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Partition Coefficients of Organic Compounds in Lipid-Water Systems and Correlations with Fish Bioconcentration Factors

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■ Triolein-water partition coefficients (K_{tw}) have been determined for 38 slightly water-soluble organic compounds, and their magnitudes have been compared with the corresponding octanol-water partition coefficients (K_{ow}). In the absence of major solvent-solute interaction effects in the organic solvent phase, the conventional treatment (based on Raoult's law) predicts sharply lower partition coefficients for most of the solutes in triolein because of its considerably higher molecular weight, whereas the Flory-Huggins treatment predicts higher partition coefficients with triolein. The data are in much better agreement with the Flory-Huggins model. As expected from the similarity in the partition coefficients, the water solubility (which was previously found to be the major determinant of the K_{ow}) is also the major determinant for the K_{tw} . When the published BCF values (bioconcentration factors) of organic compounds in fish are based on the lipid content rather than on total mass, they are approximately equal to the K_{tw} , which suggests at least near equilibrium for solute partitioning between water and fish lipid. The close correlation between K_{tw} and K_{ow} suggests that K_{ow} is also a good predictor for lipid-water partition coefficients and bioconcentration factors.

Introduction

A major problem in environmental contamination by pollutants is the extent that these pollutants may concentrate from water into aquatic organisms such as fish (1-12). The extent of such concentration is expressed as the bioconcentration factor (BCF), i.e., by the ratio of the steady-state concentration of a chemical in the organism (or a part of it) to that in water. It has been generally assumed that the mechanism leading to the uptake of organic pollutants by organisms is analogous to the partitioning between an organic phase and water. Hence, log (BCF) values of organic compounds from both laboratory bioconcentration testings and natural water systems have been correlated either with the corresponding octanol-water partition coefficients (log K_{ow}) (1, 2, 4-9, 11-13) or with their water solubilities (log S) (2, 3, 5, 6, 9, 11), to which the log K_{ow} are strongly correlated (3, 14).

Reinert (15), Anderson and Fenderson (16), Roberts et al. (17), and Sugiura et al. (18) found that concentrations of various organic compounds accumulated in fish are determined largely by fish lipid content. Hansen et al. (19) showed that residual PCB contents vary considerably in different tissues of fish, presumably because of variations in lipid content. BCF values of various chlorinated compounds in laboratory bioconcentration studies of K  nemann and van Leeuwen (8) with guppies, and of Oliver and Nimi (12) with rainbow trout, show about the same magnitudes for the same compounds, when BCF values are expressed in terms of fish lipid content. These results indicate that the lipid fraction of aquatic organisms (fish) is an important controlling factor in the bioconcentration of relatively insoluble organic compounds. The importance of lipids in bioconcentration has also been speculated in correlation analysis (8, 9, 11, 12, 18).

To better understand the effect of lipids in bioconcentration, it is of both theoretical and practical interest to examine the partition characteristics of organic compounds in lipid-water systems. This information may serve as a basis for validating the use of empirical parameters (such as log K_{ow} and log S) in the assessment of bioconcentration and for characterizing the lipophilicity of organic compounds in biochemical studies. Apart from the study by Platford (20) on the partition coefficients of three compounds (hexane, benzene, and carbon tetrachloride) in lipid (triolein)-water systems, an in-depth analysis of the subject has not been reported. The primary objectives of this study are therefore to identify the thermodynamic factors affecting the lipid-water partition coefficient (K_{tw}) and to evaluate the relationship between K_{tw} , K_{ow} , and BCF. Triolein (glyceryl trioleate) is selected in this study as the model lipid because of its abundance and its structural similarity to other triglycerides in organisms and because it is a liquid at room temperature.

Raoult's law based equation describing the partitioning of slightly water-soluble organic solutes in a solvent-water mixture, in which the solvent has small solubility in water, is given by (14)

$$\log K = -\log S - \log \bar{V}_o^* - \log \gamma_o^* - \log (\gamma_w/\gamma_w^*) \quad (1)$$

where K is the solute partition coefficient, S is the molar water solubility of the liquid or supercooled liquid solute (mol/L), \bar{V}_o^* is the molar volume of water-saturated organic phase (L/mol), γ_o^* is the solute activity coefficient (Raoult's law convention) in water-saturated solvent phase, γ_w is the solute activity coefficient in water, and γ_w^* is the solute activity coefficient in solvent-saturated water. Equation 1 has been used to analyze the relative significance of log S , log γ_o^* , and log (γ_w/γ_w^*) on log K of the solute in solvent-water systems (e.g., octanol-water and heptane-water) (14, 21), where the size difference between solute and solvent is generally small. We know, however, from the work of Flory and Huggins (22-24) that eq 1 is inappropriate for describing the partitioning of ordinary solutes into a macromolecular phase, because it does not take into account any size disparities between solute and solvent. The Flory-Huggins treatment (25) leads to the expression for the partition coefficients of dilute solutes between a macromolecular phase and water as

$$\log K = -\log S\bar{V} - (1 - \bar{V}/\bar{V}_o^*)/2.303 - \chi/2.303 - \log (\gamma_w/\gamma_w^*) \quad (2)$$

where \bar{V} is the molar volume of the solute, \bar{V}_o^* is the molar volume of water-saturated polymer phase, and χ is the Flory-Huggins interaction parameter, a sum of excess enthalpic (χ_H) and excess entropic (χ_S) contributions to the solute-polymer interaction. The magnitude of χ_S depends presumably on the characteristics of the polymer network that affect the orientation of the chain segment (26, 27). For triolein in liquid state at room temperature, χ_S should approximate zero because of flexibility of the hydrocarbon chain to assume various orientations. The $\chi_H/2.303$ term in eq 2 is equivalent to the log γ_o^* term in

eq 1. In the absence of size disparity (i.e., $\bar{V}_o^* = \bar{V}$), eq 2 is thus equivalent to eq 1.

The fundamental difference between the predictions of eq 1 and 2 may be illustrated for systems in which one postulates no excess enthalpic or entropic interactions between solute and solvent (i.e., $\chi = 0$) and where, for simplicity, there is effectively zero water miscibility of the solvent (i.e., where $\log(\gamma_w/\gamma_w^*)$ is zero). Let us consider what happens to the partition coefficient of a solute as we increase the molecular weight of the solvent to macromolecular magnitudes. Equation 2 predicts an asymptotic approach of $\log K$ to some constant value. To the extent that this constancy is followed, it can be accounted for on the basis of eq 1 only by making activity coefficient (γ_o^*) inversely proportional to an increasingly large solvent molar volume. For such systems, therefore, Raoult's law model could be reconciled with the data only by assuming a vanishingly small fractional activity coefficient that is characteristic of large specific interactions for which there is no apparent physical justification.

Although triolein is not polymeric in the ordinary sense, it is an interesting solvent (in addition to its obvious biochemical significance) because of its high molar volume relative to a common solvent (e.g., octanol), which is sufficient to distinguish between the predictions of the alternative models. In this study, partition experiments were carried out for a large group of organic compounds in the triolein-water systems to determine whether or not the effects of size disparity between solute and triolein may be safely ignored and how they are best handled if they exist. We may anticipate that the data are better fit by the Flory-Huggins model in view of its recognized success for macromolecular solvent systems; therefore, the reduction in partition coefficient that one would expect from eq 1 on going from octanol to triolein (which corresponds to about a 7-fold increase in molar volume) should not materialize.

Experimental Section

Lipid triolein ($C_{57}H_{104}O_6$, also known as glyceryl trioleate) was purchased from Nu-Check Prep Inc., Elysian, MN and used without further purification. The lipid had been analyzed previously by the supplier using gas-liquid chromatography (GLC) and thin-layer chromatography (TLC) techniques; it was claimed to have a purity greater than 99%. At room temperature, the lipid is a liquid having a density of 0.915 g/mL at 15 °C. Test compounds were reagent grades or analytical standards from Aldrich, Analabs, Mallinckrodt, and Chem Service; they were used as received. The water used was distilled and filtered through an XAD-2 column to remove residual organic contaminants.

The method used for determining the triolein-water partition coefficient is virtually the same as described for the determination of octanol-water partition coefficients (3, 14). In the present study, 0.25–0.50 mL triolein containing 1000–2000 mg/L of test compounds were added to 20 mL of water. Samples were equilibrated at 20–23 °C in 30-mL screw-capped Corex centrifuged tubes (equipped with Teflon-lined lids) for 8–16 h on a reciprocating shaker. Control experiments indicated that samples of all test compounds reached equilibrium in less than 8 h with mechanical shaking, as the observed solute partition coefficients were practically time independent after this period of equilibration.

Generally, four replicate samples were prepared for each test compound. Samples were subsequently centrifuged at 20 °C at ~3500 rpm (1560g) for 1 h to attain phase separation. Aliquots of the triolein phase were removed

and stored in 2-mL microvials for subsequent dilution and analysis. Remaining triolein was then removed from the sample tubes by using suction pipets, and glass walls previously in contact with the upper triolein phase were carefully cleaned by wiping with tissue paper. To assist in complete removal of excess triolein, the tubes were recentrifuged and the cleaning procedure repeated, as it was observed that residual triolein has a tendency to slide down the glass wall and form droplets on newly cleaned water surfaces. Following this procedure, aliquots of aqueous samples (normally, 10 mL) were removed with pipets and concentrated, when necessary, by extraction with hexane or heptane for subsequent analysis. Partition coefficients of test compounds were calculated as ratios of the concentrations in the triolein phase to those in the aqueous phase. For each compound, $\log K_{tw}$ values of the four replicate samples were averaged. Standard deviations were generally less than 0.05 for compounds with average $\log K_{tw} < 3.00$, less than 0.10 with $3.00 < \log K_{tw} \leq 5.50$, and less than 0.14 for a few compounds with $\log K_{tw} > 5.50$. For DDT and some PCBs, which have high $\log K_{tw}$ values, experiments had been carried out with more than four replicate samples to enhance accuracies; in many instances, experiments were repeated until nearly constant $\log K_{tw}$ values were obtained.

Determinations of the concentrations of most simple benzene derivatives lacking electron-capture (EC) sensitivity (most of compounds 1–15 in Table I) were done by UV. The triolein phase was diluted with heptane; the aqueous phase was analyzed either directly, or as concentrated heptane extracts (as for benzene and other relatively nonpolar compounds). Interference in UV absorption by the residual triolein in diluted samples was corrected through a blank containing equal amounts of triolein in heptane. In some cases, when concentrations of the aqueous phase had insufficient sensitivity, analyses were done by high-pressure liquid chromatography (HPLC) using a C-18 column, with methanol-water mixture as the mobile phase. Concentration analysis for compounds containing multiple chlorine atoms was carried out by GC with (^{63}Ni) EC detectors, which eliminated the triolein background problem. Whenever possible, the same technique was used to analyze concentrations in both phases. Finally, the solubility of water in triolein was determined by the standard Karl-Fisher titration method.

Results and Discussion

Determined triolein-water partition coefficients (K_{tw}), octanol-water partition coefficients (K_{ow}), solubilities in water (S), and molar volumes (\bar{V}) of 38 organic compounds at room temperatures (20–25 °C) are listed in Table I. The S values for solid solutes are values of the corresponding supercooled liquids, calculated from solid solubilities, heats of fusion ($\Delta\bar{H}_f$), and melting points (T_m) according to the method described earlier (14). For 1,2,3-trichlorobenzene, 1,3,5-trichlorobenzene, 1,2,3,4-tetrachlorobenzene, 1,2,3,5-tetrachlorobenzene, and pentachlorobenzene, which have low melting points (<370 K), calculations were made with the assumption of $\Delta\bar{H}_f = 13.5T_m$, along with solid solubilities of 16.3, 10.6, 7.18, 3.23 and 0.385 mg/L, respectively, at 23 °C. Similarly, the molar volumes are those for the solutes in the liquid state. Densities of 1,2,3-trichlorobenzene, 1,2,3,4-tetrachlorobenzene, pentachlorobenzene, hexachlorobenzene, and DDT at their melting points were determined and used to calculate their \bar{V} values. Liquid molar volumes of 1,3,5-trichlorobenzene and 1,2,3,5-tetrachlorobenzene were assumed to be the same as those of 1,2,3-trichlorobenzene and 1,2,3,4-tetrachlorobenzene, respectively. Liquid molar volumes of PCBs were

Table I. Water Solubilities (S), Liquid Molar Volumes (\bar{V}), and Partition Coefficients (K) of Selected Organic Compounds in Triolein-Water and Octanol-Water Systems: $K_{ow} = K(\text{Octanol-Water})$ and $K_{tw} = K(\text{Triolein-Water})$

	compound	\bar{V} , L/mol ^a	log S , mol/L ^b	log $S\bar{V}$	log K_{ow} ^c	log K_{tw} ^d
1	aniline	0.0911	-0.405	-1.45	0.90	0.91
2	<i>o</i> -toluidine	0.107	-0.817	-1.79	1.29	1.24
3	benzaldehyde	0.102	-1.51	-2.50	1.48	1.58
4	acetophenone	0.117	-1.31	-2.24	1.58	1.61
5	anisole	0.109	-1.85	-2.82	2.11	2.31
6	benzene	0.0894	-1.64	-2.69	2.13	2.25
7	toluene	0.106	-2.25	-3.22	2.69	2.77
8	nitrobenzene	0.102	-1.78	-2.77	1.85	2.15
9	ethylbenzene	0.123	-2.84	-3.75	3.15	3.27
10	<i>n</i> -propylbenzene	0.139	-3.30	-4.16	3.68	3.77
11	1,3,5-trimethylbenzene	0.139	-3.09	-3.95	3.42	3.56
12	fluorobenzene	0.0938	-1.80	-2.83	2.27	2.33
13	chlorobenzene	0.102	-2.36	-3.35	2.84	2.97
14	bromobenzene	0.105	-2.55	-3.53	2.99	3.12
15	iodobenzene	0.112	-2.78	-3.73	3.25	3.42
16	1,2-dichlorobenzene	0.113	-2.98	-3.98	3.38	3.51
17	1,3-dichlorobenzene	0.114	-3.04	-3.98	3.38	3.63
18	1,4-dichlorobenzene	0.118	(-3.03)	-3.96	3.39	3.55
19	hexachloroethane				4.14	4.21
20	1,2,3-trichlorobenzene	0.125	(-3.74)	-4.64	4.14	4.19
21	1,2,4-trichlorobenzene	0.125	-3.72	-4.62	4.02	4.12
22	1,3,5-trichlorobenzene	0.125	(-3.82)	-4.72	4.31	4.36
23	1,2,3,4-tetrachlorobenzene	0.142	(-4.24)	-5.09	4.60	4.68
24	1,2,3,5-tetrachlorobenzene	0.142	(-4.53)	-5.38	4.59	4.69
25	1,2,4,5-tetrachlorobenzene	0.142			4.70	4.70
26	hexachlorobutadiene	0.158	-5.01	-5.81	4.90	5.04
27	pentachlorobenzene	0.166	(-5.18)	-5.96	5.20	5.27
28	hexachlorobenzene	0.186	(-5.57)	-6.30	5.50	5.50
29	biphenyl	0.155	(-3.88)	-4.69	4.09	4.37
30	2-PCB	0.174	(-4.57)	-5.33	4.51	4.77
31	2,2'-PCB	0.189	(-5.08)	-5.57	4.80	5.05
32	2,4'-PCB	0.189	(-5.28)	-5.97	5.10	5.30
33	4,4'-PCB				5.58	5.48
34	2,4,4'-PCB	0.204	(-5.98)	-6.67	5.62	5.52
35	2,5,2',5'-PCB				5.81	5.62
36	2,4,5,2',5'-PCB				6.11	5.81
37	2,4,5,2',4',5'-PCB				6.72	6.23
38	<i>p,p'</i> -DDT	0.250	(-6.74)	-7.34	6.36	5.90

^a Calculated from molecular weights and liquid densities. ^b The 20–25 °C values cited in ref 14 and 25 for all compounds, except compounds 20–27 from this work. Numbers in parentheses are for the supercooled liquids. ^c Values cited in ref 14 and 28 for all compounds, except compounds 19–27 from this work. ^d Values from this work.

approximated by using the densities of liquid Aroclor mixtures that have approximately the same chlorine numbers as the individual PCBs.

In analyzing the partition data in triolein-water systems, the molar volume of the triolein phase was calculated based on the solubility of water in triolein and on the assumption of volume additivity of the liquids (14). The water content in triolein at 25 °C was found to be 0.11% by weight (or 5.1% by mole fraction), which is in reasonable agreement with the reported value of 0.20% by weight at 37 °C (20). This gives $\bar{V}_o^* = 0.919$ L/mol, or $\log \bar{V}_o^* = -0.037$, for water-saturated triolein at room temperature. To simplify the analysis further, the term $\log (\gamma_w/\gamma_w^*) (\geq 0)$ describing the enhancement of solute solubility in water by dissolved triolein is assumed to be zero. With small mutual solubility of triglyceride and water (28), neglect of this term will not be serious for solutes with relatively large log S .

As shown in Table I, determined log K_{tw} values are generally somewhat greater than corresponding log K_{ow} values for most relatively small nonpolar organic compounds that would not be expected to form stable associations with triolein. Platford (20) reported log $K_{tw} = 2.5 \pm 0.2$ for benzene at 20–37 °C, in reasonable agreement with the value from this study. With increasing molecular size of the solute, e.g., for larger PCBs, hexachlorobenzene, and DDT, log K_{tw} and log K_{ow} values become more comparable. The large log K_{tw} values for small solutes can be

explained by eq 1 only by assuming γ_o^* to be from 0.27 to 0.42, i.e., by an ad hoc assumption of negative deviations from Raoult's law that has no physical justification and that we may at least suspect to be an artifact of the model. In a similar study (20), less-than-one γ_o^* values (0.20–0.50) were also found for hexane, benzene, and carbon tetrachloride in triolein at dilution, based on the Raoult's law theory.

The apparent negative deviations from Raoult's law of small solutes in triolein reflect presumably the result that activities of small molecules in a polymer (or a macromolecular phase) are lower than can be expected on the mole fraction basis because of the size-disparity effect (22–25), which makes eq 1 ineffective. This occurs to practically all substituted benzenes whose molecular volumes are only small fractions of the triolein molecule (i.e., $\bar{V}_o^*/\bar{V} > 6$). In support of this view, magnitude of the size effect on γ_o^* becomes progressively reduced (i.e., γ_o^* increases) as solute size increases. For instance, the calculated log γ_o^* values by eq 1 for DDT, hexachlorobenzene, and some PCBs, which have only moderate size disparity with triolein (i.e., $\bar{V}_o^*/\bar{V} = 3.7$ –5.0), are positive (i.e., $\gamma_o^* > 1$), as is normally the case for a solute in solution. It should be noted, however, that since $\log (\gamma_w/\gamma_w^*)$ can be significant for larger solutes (which is omitted in our calculations), the actual γ_o^* values may still be < 1 for some of these compounds.

According to the Flory-Huggins model, as incorporated into eq 2, activities of the two components differing in size and shape in a binary solution will always deviate from those defined by Raoult's law theory. Although this has been well recognized in those systems where components show a large size disparity, as for small molecules in triolein, it has been difficult to verify the superiority of the Flory-Huggins model to Raoult's law model when the size disparity is only moderate. Hildebrand and Sweny (29) found that component activities in the hexadecane-hexane system ($\bar{V}_2/\bar{V}_1 = 2.25$) are very close to predictions of Raoult's law. With moderate size disparity, however, the difference between the two theories is relatively small. For instance, when \bar{V}_0^*/\bar{V} is 4, the $\log \gamma_o^*$ calculated by using eq 1 differs from $\chi/2.303$ calculated by using eq 2 by only about 0.3; with $\bar{V}_0^*/\bar{V} \leq 2$, as for common solutes in octanol, the difference is reduced to less than 0.09. We therefore made no attempts to resolve the relative merits of the two theories in this case. With $\bar{V}_0^*/\bar{V} > 6$, Raoult's law model (eq 1) obviously fails to account for the solute activity in triolein.

Since eq 2 is able to accommodate the experimental $\log K_{tw}$ values of all solutes in Table I, it is therefore used as the basis for interpreting the solute behavior. By eq 2, when \bar{V}/\bar{V}_0^* is neither constant nor approaching zero, no single "ideal line" relating $\log K_{tw}$ vs. $\log S$ or $\log K_{tw}$ vs. $\log S\bar{V}$ (14, 25) can be established to describe solute incompatibilities with triolein ($\chi/2.303$). The magnitude of $\chi/2.303$ is therefore determined individually for each solute according to eq 2, with $\log (\gamma_w/\gamma_w^*)$ assumed to be zero.

The values of $\chi/2.303$ thus calculated are generally quite small but positive (<0.25) for small benzene derivatives that have relatively large $\log S$ values; respective values are somewhat greater for larger, less-soluble solutes such as 2,4'-PCB (0.32), 2,4,4'-PCB (0.81), hexachlorobenzene (0.45), and DDT (1.1). True $\chi/2.303$ values for larger solutes are likely smaller than calculated because of the neglect of $\log (\gamma_w/\gamma_w^*)$, which can be significantly greater than zero. However, since the sum of $\chi/2.303$ and $\log (\gamma_w/\gamma_w^*)$ is nevertheless small compared to $-\log S$ for all solutes and the variation of \bar{V} is also relatively small, it is evident that $\log S$ is the major factor affecting the value of $\log K_{tw}$, similar to the effect of $\log S$ on the octanol-water partition coefficient ($\log K_{ow}$) (14). The $\log K_{tw}$ values are therefore quite comparable with respective $\log K_{ow}$ values. Data in Table I show that difference between the two is generally less than 0.2 (or, a factor of 2 between K_{tw} and K_{ow}) for all compounds except 2,4,5,2',4',5'-PCB and DDT (where the $\log K_{tw}$ could be less accurate because of experimental difficulties). Small differences between $\log K_{tw}$ and $\log K_{ow}$ appear to be related to size differences of the solutes. All simple benzene derivatives that are relatively nonpolar tend to have larger values of $\log K_{tw}$ than of $\log K_{ow}$ by about 0.10-0.20. In contrast, $\log K_{tw}$ values of larger solutes (PCBs, hexachlorobenzene, and DDT) are more comparable with (and in some cases slightly smaller than) respective $\log K_{ow}$ values, a result to be further clarified with more intensive experimental work.

Because $\log S$ is the major factor affecting both $\log K_{tw}$ and $\log K_{ow}$, $\log K_{tw}$ can therefore be estimated in terms of $\log S$ (or $\log S\bar{V}$) and $\log K_{ow}$. A plot of $\log K_{tw}$ vs. $\log S\bar{V}$ is given in Figure 1 and a plot of $\log K_{tw}$ vs. $\log K_{ow}$ in Figure 2. Results show that although $\log K_{tw}$ is closely related to $\log S\bar{V}$ and to $\log K_{ow}$, the correlations are noticeably curvilinear, rather than linear, when extended over the upper range of $\log K_{tw}$. Curvature is noted more visibly at $\log K_{tw} \approx 5$ in both plots, about the point that sepa-

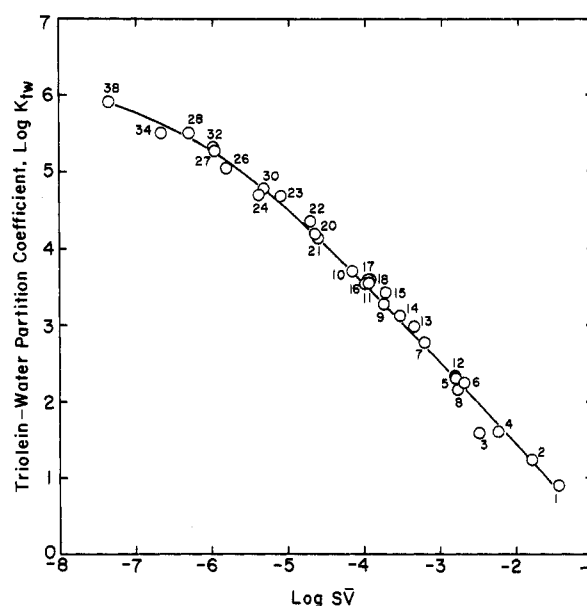


Figure 1. Plot of $\log K_{tw}$ values vs. $\log S\bar{V}$ for the selected compounds. See Table I for compound numbers.

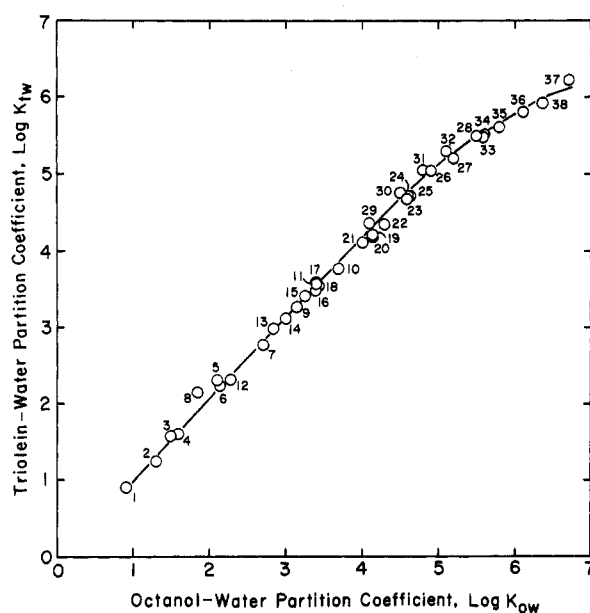


Figure 2. Correlation of $\log K_{tw}$ with $\log K_{ow}$ for the selected organic compounds. See Table I for compound numbers.

rates most benzene derivatives from relatively larger PCBs and DDT. This nonlinearity appears to result partly from the uneven size effect and partly from the difference in χ and $\log (\gamma_w/\gamma_w^*)$ on $\log K_{tw}$ for small and large solutes. According to eq 2, the size effect favors the $\log K_{tw}$ values of small molecules; consequently, a systematic increase in χ and/or $\log (\gamma_w/\gamma_w^*)$ with solutes of increasing size (of decreasing $\log S$) would result in deviations from linearity between $\log K_{tw}$ and $\log S\bar{V}$. It is possible that part of the deviation from linearity could also result from the inaccuracy of large $\log K_{tw}$ values.

Barring some unknown effects that may also contribute to the curvature in Figures 1 and 2 at high $\log K_{tw}$, the values of $\log K_{tw}$ for most substituted benzenes that have comparable molar volumes can be satisfactorily correlated in linear form with respective values of $\log S\bar{V}$ and $\log K_{ow}$. For compounds 1-25, where $\log K_{tw} < 5$, the linear regression between $\log K_{tw}$ and $\log K_{ow}$ gives

$$\log K_{tw} = 1.00 \log K_{ow} + 0.105 \quad (3)$$

Table II. Comparison of Lipid-Based Bioconcentration Factor (BCF) and Triolein-Water Partition Coefficients (K_{tw}) of Selected Organic Compounds

compound	log K_{tw}	lipid-based log (BCF)	
		guppies ^a	rainbow trout ^b
1,2-dichlorobenzene	3.51		3.51-3.80
1,3-dichlorobenzene	3.63		3.70-4.02
1,4-dichlorobenzene	3.55	3.26	3.64-3.96
hexachloroethane	4.21		3.79-4.13
1,2,3-trichlorobenzene	4.19	4.11	4.15-4.47
1,2,4-trichlorobenzene	4.12		4.19-4.56
1,3,5-trichlorobenzene	4.36	4.15	4.34-4.67
1,2,3,4-tetrachlorobenzene	4.68		4.80-5.13
1,2,3,5-tetrachlorobenzene	4.69	4.86	
1,2,4,5-tetrachlorobenzene	4.70		4.80-5.17
hexachlorobutadiene	5.04		4.84-5.29
pentachlorobenzene	5.27	5.42	5.19-5.36
hexachlorobenzene	5.50	5.46	5.16-5.37

^aData from Könemann and van Leeuwen (8). ^bData from Oliver and Nimi (12) with BCFs obtained at two exposure levels of the test compounds.

with $r^2 = 0.995$ and $n = 25$. The linear regression between $\log K_{tw}$ and $\log S\bar{V}$ for the same set (excluding compounds 19 and 25) gives

$$\log K_{tw} = -1.05 \log S\bar{V} - 0.646 \quad (4)$$

with $r^2 = 0.987$ and $n = 23$. If $\log S$ is used to replace $\log S\bar{V}$ in eq 4 the correlation gives

$$\log K_{tw} = -0.960 \log S + 0.537 \quad (5)$$

with $r^2 = 0.959$ and $n = 23$.

It is worth noting that the small curvilinearity in the plot of $\log K_{tw}$ vs. $\log K_{ow}$ at large values of $\log K_{ow}$ resembles the one noticed in the plot of $\log (BCF)$ vs. $\log K_{ow}$ in the studies of Sugiura et al. (7), Könemann and van Leeuwen (8), and Watarai et al. (13). While the nonlinearity in $\log (BCF) - \log K_{ow}$ plots appears to result partly from the use of inaccurately estimated $\log K_{ow}$ values in some studies, it has also been suggested that the curvature at large values of $\log K_{ow}$ reflects the transport resistance of large molecules across tissues and membranes in organisms (7, 13) before the system reaches a steady-state condition. In the present study of the correlation of $\log K_{tw}$ with $\log K_{ow}$, the observed nonlinearity is recognized as an equilibrium effect rather than as a kinetic effect of the solutes in triolein and octanol phases. A critical investigation of the linearity in plots of $\log (BCF)$ vs. $\log K_{ow}$ and $\log K_{tw}$ vs. $\log K_{ow}$ would require a large set of accurate data on these properties.

We now examine the relationship between $\log K_{tw}$ and $\log (BCF)$. A comparison of $\log K_{tw}$ values with corresponding $\log (BCF)$ values reported by Könemann and van Leeuwen (8) with guppies, and by Oliver and Nimi (12) with rainbow trout, expressed on the basis of the fish lipid content, is shown in Table II. Results show a close agreement between K_{tw} and BCF values for the compounds studied. In most cases, the agreement appears to be within a factor of 2, which is about as good as can be expected since the combined error associated with K_{tw} and BCF determinations can often be just as large. The $\log (BCF)$ values on the lipid basis do not appear to show systematic differences between the two fish species, when one considers the uncertainty associated with BCF values and the possible dependence of BCF on solute concentration as indicated in the study of Oliver and Nimi (12).

The proximity of $\log K_{tw}$ to $\log (BCF)$ on the lipid basis is consistent with the suggestion that the lipid content of

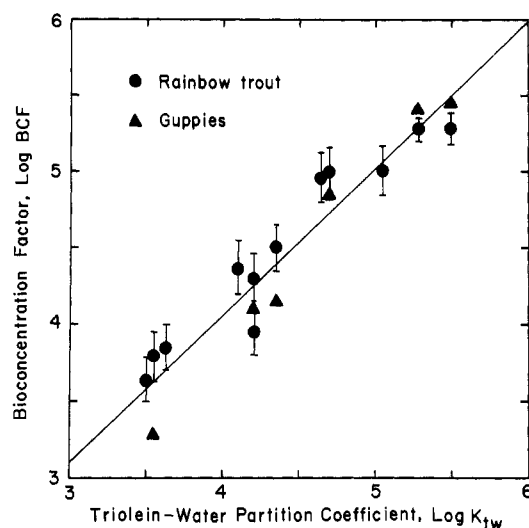


Figure 3. Correlation of $\log (BCF)$ on the basis of fish lipid content with $\log K_{tw}$ for the compounds in Table II. The BCF values for rainbow trout are the average values given in Table II. The solid line is the correlation line given by eq 6.

the fish is the principal component for achieving concentrations of (nonionic) organic compounds. The correspondence between $\log K_{tw}$ and $\log K_{ow}$ therefore supports the use of $\log K_{ow}$ in estimating $\log (BCF)$ values. A practically linear correlation is found by plotting $\log (BCF)$ vs. $\log K_{tw}$ (Figure 3) by using the BCF values of guppies from Könemann and van Leeuwen (8) and of rainbow trout from Oliver and Nimi (12). The correlation gives

$$\log (BCF) = 0.957 \log K_{tw} + 0.245 \quad (6)$$

with $n = 18$ and $r^2 = 0.915$. The fact that the slope is nearly 1 and the intercept is small further supports the postulate that lipid content mainly is responsible for the uptake of organic compounds. The correlation given by eq 6 is not statistically different from $\log (BCF) = \log K_{tw}$ at the 95% confidence level for the compounds in Table II. When $\log BCF$ values of the compounds are correlated with corresponding $\log K_{ow}$ values, the result gives

$$\log (BCF) = 0.893 \log K_{ow} + 0.607 \quad (7)$$

with $n = 18$ and $r^2 = 0.904$. Although eq 7 is statistically different from $\log (BCF) = \log K_{ow}$ at the 95% level for the range of BCF values in Table II, the difference between eq 6 and 7 is relatively small, and we cannot be sure that the correlation of $\log (BCF)$ with $\log K_{ow}$ will be statistically different from that of $\log (BCF)$ with $\log K_{tw}$ for wider or different range of data set. On the basis of the relationship between $\log K_{tw}$ and $\log K_{ow}$, and correlations of $\log (BCF)$ with $\log K_{tw}$ and $\log K_{ow}$, octanol appears to be a sufficiently good model for biological lipids in the study of bioconcentration of nonionic organic compounds, since the uncertainty of $\log (BCF)$ can be as high as 0.30 (as shown in Table II), more than the difference between $\log K_{tw}$ and $\log K_{ow}$ for most compounds.

There are several factors that can lead to discrepancies between BCF and K_{tw} (or K_{ow}). Compounds that are unstable in water or that are readily metabolized by organisms (to the extent that the rate of degradation is greater than the rate of equilibration) will give anomalous BCF values because of the inability of the system to reach true equilibrium state. Similarly, BCF values obtained with short exposure times before steady-state concentrations in both biotic and water phases are reached may be expected to differ greatly from equilibrium values. For compounds with very large $\log S$ (or very small $\log K_{ow}$),

it is also possible that the solute concentration in nonlipid phases (e.g., protein or membrane phase) of the organism may be significant (11) and consequently may affect the correlation between \log (BCF) and $\log K_{tw}$ (or K_{ow}). Certain macromolecular organic materials (e.g., humic substances) in natural waters also could significantly enhance the solubility of relatively insoluble solutes (30, 31), thus decreasing apparent BCF values. Thus, BCF values from laboratory experiments must be considered to be somewhat "idealized". Nonetheless, they provide useful references in fate assessment, particularly in situations where experimental BCF values are not available. Estimation of BCF values in fish for relatively stable compounds (such as chlorinated hydrocarbons) on the basis of K_{tw} or K_{ow} and fish lipid content would seem to be a convenient and economical approach. To substantiate the effect of lipids and the use of K_{tw} and K_{ow} in estimating bioconcentration, the relationship between K_{tw} (or K_{ow}) and (lipid-based) BCF needs to be further evaluated with more compounds in the range of $5 < \log$ (BCF) < 3 .

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