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DETERMINATION OF HYDROCARBON–WATER PARTITION COEFFICIENTS FROM CHROMATOGRAPHIC DATA AND BASED ON SOLUTION THERMODYNAMICS AND THEORY

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SUMMARY

The octanol–water and hexadecane–water partition coefficients for series of alkylbenzenes, alkanes, alkenes, alcohols, and bromoalkanes were determined by the generator column technique and compared favorably to those calculated from the activity coefficients in each phase. A lattice-model theory suggested and the data confirmed that the logarithms of the partition coefficients are linearly related to each other and to the solute molar volume for each homologous series. As predicted by the theory, the slopes of the linear relationships between the logarithms of the partition coefficients and solute molar volume were the same for all homologous series studied. Furthermore, the logarithms of the octanol–water partition coefficients were linearly related ($r^2 = 0.993$) to the logarithms of the reversed-phase liquid chromatographic adjusted retention volumes determined by extrapolation to 100% water as the mobile phase for a variety of the solutes.

INTRODUCTION

The distribution of organic solutes between water and an immiscible lipophilic solvent provides data on the intramolecular and intermolecular forces acting between the solute and each solvent. The partition coefficient (K) is defined according to the Nernst partition law as the ratio at equilibrium of the concentration of dissolved substance (solute) in a two-phase system consisting of two largely-immiscible solvents[1]. Due to the extensive work by Hansch and Leo[2], the octanol–water system has become the standard for determining lipophilic solvent–water partition coefficients. At equilibrium, however, octanol contains 1.7 mol/l water and water contains $4.5 \cdot 10^{-3}$ mol/l octanol[3].

If one chooses an *n*-alkane solvent in which to determine partition coefficients, there is no hydrogen bonding interaction between solvent and solute so the partition coefficient is determined by desolvation of water from the solute and the free energy

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required to break any hydrogen bonding or dipolar interactions between the solute and water. The disadvantage of using an *n*-alkane solvent is that the possibility of dimerization of the solute is maximized. Costas and Patterson[4] measured apparent molar heat capacities and volumes for methanol in *n*-hexane, 1-hexanol in *n*-dodecane, and 1-decanol in decane. They noted concentration and temperature dependencies which indicated alcohol self-association in the alkane solvent through hydrogen bonds.

Collander[5] suggested a simple linear relationship between partition coefficients in different lipophilic solvent systems, 1 and 2, *i.e.*

$$\ln K_{2-\mathrm{w}} = a \ln K_{1-\mathrm{w}} + b \tag{1}$$

The slope, a, is a measure of the solvent system's sensitivity to changes in hydrophobicity of the solute. Leo and Hansch[6] postulated that other than hydrogen bonding the partition process should be the same for solutes in each solvent system. Therefore, if one corrects for the hydrogen bonding ability of the solvents and solutes, the slope, a, should be equal to one. This linear relationship between partition coefficients in different solvent systems is said to hold if[2]: (1) the primary solvation forces in the two solvent systems are similar; or (2) the solute set is an homologous series.

In addition to experimental determination, group contribution methods have been used to estimate partition coefficients[2]. For instance, the π constant is a free-energy-related constant for a functional group defined as:

$$\pi = \log (K_{\mathrm{x}}/K_{\mathrm{h}}) \tag{2}$$

where K_{h} is the partition coefficient of the parent compound and K_{x} is the partition coefficient of a derivative. The values are additive as long as no new effects in summation are encountered. In other words, as long as only effects, such as intermolecular interactions, found in the constituent parts are encountered.

Octanol–water partition coefficients have also been estimated by correlating retention in a reversed-phase liquid chromatographic (RPLC) system with known partition coefficients. For instance, Veith *et al.*[7] using methanol–water (85:15), Konemann *et al.*[8] using methanol–water (70:30), and McDuffie[9] using methanol–water (75:25) have correlated RPLC retention data with $K_{\mathrm{o-w}}$ values. More recently, Camps *et al.*[10] noted that the correlation coefficient between RPLC retention and $K_{\mathrm{o-w}}$ (where o = octanol and w = water) increased with decreasing methanol percentages.

Other workers[11–13] have used octanol-coated columns and octanol-saturated water mobile phases in RPLC systems for determination of $K_{\mathrm{o-w}}$ values. The disadvantages of an octanol-coated column, however, include: (1) substances of low aqueous solubility (1 ppm or less) are undetectable by UV or fluorescence analysis, (2) stripping of the physically supported octanol creates baseline stabilization problems, and (3) elution of fairly lipophilic compounds can take several hours with consequent band broadening difficulties. This leaves capacity factors or adjusted retention volumes (from C_{18} bonded phases) as the best RPLC estimate of $K_{\mathrm{o-w}}$.

In this study, octanol–water ($K_{\mathrm{o-w}}$) and hexadecane–water ($K_{\mathrm{h-w}}$) partition coefficients have been determined at 25°C for a series of alkylbenzenes, alkanes, alkenes, alcohols, and bromoalkanes using the generator column technique[14,15]. The importance of this data is both environmental and as a measure of preference of solute and solute functional groups for aqueous *versus* hydrocarbon environments. Due to the time and thus expense involved in doing these measurements, it is desirable to be able to estimate partition data from molecular parameters or from other measurements. The lattice model theory which is described in the next section suggests linear relationships between ln K_{o-w} and ln K_{h-w} and between either ln K_{o-w} or ln K_{h-w} and the solute molar volume. Also, the theory validates the group contribution method for estimating partition coefficients. Furthermore, since well characterized adjusted retention volumes are available at several volume fractions of water in methanol[16], these are extrapolated to retention in 100% water which is then correlated with the octanol–water partition coefficients.

From thermodynamics, the octanol–water or hexadecane–water partition coefficient can be expressed as the ratio of the solute's, component a, volume-fraction-based activity coefficient at infinite dilution in water, component b, ($\gamma_{a(b)}$) to that in the organic solvent, component c, either octanol ($\gamma_{a(o)}$) or hexadecane ($\gamma_{a(h)}$), as follows[17]:

$$K_{o-w} = \gamma_{a(b)}/\gamma_{a(o)} \tag{3}$$

$$K_{h-w} = \gamma_{a(b)}/\gamma_{a(h)} \tag{4}$$

The quantity $\gamma_{a(b)}$ is generally determined (for sparingly soluble solutes) as the reciprocal of the volume fraction of the solute in water, *i.e.* $1/\Phi_{a(b)}$, and is expressed as the reciprocal of the solute concentration in water ($C_{a(b)}$) times the molar volume of the solute (V_a^*), $1/[C_{a(b)}V_a^*]$. In this study, the activity coefficients in octanol or hexadecane have been determined by gas chromatography (GC) for the solutes of interest.

Note that the partition coefficients calculated from the activity coefficients may be different than those determined experimentally. In the generator column measurement, the octanol or hexadecane phase is saturated with water, and the water phase is saturated with either octanol or hexadecane. In the activity coefficient determination, however, one is dealing with pure organic phase and pure water. This comparison should shed some light on the importance, or lack thereof, of phase saturation.

BACKGROUND THERMODYNAMICS

The octanol–water partition coefficient, K_{o-w}, and hexadecane–water partition coefficient, K_{h-w}, are defined as the ratio of the molar concentration of solute in octanol ($C_{a(o)}$) and hexadecane ($C_{a(h)}$), respectively, saturated with water to its concentration in water saturated with octanol and hexadecane, respectively, ($C_{a(b)}$) under equilibrium conditions:

$$K_{o-w} = C_{a(o)}/C_{a(b)} \tag{5}$$

$$K_{h-w} = C_{a(h)}/C_{a(b)} \tag{6}$$

Furthermore, the chemical potential of the solute in water, $\mu_{a(b)}$, in octanol, $\mu_{a(o)}$, and in hexadecane, $\mu_{a(h)}$, may be expressed by the following equations:

$$\mu_{a(b)} = \mu_a^* + RT \ln \gamma_{a(b)}\Phi_{a(b)} \tag{7}$$

$$\mu_{a(o)} = \mu_a^* + RT \ln \gamma_{a(o)}\Phi_{a(o)} \tag{8}$$

$$\mu_{a(h)} = \mu_a^* + RT \ln \gamma_{a(h)}\Phi_{a(h)} \tag{9}$$

where μ_a^* is the chemical potential of the pure liquid, R is the gas constant, T is the temperature of the system in Kelvin, $\Phi_{a(b)}$, $\Phi_{a(o)}$, and $\Phi_{a(h)}$ are, respectively, the solute volume fractions in the aqueous phase, octanol phase, and hexadecane phase, and $\gamma_{a(b)}$, $\gamma_{a(o)}$, and $\gamma_{a(h)}$ are the solute activity coefficients on a volume-fraction-basis ($\gamma_a \rightarrow 1$ as $\Phi_a \rightarrow 1$) in water, octanol, and hexadecane, respectively.

Under equilibrium conditions, $\mu_{a(b)} = \mu_{a(o)}$ and $\mu_{a(b)} = \mu_{a(h)}$; hence,

$$\gamma_{a(b)}\Phi_{a(b)} = \gamma_{a(o)}\Phi_{a(o)} \tag{10}$$

$$\gamma_{a(b)}\Phi_{a(b)} = \gamma_{a(h)}\Phi_{a(h)} \tag{11}$$

Recognizing that $C_{a(i)}V_{a(i)} = \Phi_{a(i)}$ where $V_{a(i)}$ is the partial molar volume of the solute, and combining eqns. 5 and 10 as well as 6 and 11, one obtains

$$\ln K_{o-w} = \ln \gamma_{a(b)} - \ln \gamma_{a(o)} \tag{12}$$

$$\ln K_{h-w} = \ln \gamma_{a(b)} - \ln \gamma_{a(h)} \tag{13}$$

where it has been assumed that $V_{a(b)} \approx V_{a(o)} \approx V_{a(h)} \approx V_a^*$, the last being the molar volume of the pure liquid solute. Note that here one is assuming that the activity coefficients in octanol- or hexadecane-saturated water are approximately the same as those in pure water and those in water-saturated octanol or hexadecane are the same as in pure octanol or hexadecane. This assumption seems to hold fairly well as will be seen later.

Activity coefficients of the solute in the aqueous phase in equilibrium with essentially pure solute may be expressed as

$$\gamma_{a(b)}\Phi_{a(b)} = \gamma_{a(a)}\Phi_{a(a)} \tag{14}$$

where $\gamma_{a(a)}$ and $\Phi_{a(a)}$ are, respectively, the solute activity coefficient and volume fraction in the solute. Under experimental conditions, $\gamma_{a(a)}$ approaches unity as $\Phi_{a(a)}$ approaches unity; hence,

$$\gamma_{a(b)} = (\Phi_{a(b)})^{-1} = (C_{a(b)}V_a^*)^{-1} \tag{15}$$

Therefore, the solute volume-fraction-based activity coefficient can be calculated from the solute's aqueous solubility and molar volume.

The solute activity coefficients in the organic phase are determinable by GC measurements. From these measurements, one must first calculate the solute's specific retention volume (V_g) using the following equation[18]:

$$V_g = [(t_r'F)/w][(P_o - P_w)/P_o](273.2/T_a)\,(3/2)\{[(P_i/P_o)^2 - 1]/[(P_i/P_o)^3 - 1]\} \quad (16)$$

where t_r' is the solute retention time minus the air peak retention time in minutes, F is the carrier gas flow-rate in ml/min, P_i is the column inlet pressure in torr, P_o is the atmospheric (outlet) pressure in torr, P_w is the saturated water vapor pressure in torr at the room temperature (T_a), and w is the weight in grams of the stationary phase in the column. Next, the specific retention volumes must be corrected for vapor phase nonideality in order to obtain the solute activity coefficient so that

$$\ln \gamma_a = \ln(273.2R)/(P_a V_g V_a^* d) - (P_a B_{aa})/RT \quad (17)$$

where d is the density of the stationary phase at the temperature (T) of the measurements, P_a and B_{aa} are the vapor pressure and gas phase second virial coefficient of the solute at T, and V_a^* is the liquid molar volume of the solute at T. The virial coefficients are calculated from the modified corresponding states equation of McGlashan and Potter[19].

From the Flory–Huggins theory, which is based on a random mixing (Bragg–Williams) approximation, the volume-fraction-based solute activity coefficients at infinite dilution in water and organic solvent are given by[20]

$$\ln \gamma_{a(b)} = [1 - (r_a/r_b)] + r_a X_{ab} \quad (18)$$

$$\ln \gamma_{a(c)} = [1 - (r_a/r_c)] + r_a X_{ac} \quad (19)$$

in these equations, r_i is the total number of segments in a molecule of component i which is proportional to V_i, the molar volume of component i. Also, X_{ij} is the segmental interaction parameter.

The solute, a, is composed of group type 1, the methyl and methylene groups and group type 2, the substituent group. Water, component b, is composed of group type 3. The organic solvent, either octanol or hexadecane, is component c composed of group types 1, the methyl and methylene groups, and 4, the –OH or –CH$_2$OH group of octanol. Expanding eqns. 18 and 19 to include the group types and substituting the results into eqns. 12 and 13, one obtains the following expressions:

$$\ln K_{h-w} = r_{1a}(X_{13} + 1/r_h - 1/r_b) + r_{2a}(X_{23} - X_{12} + 1/r_h - 1/r_b) \quad (20)$$

$$\begin{aligned}\ln K_{o-w} = {} & r_{1a}(X_{13} - f_{4o}^2 X_{14} + 1/r_o - 1/r_b) + r_{2a}[X_{23} - X_{12} - \\ & f_{4o}^2 X_{14} + 1/r_o - 1/r_b + f_{4o}(X_{12} + X_{14} - X_{24})]\end{aligned} \quad (21)$$

Note that f_{4o} is the fraction of segments of type 4 (–OH) in the octanol molecule. Also, the number of segments in component a which are of group type 1 (r_{1a}) is given by

$$r_{1a} = r_a - r_{2a} \quad (22)$$

In eqns. 20 and 21, the X values are group interaction parameters. It is interesting to note that equations similar to eqns. 20 and 21 were derived previously to describe weak complexes[21].

Furthermore, r_a is proportional to the molar volume of the solute, V_a^*, and r_{2a} is proportional to the molar volume of the solute functional group x, V_{2a}^*. Eqns. 20 and 21 can now be rewritten as

$$\ln K_{h-w} = V_a^* C(X_{13} + 1/r_h - 1/r_b) + V_{2a}^* C(X_{23} - X_{12} - X_{13}) \tag{23}$$

$$\begin{aligned}\ln K_{o-w} = {} & V_a^* C(X_{13} - f_{4o}^2 X_{14} + 1/r_o - 1/r_b) + \\ & + V_{2a}^* C\,[(X_{23} - X_{12} - X_{13}) + f_{4o}(X_{12} + X_{14} - X_{24})]\end{aligned} \tag{24}$$

where C is a constant. Note the linear relationship between $\ln K_{h-w}$ and V_a^* and $\ln K_{o-w}$ and V_a^*. In eqn. 24, the $f_{4o}^2 X_{14}$ term is negligible since the fraction of an octanol molecule which is an hydroxy-term (f_{4o}) is small. Also, the $1/r_o - 1/r_b$ and $1/r_h - 1/r_b$ terms in eqns. 24 and 23 are small; therefore, the slopes of $\ln K_{h-w}$ or $\ln K_{o-w}$ *versus* V_a^* should be dominated by the X_{13} term which is positive and approximately the same for both systems.

The intercepts in eqns. 23 and 24 for plots of $\ln K_{h-w}$ or $\ln K_{o-w}$ *versus* V_a^* are more difficult to interpret due to the combination of unknown X values involved. The extra $f_{4o}(X_{12} + X_{14} - X_{24})]$ term in eqn. 24 indicates that the intercepts should be different for the two systems unlike the slopes.

As mentioned in the Introduction, Hansch and Leo[2] have used the π method for estimating octanol–water partition coefficients. The π constants are free-energy-related constants which are determined for each solute group type by eqn. 2. In order to demonstrate the validity of group additivity, one lets

$$r_{1a} = n_{CH_2} r_{CH_2} + n_{CH_3} r_{CH_3} \tag{25}$$

$$r_{2a} = r_x \tag{26}$$

where n_{CH_2} and n_{CH_3} are the number of methylene and methyl groups, respectively. Substituting eqns. 25 and 26 into eqn. 21, one obtains

$$\begin{aligned}\ln K_{o-w} = {} & n_{CH_2} r_{CH_2}(X_{CH_{2-3}} - f_{4o}^2 X_{CH_{2-4}} + 1/r_o - 1/r_b) + \\ & + n_{CH_3} r_{CH_3}(X_{CH_{2-3}} - f_{4o}^2 X_{CH_{3-4}} + 1/r_o - 1/r_b) + r_x[X_{3x} - \\ & X_{1x} - f_{4c}^2 X_{14} + 1/r_o - 1/r_b + f_{4o}(X_{1x} + X_{14} - X_{4x})]\end{aligned} \tag{27}$$

which is of the form

$$\ln K_{o-w} = n_{CH_2} \ln K_{CH_2} + n_{CH_3} \ln K_{CH_3} + \ln K_x \tag{28}$$

The free energy of transfer from water to octanol, ΔG_{o-w}, is related to K_{o-w} by

$$-\Delta G_{o-w} = RT \ln K_{o-w} \tag{29}$$

Therefore, eqn. 28 can be rewritten as

$$RT \ln K_{o-w} = -(n_{CH_2}\Delta G_{CH_2} + n_{CH_3}\Delta G_{CH_3} + \Delta G_x) \tag{30}$$

thus indicating the additivity of the free energies of transfer.

The lattice model theory also suggests a linear relationship between ln K_{o-w} and ln K_{h-w}. Combining eqns. 20 and 21 using eqns. 25 and 26 and letting c = o for octanol and c = h for hexadecane, one finds the following relationship

$$\begin{aligned}\ln K_{o-w} = \ln K_{h-w} &+ n_{CH_2}r_{CH_2}(1/r_o - 1/r_h - f_{4o}^2X_{14}) + \\ &n_{CH_3}r_{CH_3}(1/r_o - 1/r_h - f_{4o}^2X_{14}) + r_x[1/r_o - 1/r_h - f_{4o}^2X_{14} + \\ &+ f_{4o}(X_{14} + X_{12} - X_{24})]\end{aligned} \tag{31}$$

This equation is of the general form

$$\ln K_{o-w} = \ln K_{h-w} + an_{CH_2} + b \tag{32}$$

where $a = r_{CH_2}(1/r_o - 1/r_h - f_{4o}^2X_{14})$. Strictly then, the intercept of a plot of ln K_{o-w} *versus* ln K_{h-w} should show, to some extent, a dependence on solute chain length which could lead to "skewing" and a slope slightly different from unity.

EXPERIMENTAL*

The solutes used in this study were obtained either from Aldrich (Metuchen, NJ, U.S.A.) or Wiley Organics (Columbus, OH, U.S.A.). The purities determined by high-temperature GC were 99% and greater. Both the 1-octanol and *n*-hexadecane had a purity in excess of 99%. Baker analyzed RPLC-grade methanol and water were used to prepare the mobile phase for liquid chromatography. Distilled water was used for other aqueous solutions.

The generator column RPLC method as described by DeVoe *et al.*[22] was used to determine the K_{o-w} and K_{h-w} values for the bromoalkanes and alkylbenzenes. The generator column GC method as described by Tewari *et al.*[23] was used to determine the K_{o-w} and K_{h-w} values for the alkanes, alkenes, and alcohols.

For partition coefficient measurements, approximately 2 ml of 1-octanol or *n*-hexadecane containing about 1% (w/w) of solute were used to saturate the solid support contained in the generator column. Note that the solute–octanol or solute–hexadecane mixtures were previously equilibrated with water using gentle stirring for several hours. A portion of this equilibrated mixture was taken for analysis by either RPLC or GC.

The water used for partition coefficient measurements, however, was not presaturated with 1-octanol or *n*-hexadecane. *n*-Hexadecane has a low solubility in water

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* 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 nor does it imply that the products are necessarily the best available for the purpose.

[$33.8 \cdot 10^{-10}$ mol/l at 25°C (ref. 24)]. For 1-octanol, it has been reported[25] that the solubilities in water are identical within experimental error to those in octanol-saturated water.

The activity coefficients in hexadecane and octanol were determined by GC for the alkanes, alkenes, alcohols, bromoalkanes, and alkylbenzenes. The stationary phases, 1-octanol or *n*-hexadecane, were coated onto the support material, Chromosorb W-HP, 100–120 mesh, and the weight percent of coating was determined by an ashing method[26]. In the case of the 1-octanol phase, two different weight percent coatings were used, 6.93 ± 0.08% and 15.97 ± 0.04%. For *n*-hexadecane, only one weight percent coating was used, 11.84 ± 0.05%. Stainless-steel columns [1/8 in. (3.2 mm) O.D.], both 3 ft. (90 cm) and 1.5 ft. (45 cm) lengths, were packed with known amounts of coated support and connected to a heated injection port and a thermal conductivity detector. The column temperature was controlled by a water bath at 25.0 ± 0.1°C.

A Nagretti–Zamba precision pressure regulator was used to regulate the column inlet pressure which was measured by determining the difference in mercury heights in a U-tube. The carrier gas (helium) flow-rate through the column was measured by connecting a soap bubble flow-meter to the outlet of the thermal conductivity detector. Flow-rates were taken periodically throughout a series of runs.

The peak midpoint at which retention times were determined was found by drawing tangents at points of inflection on both sides of the peak, extrapolating to baseline and thereby finding the midpoint[27]. Since the retention times decreased as the experiment progressed due to column loss of the 1-octanol and *n*-hexadecane, benzene was used as a reference retention time standard and injected with each solute. The measured retention times were then corrected for any bleeding using the reference solute retention time.

The solute specific retention volumes were calculated using eqn. 16, and the corrected activity coefficients were calculated using eqn. 17. The physical properties needed for these calculations can be found in refs. 28–33. Considering the uncertainties in experimental determinations and required constants for calculations, the uncertainty in the activity coefficients is less than 2%.

RESULTS AND DISCUSSION

The results for the activity coefficients in octanol ($\gamma_{a(o)}$), hexadecane ($\gamma_{a(h)}$), and water ($\gamma_{a(b)}$) are given in Table I for octanol–water and Table II for hexadecane–water. Also given in the tables are the partition coefficients calculated using eqns. 12 and 13 and those determined experimentally by the generator column technique. To check the validity of the alcohol in hexadecane activity coefficients, literature values for the specific retention volumes of 1-butanol in *n*-heptadecane[26] and 1-butanol in *n*-octadecane[34] as a function of temperature were extrapolated to 25°C, and the activity coefficients were calculated. The ln γ value obtained for 1-butanol in heptadecane is 4.61 and for 1-butanol in octadecane is 4.84. Extrapolating the above values to *n*-hexadecane at 25°C, one finds ln γ = 4.38 compared to the activity coefficient for 1-butanol in hexadecane determined here of 4.42 (Table II).

As can be seen in Tables I and II except for the case of the hexadecane–water partition coefficients for the alcohols, the agreement between the partition coefficients

TABLE I

RELATIONSHIP BETWEEN VOLUME-FRACTION-BASED ACTIVITY COEFFICIENTS IN WATER ($\gamma_{a(b)}$) AND OCTANOL ($\gamma_{a(o)}$) AND THE OCTANOL–WATER PARTITION COEFFICIENTS

Compound	*ln* $\gamma_{a(b)}$	*ln* $\gamma_{a(o)}$*	*ln* K_{o-w}		
			*Calculated***	*Experimental*	*Calc. − Exp.*
Benzene	5.96	1.39 (1.30)	4.57	4.63	−0.06
Toluene	7.30	1.23 (1.17)	6.07	6.10	−0.03
Ethylbenzene	8.45	1.22 (1.17)	7.23	7.21	0.02
n-Propylbenzene	9.72	1.18 (1.14)	8.54	8.50	0.04
n-Butylbenzene	11.03	1.03	10.00	9.88	0.12
n-Pentane	9.65	1.36 (1.28)	8.29	8.34	−0.05
n-Hexane	10.89	1.32 (1.22)	9.57	9.46	0.11
n-Heptane	12.16	1.28 (1.19)	10.88	10.73	0.15
n-Octane	13.35	1.28 (1.18)	12.07	11.93	0.14
n-Hex-1-ene	9.16	1.33 (1.16)	7.83	7.81	0.02
n-Hept-1-ene	10.55	1.21	9.34	9.19	0.15
n-Oct-1-ene	12.07	1.20 (1.10)	10.87	10.52	0.35
n-Non-1-ene	13.38	1.16 (1.08)	12.22	11.86	0.36
1-Bromobutane	7.46	1.37 (0.86)	6.09	6.33	−0.24
1-Bromopentane	8.96	1.31	7.65	7.76	−0.11
1-Bromohexane	9.99	1.23	8.76	8.75	0.01
1-Bromoheptane	11.35	1.12	10.23	10.04	0.19
1-Bromooctane	12.64	0.93	11.71	11.26	0.45
1-Butanol	2.56	0.75 (0.77)	1.85	1.81	0.04
1-Pentanol	4.24	0.68	3.56	3.52	0.04
1-Hexanol	5.25	0.53	4.72	4.67	0.05
1-Heptanol	6.45	0.54	5.91	5.92	−0.01

* Numbers in parentheses are preliminary results from Tewari *et al.*[17].

** $\ln K_{o-w} = \ln \gamma_{a(b)} - \ln \gamma_{a(o)}$.

calculated from the activity coefficients and those determined experimentally is relatively good. This indicates that the assumption concerning the equivalence between the activity coefficients in octanol- or hexadecane-saturated water and pure water and those in water-saturated octanol or hexadecane and pure octanol or hexadecane is good.

Aveyard and Mitchell[35] also determined hexadecane–water partition coefficients for some 1-alcohols. The ln K_{h-w} values which they determined are[35]: −1.08 for 1-butanol, −0.90 for 1-pentanol, 0.25 for 1-hexanol, and 1.77 for 1-heptanol. These values, except for 1-butanol, are less than those determined by the generator column technique or calculated from the activity coefficients. Given that the alcohol activity coefficients agreed with the literature values, there is an indication of deviation from infinite dilution or limiting behavior in the hexadecane phase during the actual partitioning experiment. Costas and Patterson[4] noted self-association of alcohols in alkane solvents through hydrogen bonds for methanol in *n*-hexane, 1-hexanol in dodecane, and 1-decanol in decane.

When considering activity coefficients in water, one must be concerned whether calculating them from the aqueous solubility gives a value comparable to the infinite dilution activity coefficient. Medir and Giralt[36] reported infinite dilution activity

TABLE II

RELATIONSHIP BETWEEN VOLUME-FRACTION-BASED ACTIVITY COEFFICIENTS IN WATER ($\gamma_{a(b)}$) AND HEXADECANE ($\gamma_{a(h)}$) AND THE HEXADECANE–WATER PARTITION COEFFICIENT (K_{h-w})

Compound	*ln* $\gamma_{a(b)}$	*ln* $\gamma_{a(h)}$	*ln* K_{h-w}		
			*Calculated**	*Experimental*	*Calc. – Exp.*
Benzene	5.96	1.28	4.67	4.77	−0.10
Toluene	7.30	1.04	6.26	6.24	0.02
Ethylbenzene	8.45	1.01	7.44	7.41	0.03
n-Propylbenzene	9.72	0.87	8.85	8.82	0.03
n-Butylbenzene	11.03	0.76	10.27	10.50	−0.23
n-Pentane	9.65	0.83	8.82	9.21	−0.39
n-Hexane	10.89	0.74	10.15	10.22	−0.07
n-Heptane	12.16	0.62	11.54	11.95	−0.41
n-Octane	13.35	0.53	12.82	13.01	−0.19
n-Hex-1-ene	9.16	0.78	8.38	8.82	−0.44
n-Hept-1-ene	10.55	0.69	9.86	9.86	0.00
n-Oct-1-ene	12.07	0.58	11.49	11.12	0.37
n-Non-1-ene	13.38	0.55	12.83	12.34	0.49
1-Bromobutane	7.46	1.18	6.28	6.68	−0.40
1-Bromopentane	8.96	1.06	7.90	8.20	−0.30
1-Bromohexane	9.99	0.93	9.06	8.98	0.08
1-Bromoheptane	11.35	0.80	10.55	10.48	0.07
1-Butanol	2.56	4.42	−1.86	−2.22	0.36
1-Pentanol	4.24	4.37	−0.13	−0.70	0.57
1-Hexanol	5.25	4.26	0.99	1.23	−0.24
1-Heptanol	6.45	3.98	2.47	2.53	−0.06

* $\ln K_{h-w} = \ln \gamma_{a(b)} - \ln \gamma_{a(h)}$.

coefficients for several organic compounds in water. Representative values are given in Table III along with the activity coefficients calculated from the aqueous solubilities. Note that there is relatively good agreement between all of the values indicating that the solubility calculation is a reasonable method for determining activity coefficients in water.

A linear relationship between ln K_{o-w} and solute molar volume, V_a^*, and ln K_{h-w} and V_a^* is suggested by the lattice model, eqns. 23 and 24. The plots are shown in Figs. 1 and 2 for K_{o-w} and K_{h-w}, respectively. Note that for the hexadecane–water partition coefficients of the alcohols, the ln K_{h-w} calculated from the activity coefficients (Table II) are used.

In eqns. 23 and 24, one notes that the slopes of either ln K_{o-w} *versus* V_a^* or ln K_{h-w} *versus* V_a^* should be the same for all functional group solutes. For the octanol–water partition coefficients, the following slopes were found: alkylbenzenes 0.077, alkanes 0.076, alkenes 0.083, bromoalkanes 0.073, and alcohols 0.082. The slopes for the hexadecane–water system are: alkylbenzenes 0.083, alkanes 0.082, alkenes 0.073, bromoalkanes 0.072, and alcohols 0.085. (If one uses the experimental ln K_{h-w} values for the alcohols to plot against V_a^*, the slope found is 0.103 which may indicate self-association of the alcohols in the hexadecane phase.)

Looking back at the respective slopes for the octanol–water and hexa-

TABLE III

COMPARISON OF MOLE-FRACTION-BASED ACTIVITY COEFFICIENTS IN WATER DETERMINED AT INFINITE DILUTION $(\gamma^{\infty}_{a(b)})$ AND CALCULATED FROM AQUEOUS SOLUBILITIES $(\gamma^{SOLUB}_{a(b)})$

Compound	*ln* $\gamma^{\infty}_{a(b)}$*	*ln* $\gamma^{SOLUB}_{a(b)}$**
n-Pentane	11.55	11.51
n-Hexane	13.13	12.88
n-Heptane	14.46	14.26
n-Octane	16.08	15.55
n-Hex-1-ene	11.45	11.10
n-Oct-1-ene	14.65	14.24
Benzene	7.78	7.56
Toluene	9.20	9.08
Ethylbenzene	10.57	10.37
n-Propylbenzene	11.75	11.77
n-Butylbenzene	13.29	13.19
Biphenyl	12.98	14.05

* Medir and Giralt[36].

** From solubility data reported in ref. 23.

decane–water partition coefficients *versus* solute molar volume (eqns. 23 and 24), one notes that both slopes are dominated by the X_{13} term, as mentioned previously. Therefore, one would expect the octanol–water and hexadecane–water slopes to be close to one another which they are. The average value of the slope for the octanol–water system is 0.078 and for the hexadecane–water system is 0.079.

Molar volume correlations could prove beneficial in predicting partition coefficients for other members of solute classes. The data obtained and the lattice model, however, do not predict the "leveling off" of the partition coefficients at higher molecular volumes suggested by Mackay *et al.*[37].

Having determined the partition coefficients in two different solvent systems, it is interesting to examine the relationship between the partition coefficients. Using the lattice model theory, eqn. 31 predicts a linear relationship between the octanol–water and hexadecane–water partition coefficients of the form:

$$\ln K_{o-w} = \ln K_{h-w} + an_{CH_2} + b \tag{32}$$

A plot of ln K_{o-w} *versus* ln K_{h-w} for a given homologous series should show some dependence on solute chain-length through the an_{CH_2} term. This may lead to skewing and a slope which is slightly different from unity. Note that the slope would be unity if the intercept ($an_{CH_2} + b$) were independent of solute size.

The plots of ln K_{o-w} *versus* ln K_{h-w} are shown in Fig. 3. Note that for the alcohols, the K_{h-w} values calculated from the activity coefficient data (Table II) are used for the correlations since some aggregation of the alcohols in the hexadecane phase during partitioning is suspected. The slopes are close to unity. They are: for the alkylbenzenes 0.92, alkanes 0.91, alkenes 1.14, bromoalkanes 1.02, and alcohols 0.96. Since none of the slopes is unity, the suspected dependence of the intercept on solute size does occur. Such linearity between partition coefficients from two solvent

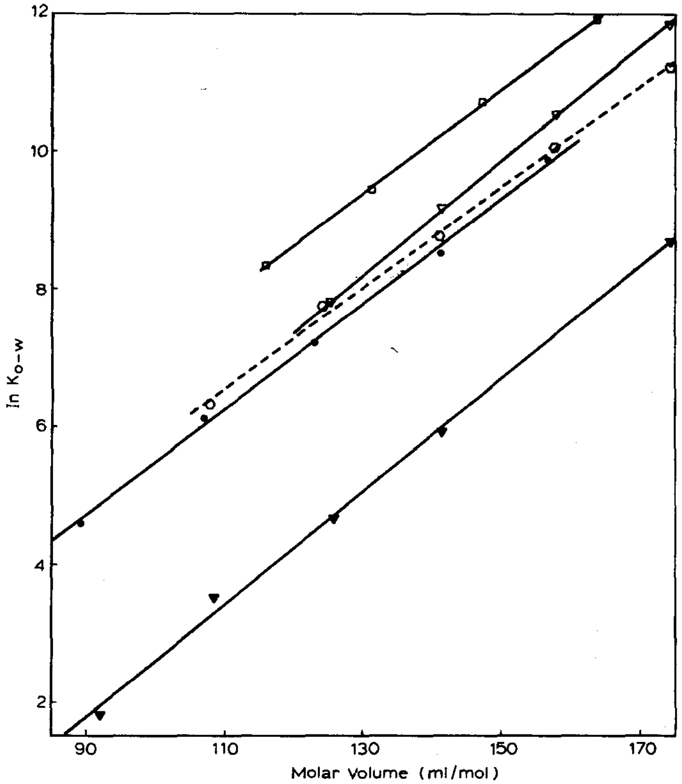

Fig. 1. Plots of ln K_{o-w} *versus* molar volume of the solute. Alkylbenzenes (●): ln K_{o-w} = 0.077 (±0.003)V_s^* − 2.16 (±0.03), r^2 = 0.999 (±0.019). Alkanes (□): ln K_{o-w} = 0.076 (±0.004)V_s^* − 0.43 (±0.01), r^2 = 0.999 (±0.014). Alkenes (▽): ln K_{o-w} = 0.083 (±0.001)V_s^* − 2.58 (±0.06), r^2 = 0.999 (±0.037). Bromoalkanes (○): ln K_{o-w} = 0.073 (±0.003)V_s^* − 1.50 (±0.10), r^2 = 0.998 (±0.013). Alcohols (▼): ln K_{o-w} = 0.082 (±0.003)V_s^* − 5.54 (±0.08), r^2 = 0.997 (±0.018). The values in parentheses indicate the standard deviations of the slope, intercept, and coefficient of determination, respectively, for each equation (Figs. 2–4).

systems occurs if the primary solvation forces in the two solvent systems or solutes under consideration are sufficiently similar[38], *i.e.*, solutes in a homologous series as reported here.

Watari *et al.*[39] examined the partitioning of chlorobenzene and bromobenzene derivatives in a heptane–water system and in a 1-octanol–water system. These workers observed no significant difference in the interaction energies of 1-octanol and heptane and concluded that partition coefficients are governed principally by differences in cavity formation energy. However, Lyman *et al.*[40] observed a poor correlation between the partition coefficients for alcohols in a heptane–water and 1-octanol–water system (r^2 = 0.584). This poor fit was attributed to hydrogen bonding between solutes in the heptane phase. Octanol which dissolves a greater amount of water than heptane tends to inhibit solute–solute hydrogen bonding[40]. The data presented here do not indicate a poorer correlation for the alcohols between *n*-hexadecane–water and 1-octanol–water systems (r^2 = 0.998), probably because the

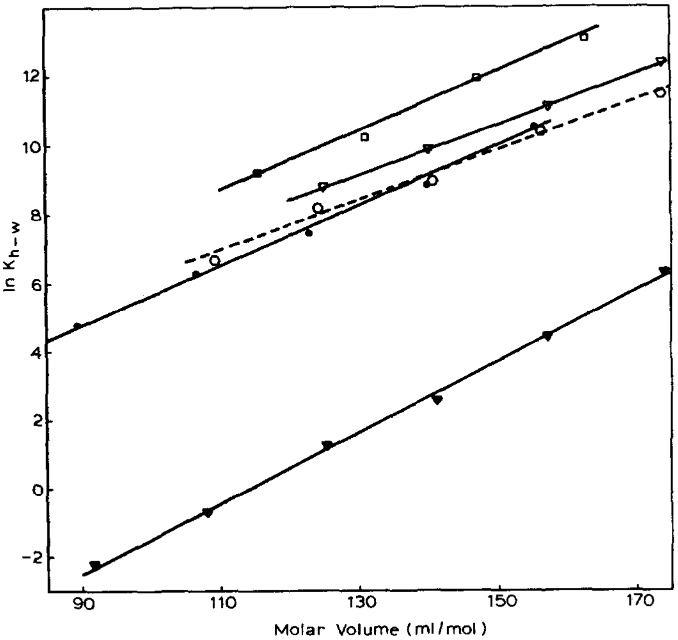

Fig. 2. Plots for ln K_{h-w} *versus* molar volume of the solute. Alkylbenzenes (●): ln K_{h-w} = 0.083 (±0.003)V_2^* − 2.71 (±0.04), r^2 = 0.997 (±0.019). Alkanes (□): ln K_{h-w} = 0.082 (±0.002)V_2^* − 0.40 (±0.01), r^2 = 0.989 (±0.022). Alkenes (▽): ln K_{h-w} = 0.073 (±0.003)V_2^* − 0.36 (±0.01), r^2 = 0.998 (±0.014). Bromoalkanes (○): ln K_{h-w} = 0.072 (±0.002)V_2^* − 0.96 (±0.02), r^2 = 0.992 (±0.016). Alcohols (▼): ln K_{h-w} = 0.085 (±0.003)V_2^* − 9.58 (±0.10), r^2 = 0.992 (±0.021).

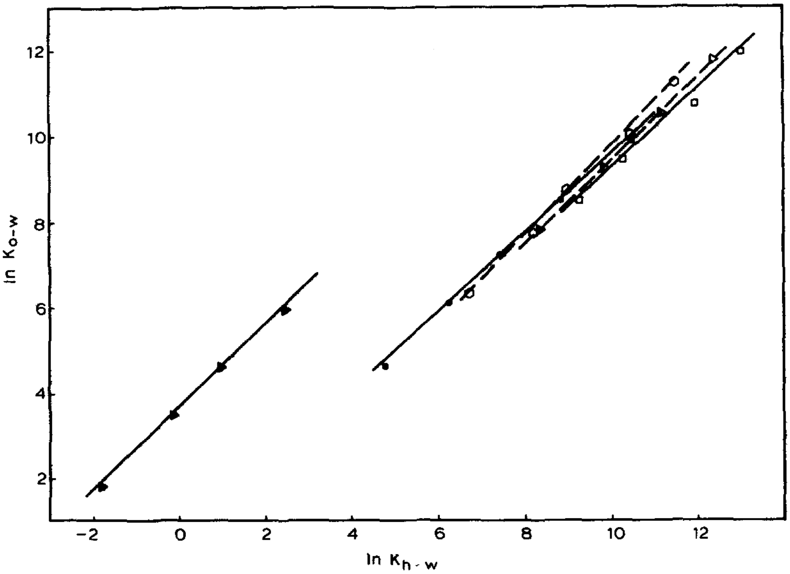

Fig. 3. Plots of ln K_{o-w} *versus* ln K_{h-w}. Alkylbenzenes (●): ln K_{o-w} = 0.92 (±0.02) ln K_{h-w} + 0.34 (±0.01), r^2 = 0.998 (±0.026). Alkanes (□): ln K_{o-w} = 0.91 (±0.02) ln K_{h-w} + 0.03 (±0.00), r^2 = 0.992 (±0.015). Alkenes (▽): ln K_{o-w} = 1.14 (±0.03) ln K_{h-w} − 2.14 (±0.03), r^2 = 0.998 (±0.019). Bromoalkanes (○): ln K_{o-w} = 1.02 (±0.02) ln K_{h-w} − 0.48 (±0.01), r^2 = 0.997 (±0.018). Alcohols (▼): ln K_{o-w} = 0.96 (±0.05) ln K_{h-w} + 3.63 (±0.09), r^2 = 0.998 (±0.032).

activity coefficients are used to calculate the hexadecane–water partition coefficients. The alcohols do, however, fall outside the cluster of the other data (Fig. 3).

As seen in eqn. 30, the lattice model validates the idea of additivity of free energies of transfer, *i.e.* the octanol–water partition coefficient can be divided into contributions to the free energies of transfer from the methyl, methylene, and functional groups. The group contributions to ln K_{o-w} calculated from this data are compared to those compiled by Hansch and Leo[2] in Table IV. The comparison between the group contributions determined here and those compiled by Hansch and Leo[2] is fairly good.

Also given in Table IV is the free energy of transfer from water to octanol (ΔG_i) for each solute group (i). Note that a negative ΔG_i implies favorable conditions for transfer from water to octanol; whereas, positive ΔG_i implies unfavorable conditions for the transfer. For the solute groups studied, only the hydroxy group of the alcohols preferred to remain in the water phase as compared to the octanol phase.

The group contributions and free energies of transfer depend on intrinsic energetics of the solutes and solvents and the size of the solute group. The ratio of the group contribution for the methyl group to that for the methylene group is 1.65 which is larger than the ratio of the respective group volumes (1.34) or group areas (1.57). This suggests that the segmental interaction parameter between the methyl group and water (X_{CH_3-3}) is greater than that between the methylene group and water (X_{CH_2-3}).

As noted in the introduction, several workers have correlated capacity factors (k') obtained from RPLC measurements with K_{o-w} values. This is indeed a rapid and widely applicable method for determining K_{o-w} values; however, Veith *et al.*[7] had a mean standard deviation of 0.64 in log K_{o-w} for eighteen compounds. This poor correlation is probably due to differences in hydrogen bonding properties of the two systems. Camps *et al.*[16] noted that the correlation coefficients obtained by correlating K_{o-w} with k' increased with decreasing methanol percentages. The r^2 values which they obtained for these plots were 0.759 for water–methanol (10:90), 0.949 for water–methanol (30:70), and 0.984 for 100% water as the mobile phase.

Martire and Boehm[41] noted that neglecting the effect of the –OH group on

TABLE IV

GROUP CONTRIBUTIONS TO OCTANOL–WATER PARTITION COEFFICIENT (ln K_{o-w})

Group	*π*		*ΔG_{o-w}*** *(cal/mol)*
	*Experimental**	*From ref. 2*	
$-CH_3$	2.13	2.05	−1263
$-CH_2-$	1.30	1.24	− 770
$CH_2=CH_2$	1.86	2.03	−1102
–Phenyl ring	3.89	4.37	−2307
–Br	0.18	0.46	− 105
–OH	−3.91	−3.78	2317

* Determined from data in Table I.

** Free energies of transfer from water to octanol ($RT \ln K_{o-w} = -\Delta G_{o-w}$) calculated using experimental data.

TABLE V

RELATIONSHIP BETWEEN ln K_{o-w} AND ln $V_n(\Phi_b = 1)$

Compound	*ln $V_n(\Phi_b = 1)$**	*ln K_{o-w}*
Benzene	6.20	4.63
Biphenyl	11.82	8.66
Toluene	7.91	6.10
Ethylbenzene	9.37	7.21
n-Propylbenzene	11.27	8.50
n-Butylbenzene	12.74	9.88
n-Pentylbenzene	14.12	11.28
n-Hexylbenzene	15.71	12.71
n-Heptane	13.80	10.73
n-Butanol	2.68	1.81
n-Pentanol	4.22	3.52
n-Hexanol	6.60	4.67
n-Heptanol	7.75	5.92

* Ref. 16: adjusted retention volumes using the 25 cm Zorbax ODS column thermostatted at 25°C extrapolated to 100% water (from methanol–water mixtures) as the mobile phase (Φ_b = 1).

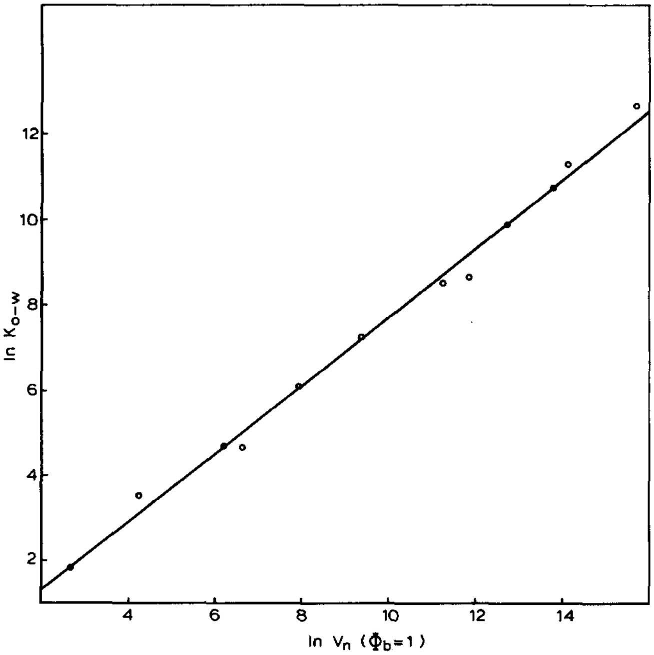

Fig. 4. Correlation between ln K_{o-w} and ln V_n (Φ_b = 1). ln K_{o-w} = 0.81 (±0.02) ln V_n (Φ_b = 1) − 0.34 (±0.01), r^2 = 0.993 (±0.023).

1-octanol, the main difference between the RPLC capacity factor in pure water and K_{o-w} is the translational freedom and structure of the respective hydrocarbon phases. This implies that by extrapolating the capacity factors to pure water, one can obtain a reasonable estimate of K_{o-w}. Thus and Kraak[42] also found that the correlation for k' at 100% water was better with K_{o-w} than k' at a fixed mobile phase composition. Jinno[43], however, found that extrapolation to 100% water was no better than at other compositions.

Using adjusted retention volumes (V_n) determined on a 25 cm × 4.6 mm I.D. Zorbax ODS column extrapolated to 100% water at 25°C (ref. 16), ln K_{o-w} are correlated with RPLC retention volumes. For the adjusted retention volumes, ^2H_2O was used as the unretained solute. The data are given in Table V and plotted in Fig. 4. The correlation between ln K_{o-w} and ln V_n at 100% water, $\Phi_b = 1$, is fairly good, $r^2 = 0.993$. This indicates that Martire and Boehm[41] may be correct in suggesting that by extrapolating the capacity factors (or adjusted retention volumes) to pure water, one can obtain reasonable estimates of K_{o-w}.

CONCLUSIONS

The lattice model theory developed suggests and the data gathered using the generator column technique confirm that the partitioning characteristics of organic solutes are predictable from other partitioning measurements, molar volumes, group contributions, or ODS retention properties. Octanol–water partition coefficients and hexadecane–water partition coefficients are linearly related to each other (approximately) and to solute molar volume for the solute group types studied. These partition coefficients may also be calculated with reasonable accuracy from the solute activity coefficients in either octanol or hexadecane determined by GC and in water calculated from the aqueous solubilities. Therefore, at least for these two solvent systems, the influences from mutual solubility of the two phases are minimal. The octanol–water partition coefficient is also separable into group contributions from the methyl, methylene, and functional groups.

Relating the octanol–water partitioning data to retention in RPLC, one finds that partition coefficients may be reasonably predicted from adjusted retention volumes extrapolated to 100% water as the mobile phase. Therefore, neglecting the effect of the –OH group on 1-octanol, the main difference between the reversed-phase retention volume in pure water and octanol–water partitioning is the translational freedom and structure of the respective hydrocarbon phases as suggested earlier[41].

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