^{-2} (*4*)	2.30	1.98 (a)	1.79*
2-octanone	8.85×10^{-3} (a)		2.86	2.76 (a)	
2-nonanone	2.61×10^{-3} (a)		3.35	3.18 (a)	
2-decanone	5.03×10^{-4} (a)		4.02	3.81 (a)	
acetal	0.75 (b)	0.42 (*9*)	0.97	0.36 (b)	
2-furaldehyde	0.81 (a)	0.85 (*4*)	1.17	0.52 (a)	

[a] See footnote to Table III.

Table VI. Aqueous Solubilities and Octanol/Water Partition Coefficients of Esters[a]

	aqueous concn, mol/L			$\log K_{o/w}$	
solute	this study	lit.	$\log \gamma_s^w$	this study	ref *4*
methyl nonanoate	1.33×10^{-4} (b)		4.58	4.32 (b)	
methyl decanoate	2.05×10^{-5} (b)		5.36	4.41 (b)	
ethyl acetate	0.726 (b)	0.912 (*4*)	1.15	0.68 (b)	0.73*
n-propyl acetate	0.200 (b)	0.185 (*4*)	1.64	1.24 (b)	1.23*
n-butyl acetate	5.77×10^{-2} (b)	0.203 (*4*)	2.12	1.82 (b)	1.73*
ethyl propionate	0.148 (b)	0.187 (*9*)	1.77	1.43 (b)	
2-bromoethyl acetate	0.212 (a)		1.63	1.11 (a)	

[a] See footnote to Table III.

Table VII. Aqueous Solubilities and Octanol/Water Partition Coefficients of Alcohols[a]

	aqueous concn, mol/L			$\log K_{o/w}$	
solute	this study	ref *9*	$\log \gamma_s^w$	this study	lit.
1-butanol	0.854 (b)		1.10	0.785 (b)	0.84 (*4*)*
1-pentanol	0.133 (b)	0.249	1.84	1.53 (b)	1.34 (*3*)*
1-hexanol	4.14×10^{-2} (b)		2.28	2.03 (b)	1.84 (*4*)*
1-heptanol	1.13×10^{-2} (b)		2.80	2.57 (b)	2.34 (*4*)*
1-nonanol	7.35×10^{-4} (b)		3.89	3.77 (b)	
2-ethyl-1,3-hexanediol	1.56×10^{-3} (b)		3.61	3.22 (b)	

[a] See footnote to Table III.

measurement also required accurate analysis of the 1% solute in 1-octanol solution.

Analysis

The solute concentration in the aqueous phase was analyzed by either a high-pressure liquid chromatographic (HPLC) or a gas chromatographic (GC) method. The method employed to collect the water (containing solute) from the generator column depended on the technique used for analysis of the aqueous phase. The HPLC method, which was used for solutes that absorbed in the UV region, has been described elsewhere (*6*) and will not be discussed here.

In the GC method aqueous solutions from the generator column entered a collecting vessel (Figure 1) containing a known weight of extracting solvent which was immiscible with water. The outlet of the generator column was positioned such that the aqueous phase always entered below the extracting solvent. After the aqueous phase was collected, the collecting vessel was stoppered with a $^{3}/_{8}$-in. Teflon Swagelok cap, and the quantity of aqueous phase was determined by weighing. The solvent and the aqueous phase were equilibrated either by stirring with a glass-enclosed magnet or by rotating the collecting vessel at the rate of 2 rpm for 5 min. It was found that rotating the collecting vessel for longer than 5 min did not increase the amount of solute extracted into the extracting solvent. A small amount of the solvent was then injected into a gas chromatograph equipped with a flame ionization detector, and the solute concentration in the aqueous phase was determined from a calibration curve constructed by using known concentrations of the solute. In order to determine the partition coefficient, $K_{o/w}$, we injected samples of the 1% (by weight) solute in 1-octanol solution into the GC, and the concentration of the solute in the octanol phase was similarly calculated from a calibration curve.

Table VIII. Coefficients of the Regression Equation and the Correlation Coefficient of the Solutes

compd type	no. of compds	c[a]	d[b]	r[c]
aromatic hydrocarbons	18	1.056 ± 0.026	−0.768 ± 0.100	0.995
unsaturated hydrocarbons	6	0.908 ± 0.063	−0.250 ± 0.105	0.993
halogenated hydrocarbons	13	0.907 ± 0.033	−0.323 ± 0.133	0.993
normal hydrocarbons	4	0.972 ± 0.016	−0.468 ± 0.081	0.999
aldehydes and ketones	8	1.079 ± 0.065	−0.465 ± 0.155	0.989
esters	7	0.932 ± 0.05	−0.285 ± 0.167	0.991
alcohols	6	1.030 ± 0.011	−0.348 ± 0.112	0.997
all compounds	62	0.944 ± 0.018	−0.311 ± 0.066	0.990

[a] Slope. [b] Intercept. [c] Correlation coefficient.

Results and Discussion

The experimentally determined values of $K_{o/w}$ and C_s^w, and the calculated values of γ_s^w (from eq 7), are listed in Tables I–VII for several classes of compounds. The notations a and b refer respectively to the HPLC and GC methods of analysis. Each reported solubility and octanol/water partition coefficient is an average of at least three measurements. The experimental uncertainties in $K_{o/w}$ and C_s^w are around 1.0%. An asterisk is used to indicate that the literature data are calculated values according to Hansch, Quinlan, and Lawrence (*4*). Our results are generally in good agreement with available experimental literature data.

The present data were subjected to a linear regression of log $K_{o/w} = c \log \gamma_s^w + d$ for each class of compound and for all compounds taken together. The results of these analyses are shown in Table VIII.

According to eq 5, the slope for each class should be unity and the negative of the intercept is log γ_s° (assumed to be relatively constant). Examination of Table VIII shows that the slopes are indeed close to unity, ranging between 0.91 and 1.08. The small deviations are most likely caused by slight variations in log γ_s° within each class (*11*). For example, the average of the difference between log γ_s^w and log $K_{o/w}$ for the aromatic compounds of Table I is 0.56 and for halogenated hydrocarbons of Table III is 0.68, whereas their least-squares values listed in Table VIII for the intercepts are respectively -0.77 and -0.32. Therefore, the intercepts represent only approximate (averaged) values of log γ_s° for each class.

These findings show that the octanol/water partition coefficient of a solute may be estimated with reasonable accuracy from knowledge of its aqueous solubility, its molar volume, and the regression equation for compounds of its class. Also, this study establishes that the generator column method coupled with either HPLC or GC modes of analysis provides an accurate and rapid method for systematic determination of $K_{o/w}$ and C_s^w for organic compounds.

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(12) Certain trade names and company products are identified in order to adequately specify the experimental procedure. In no case does such identification imply recommendation or endorsement by the National Bureau of Standards, or does it imply that the products are necessarily the best available for the purpose.

Received for review October 28, 1981. Accepted April 5, 1982. We gratefully acknowledge the financial support of the Environmental Protection Agency and the Toxic Control Act.

Isopiestic Determination of the Activity Coefficients of Some Aqueous Rare-Earth Electrolyte Solutions at 25 °C. 6. $Eu(NO_3)_3$, $Y(NO_3)_3$, and YCl_3

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The osmotic coefficients of aqueous $Eu(NO_3)_3$, $Y(NO_3)_3$, and YCl_3 have been measured at 25 °C from dilute solution to supersaturated concentrations with the isopiestic method. Least-squares equations were fitted to these osmotic coefficients, which were then used to calculate water activities and mean molal activity coefficients. Pitzer's equations were also fitted to the lower-concentration data. These results are compared to published activity data for rare-earth chlorides, perchlorates, and nitrates. A total of 40 rare-earth salts have now been studied, and their activities are discussed in terms of cation hydration and anion–cation interactions. Density data are also reported for $Y(NO_3)_3$ solutions.

Introduction

In the late 1940s activity coefficient measurements began at Ames Laboratory for dilute rare-earth halide solutions at 25 °C, using emf measurements. Data were ultimately published for 14 rare-earth chlorides and 9 rare-earth bromides (*1*, *2*). In the 1950s isopiestic measurements were started for rare-earth electrolyte solutions at higher concentrations. This research was moved to Lawrence Livermore National Laboratory (LLNL) in 1977. Isopiestic data have already been published for 14 rare-earth chlorides, 12 perchlorates, and 12 nitrates at 25 °C (*3*-*7*).

Activity data for aqueous rare-earth salts are interesting for several reasons. The weakly complexed chlorides, bromides, and perchlorates show S-shaped series trends at constant molality, which are mainly due to total hydration trends for the cations. These trends are strongly influenced by an inner-sphere hydration number decrease between Nd^{3+} and Tb^{3+} and its concomitant contraction of the inner-sphere hydrated radius (*8*, *9*). In contrast, rare-earth nitrate solutions contain mixtures of inner- and outer-sphere complexes which cause these S-shaped series trends to disappear at fairly low concentrations (*7*).

A so-called gadolinium break appears in many properties of rare-earth complexes, but it is conspicuously absent for most thermodynamic (*3*, *4*, *10*, *11*) and transport properties (*12*, *13*) of rare-earth chlorides and perchlorates. However, most properties of rare-earth nitrates have a "bulge" in the middle

0021-9568/82/1727-0454$01.25/0