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Tricaprylin−Water Partition Coefficients and Their Temperature Dependence for Selected Chlorobenzenes

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Measurements of partition coefficients between tricaprylin (glyceryl tri-*n*-octanoate) and water are reported for seven chlorobenzenes (1,2-dichlorobenzene, 1,4-dichlorobenzene, 1,3,5-trichlorobenzene, 1,2,3,4-tetrachlorobenzene, 1,2,3,5-tetrachlorobenzene, pentachlorobenzene, and hexachlorobenzene) between 5 °C and 45 °C. The values are compared with reported data on octanol−water and triolein−water partition coefficients. The van't Hoff plots of log K_{OW} versus T^{-1} exhibit linearity with values of K_{OW} increasing by 5%−8% over this temperature range, and the enthalpy of phase change varies from 9.7 to 16 kJ/mol. Several reasons are suggested why tricaprylin−water partition coefficients may be preferable to octanol−water and triolein−water partition coefficients when quantifying a substance's hydrophobicity. The mutual solubilities of tricaprylin and water are less than that of octanol and water. Tricaprylin is less volatile than octanol and, being a triglyceride, is structurally more similar to lipids. Tricaprylin is easier to purify than triolein and, because of its lower molecular mass, is easier to analyze by gas chromatography.

Introduction

The environmental fates and effects of chemicals are largely controlled by the key physical−chemical properties of solubility in water, vapor pressure, octanol−water partition coefficient (K_{OW}), and the susceptibility of the substance to degradation or transformation reactions. A direct estimate of hydrophobicity (i.e., activity coefficient in aqueous phases) and the partitioning tendency from water to organic media such as lipids, waxes, and natural organic matter present in soils and sediments has proved invaluable for predicting soil adsorption (Karickhoff et al., 1979) and uptake in organisms (Thomann, 1989; Gobas et al., 1987, 1988; Clark and Mackay, 1991; Mackay, 1982). The success of octanol in this context is attributed to it having solvent properties similar to that of lipids, which are esters of glycerol and long-chain fatty acids. The lipid content of organisms such as fish is the critical controlling factor in the bioconcentration of relatively hydrophobic organic compounds since it is into lipids that these compounds primarily partition.

There are concerns that octanol may not be the best surrogate for lipids. Its surfactant properties can result in the formation of emulsions during the experimental determinations of K_{OW}. It may not be structurally ideal from the viewpoint of polar/nonpolar balance. It contains an hydoxyl group that can undergo hydrogen bonding. The thermodynamic studies by Beezer et al. (1983) have suggested that octanol is not a satisfactory solvent to mimic a biological lipid phase. Among solvents considered as lipid surrogates is triolein. Triolein, being a high molecular mass unsaturated triglyceride (M_W: 885), and thus somewhat reactive, is difficult to purify and does not easily elute during gas chromatography. It may contaminate GC columns and eventually reduce the sensitivity of the detector.

Another candidate is tricaprylin ($C_{27}H_{50}O_6$), also known as glyceryl tricaprylate or glycerol tri-*n*-octanoate, which is assessed here as a surrogate lipid that may have several advantages over octanol and triolein. Tricaprylin is a relatively low molar mass triglyceride (M_W: 470), it is viscous, it is more volatile than triolein, and it is therefore more easily analyzed by GC. On the basis of its structure, it is expected to act more like a naturally occurring lipid than octanol.

In this study the tricaprylin−water partition coefficients (K_{TcW}) were measured for a series of chlorobenzenes and the values compared with the corresponding values of octanol−water (K_{OW}) and triolein−water (K_{TrW}) partition coefficients. Their temperature dependence was measured by determining the partition coefficients at 10° intervals from 5 to 45 °C. The logarithms of the partition coefficients were correlated with the inverse of absolute temperature to obtain the thermodynamic relationship between K_{TcW} and temperature expressed as enthalpies of transfer from tricaprylin to water.

Experimental Section

Materials. 1,2-Dichlorobenzene 98.6%, 1,4-dichlorobenzene 99%, 1,3,5-trichlorobenzene 98%, 1,2,3,4-tetrachlorobenzene 98%, 1,2,3,5-tetrachlorobenzene 99%, and pentachlorobenzene 98% were obtained from Aldrich Chemical Co., Milwaukee, WI; OAS grade hexachlorobenzene was obtained from BDH Chemicals Ltd., Toronto, Ontario. Tricaprylin with a purity of 97−98% was purchased from Sigma Chemical Co., St. Louis, MO. All chemicals were used as purchased without further purification. Milli-Q ultrapure deionized water (Millipore Corp., Milford, MA) was used for all experiments. HPLC grade hexane was obtained from Caledon Laboratories, Georgetown, Ontario.

The solubility of water in tricaprylin was determined by the Karl Fischer titration method conducted by Guelph Chemical Laboratories, Guelph, Ontario.

Preparation of Solutions. Except for hexachlorobenzene, a stock solution of approximately 1 g/L of the compound in

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Table 1. Logarithm of Tricaprylin−Water Partition Coefficients[a] (K_{TcW}) of Selected Chlorobenzenes at 25 °C (with Precision Expressed as ± Standard Deviation), Compared with Literature Values of log K_{TrW}[b] and log K_{OW}[c]

			literature values at 25 °C	
chlorobenzene	log K_{TcW}	log K_{OW}[c]	log K_{TrW}[b]	log K_{OW}
1,2-di-	3.56 ± 0.07	3.29 ± 0.05	3.51	3.38;[d,e] 3.40;[f,g] 3.34;[h] 3.55;[i] 3.43;[j] 3.49[k]
1,4-di-	3.61 ± 0.04	3.23 ± 0.03	3.55	3.37;[d,f,l] 3.38;[e] 3.46;[h] 3.62;[i] 3.52;[g] 3.44[j]
1,3,5-tri-	4.50 ± 0.06	4.34 ± 0.04	4.36	4.15;[i] 4.17;[g,h] 4.02;[e] 4.18;[n] 4.31;[k,o] 4.40[j]
1,2,3,4-tetra-	4.63 ± 0.09	4.41 ± 0.06	4.68	4.46;[i] 4.37;[g] 4.60;[k,o] 4.63;[j] 4.55;[e] 4.41;[h] 4.75[p]
1,2,3,5-tetra-	4.65 ± 0.05	4.55 ± 0.02	4.69	4.50;[i] 4.46;[l] 4.52;[f] 4.56;[g] 4.53;[h] 4.51;[e] 4.61;[n] 4.59;[k,o] 4.66[j]
penta-	5.09 ± 0.03	4.94 ± 0.03	5.27	4.88;[i] 4.94;[f,l,n] 5.17;[g,m] 5.06;[h] 5.69;[p] 5.03;[e] 5.20;[k,o] 5.18[j]
hexa-	5.59 ± 0.02	5.46 ± 0.02	5.50	5.0;[i] 6.22;[q] 5.50;[k,o] 5.66;[h] 5.40;[g] 5.47;[e] 5.60;[r] 5.64;[s] 5.73[j]

[a] Number of repetitions ≥3. [b] Triolein−water partition coefficients (Chiou et al., 1985). [c] Octanol−water partition coefficients (Bahadur et al., 1997). [d] Wasik et al., 1983. [e] Miller et al., 1984. [f] Banerjee et al., 1980. [g] Wateral et al., 1982. [h] Hammers et al., 1982. [i] Könemann et al., 1979. [j] De Bruijn et al., 1989. [k] Pereira et al., 1988. [l] Veith et al. 1980. [m] Banerjee, 1984. [n] Garst, 1984. [o] Chiou, 1985. [p] Bruggeman et al., 1982. [q] McDuffie 1981. [r] Brooke et al., 1986. [s] Mailhot 1987.

Table 2. Tricaprylin−Water Partition Coefficients[a] of Selected Chlorobenzenes in the Range 5 °C−45 °C

	log K_{TcW}					
chlorobenzene	5 °C	15 °C	25 °C	35 °C	45 °C	d(log K_{TcW})/dT
1,2-di-	3.65 ± 0.07	3.61 ± 0.04	3.56 ± 0.07	3.51 ± 0.03	3.41 ± 0.05	−0.006
1,4-di-	3.71 ± 0.03	3.66 ± 0.05	3.61 ± 0.04	3.56 ± 0.03	3.46 ± 0.04	−0.0063
1,3,5-tri	4.60 ± 0.04	4.58 ± 0.08	4.50 ± 0.06	4.44 ± 0.04	4.35 ± 0.05	−0.0063
1,2,3,4-tetra-	4.75 ± 0.06	4.68 ± 0.07	4.63 ± 0.09	4.50 ± 0.06	4.43 ± 0.03	−0.008
1,2,3,5-tetra-	4.81 ± 0.07	4.75 ± 0.03	4.65 ± 0.05	4.56 ± 0.05	4.53 ± 0.09	−0.007
penta-	5.27 ± 0.05	5.22 ± 0.03	5.09 ± 0.03	5.07 ± 0.06	4.91 ± 0.03	−0.009
hexa-	5.80 ± 0.09	5.63 ± 0.06	5.59 ± 0.02	5.50 ± 0.02	5.39 ± 0.07	−0.0103

[a] Number of repetitions ≥3.

tricaprylin was prepared, this concentration being well below the solubility limit. A 2 mL aliquot of stock solution and 20 mL of deionized water were added to a 125 mL Erlenmeyer flask. The flasks were set in a wrist-action shaker temperature bath with refrigeration unit (Gilson Differential Respirometer) and were gently shaken for 24 h to avoid emulsion formation. The flasks were immersed in the temperature bath and maintained within ±0.1 K of the required temperature. The contents were then allowed to settle in the temperature bath for at least 48 h to ensure full phase separation at the desired temperature. For hexachlorobenzene, near-saturated solutions of approximately 0.7 g/L in tricaprylin were prepared using a 15 mL aliquot of stock solution and 150 mL of water in a 250 mL Erlenmeyer flask.

Gas Chromatographic Measurements. The aqueous and tricaprylin phases were separated and analyzed individually. The aqueous phase was extracted with hexane (2 mL), and then a 0.5 μL sample was directly injected (splitless) onto the gas chromatographic column. The tricaprylin phase was diluted 20 to 2000-fold as required. Analyses were performed on a Hewlett-Packard 5890 gas chromatograph equipped with a ^{63}Ni electron capture (EC) detector. A 0.32 mm i.d. by 30 m long J&M DB-17 fused silica capillary column was used for separation. The makeup and carrier gas was a 95:5 by volume argon−methane mixture. Operating conditions were as follows: injection port at 250 °C, oven in isothermal mode between 110 and 210 °C depending on the boiling point of the chemical, detector at 300 °C. Carrier gas flow rate was 3.1 mL/min. Peak areas were recorded on a Hewlett-Packard 3392A integrator. Calibration standards were prepared in hexane.

Results

The measured values of log K_{TcW} at 25 °C are listed in Table 1 and are compared with the K_{OW} data from Bahadur et al. (1997) as well as previously reported literature values. Triolein−water partition coefficients (K_{TrW}) from Chiou (1985) are also included. The mean K_{TcW} measurements, calculated from three replicates for each compound, are presented in Table 2 for the temperature range 5 to 45 °C. The estimated precison expressed as a standard deviation is ±9%. In Figure 1 the plots of log K_{TcW} values as a function of reciprocal absolute temperature show linear behavior with log K_{TcW} increasing by 5%−8% over the temperature range 5 to 45 °C. The variation of log K_{TcW} with T, i.e., d(log K_{TcW})/dT, is between −0.006 and −0.010 K^{-1} with a mean of −0.008 K^{-1}. The log linear increase in K_{TcW} with $1/T$ is slightly less than that for log K_{OW} reported by Bahadur et al. (1997). Thus K_{TcW} is less sensitive to temperature variation than K_{OW}.

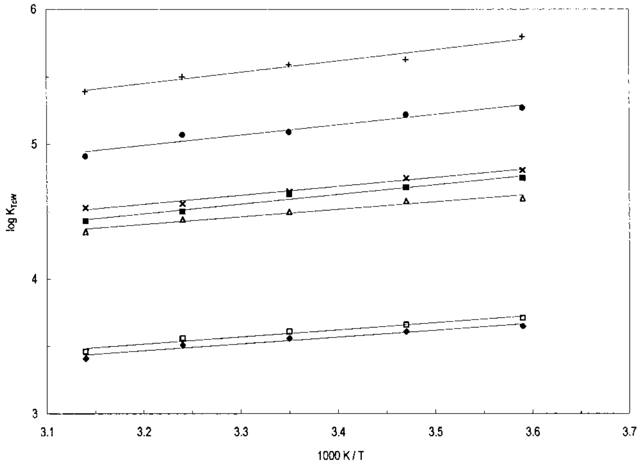

Figure 1. Van't Hoff plot of log K_{TcW} versus reciprocal absolute temperature for 1,2-dichlorobenzene □, 1,4-dichlorobenzene ◆, 1,3,5-trichlorobenzene △, 1,2,3,4-tetrachlorobenzene ■, 1,2,3,5-tetrachlorobenzene ×, pentachlorobenzene ●, and hexachlorobenzene +.

The experimental data were regressed using the following equation:

$$\log K_{TcW} = A - \Delta H/2.303RT = A - B/T \qquad (1)$$

The regression coefficients A, B, and enthalpies of phase transfer (ΔH) are shown in Table 3. The partitioning of

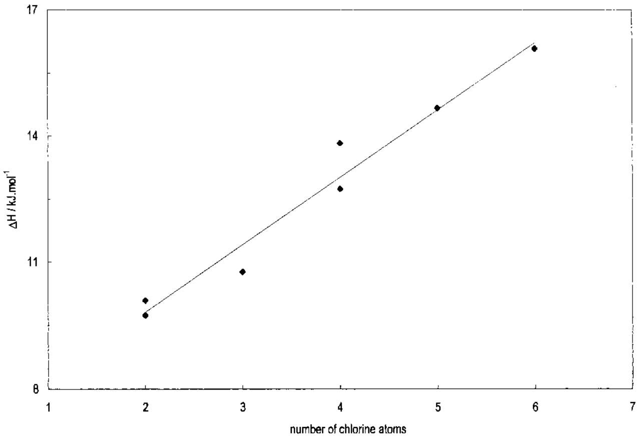

Figure 2. Relationship between ΔH and number of chlorine atoms.

Table 3. Regression Constants in Eq 1 and Enthalpy of Phase Change

chlorobenzene	A	B	ΔH/kJ·mol^{-1}	r^2
1,2-di-	1.8391	508.9	−9.74	0.949
1,4-di-	1.8301	527.1	−10.09	0.960
1,3,5-tri	2.6049	562.6	−10.77	0.995
1,2,3,4-tetra-	2.1722	722.4	−13.83	0.972
1,2,3,5-tetra-	2.4254	665.5	−12.74	0.983
penta-	2.5407	765.7	−14.66	0.941
hexa-	2.7613	840.0	−16.08	0.965

chlorobenzenes from water to tricaprylin is exothermic with the enthalpy increasing with increased chlorine number, similar to that for the corresponding octanol−water system (Bahadur et al., 1997). The ΔH values range from 9.7 kJ·mol^{-1} for 1,2-dichlorobenzene to 16.1 kJ.mol^{-1} for hexachlorobenzene. The relationship between ΔH and number of chlorine atoms (N_{Cl}) in the molecule illustrated in Figure 2 can be expressed as

$$\Delta H/\mathrm{kJ{\cdot}mol^{-1}} = 6.6 + 1.6N_{\mathrm{Cl}} \tag{2}$$

Discussion

As shown in Table 1, measured log K_{TcW} values are somewhat greater than log K_{OW} values from Bahadur et al. (1997) with larger deviations being observed for lower molecular weight chlorobenzenes. The log K_{TcW} values exceed log K_{OW} by 0.38 and 0.27 units for 1,4- and 1,2-dichlorobenzene, respectively. Chiou (1985) also reported higher values for triolein−water partition coefficients and observed larger deviations for less chlorinated compounds.

A plot of log K_{TcW} vs log K_{OW} values at 25 °C is given in Figure 3. The 1:1 relationship is shown by the broken line. The linear relationship is given by the following equation:

$$\log K_{\mathrm{TcW}} = 0.90 \log K_{\mathrm{OW}} + 0.615 \qquad (r^2 = 0.99) \tag{3}$$

The log K_{TrW} values are generally within 2% of the log K_{TcW} values reported by Chiou (1985). A plot of log K_{TcW} and log K_{TrW} is shown in Figure 4, giving the following correlation equation:

$$\log K_{\mathrm{TcW}} = 0.94 \log K_{\mathrm{TrW}} + 0.268 \qquad (r^2 = 0.97) \tag{4}$$

The observation that the slope is close to 1 and the intercept is small shows that log K_{TcW} and log K_{TrW} are very similar in solvent properties.

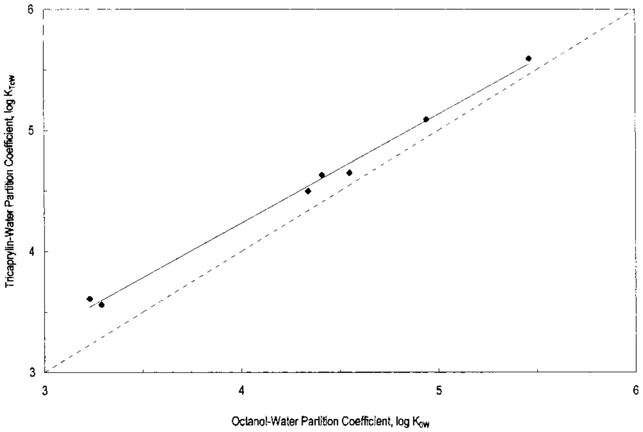

Figure 3. Correlation of log K_{TcW} with log K_{OW}.

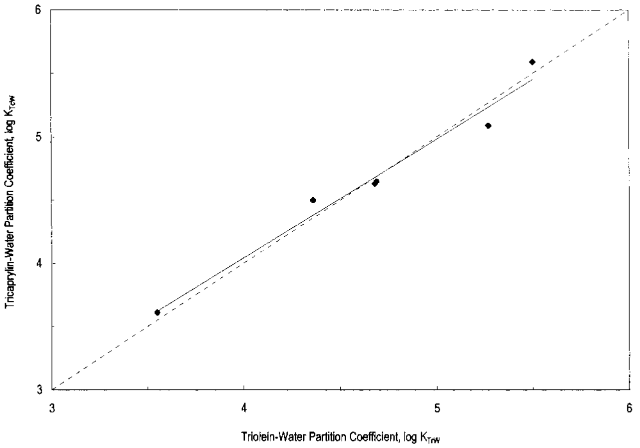

Figure 4. Correlation of log K_{TcW} with log K_{TrW}.

Tricaprylin has several advantages as listed below:

(1) It is less soluble than octanol in water by a factor of 4 (solubility of tricaprylin in water, (0.0134 ± 0.003) g/100 g; solubility of octanol in water (IUPAC, 1984), (0.054 ± 0.005) g/100 g at 25 °C).

(2) The solubility of water in tricaprylin, (0.4 g/100 g), is a factor of 11 smaller than the solubility of water in octanol (4.5 ± 0.1) g/100 g, (IUPAC, 1984) at 25 °C.

(3) It has lower vapor pressure than octanol (b.p. of tricaprylin, 233 °C; b.p. of octanol, 196 °C).

We thus suggest that tricaprylin may be preferable as a solvent for assessing partition coefficients with respect to air, that is, K_{TcA} vs K_{OA}. Tricaprylin−air partition coefficients may be good indicators of partitioning behavior from the atmosphere to vegetation, aerosols, and soil. It is likely that K_{TcA} may be estimated from the ratio of K_{TcW} and K_{AW} with more reliability than is the case for octanol since mutual solubilities of tricaprylin and water are less than in the octanol/water system.

Conclusions

Although this study reports only data for tricaprylin−water partitioning coefficients, we note the desirability of obtaining consistent data for all three partition coefficients, i.e., organic−water, air−water, and organic−air, each of which is of value for estimating partitioning in environmental systems. Tricaprylin−air partition coefficients may be good indicators of partitioning from the atmosphere to vegetation, aerosols, and soils; tricaprylin may be preferable to octanol for this purpose because of the lower mutual solubilities noted above, and a consistency test of the three partition coefficient is more rigorous.

We acknowledge that it is unlikely that tricaprylin will replace octanol because of the well-established predictive methods for K_{OW} and its widespread use in characterizing hydrophobicity of chemicals in environmental, pharmaceutical, and regulatory contexts. There may, however, be applications in which close simulation of lipid partitioning is required.

To assess more completely the suitability of tricaprylin as a surrogate lipid, further studies are required with more compounds to determine the relationship between log K_{TcW} (or log K_{OW}) and (lipid-based) bioconcentration factors (BCF) and to determine if correlations of log BCF with log K_{TcW} are statistically different and superior to that of log BCF with log K_{OW}.

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