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A THERMODYNAMIC ANALYSIS OF THE RELATIONSHIPS BETWEEN MOLECULAR SIZE, HYDROPHOBICITY, AQUEOUS SOLUBILITY AND OCTANOL-WATER PARTITIONING OF ORGANIC CHEMICALS

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ABSTRACT

This study presents a thermodynamic analysis of the relationship between molecular size, hydrophobicity, aqueous solubility and octanol-water partitioning for several classes of hydrophobic organic compounds including chlorinated dibenzo-*p*-dioxins, PCBs, polynuclear aromatic hydrocarbons, alkylbenzenes, linear alcohols and alkanes. The purpose of the thermodynamic analysis is to explore the contribution of chemical-water and chemical-chemical interactions involved in the aqueous solution process. This is important for the development of relationships between the molecular structure and environmentally relevant properties of organic chemicals. The results show that the free energy of aqueous solvation is virtually independent on the molar volume of the solute for each of the congeneric series that was investigated. Within each congeneric series, congeners are therefore approximately equally "hydrophobic", and the relationship between the aqueous solubility of (subcooled) liquid hydrophobic chemicals and molecular volume predominantly reflects the dependence of chemical-chemical interactions on the molecular volume in the (subcooled) liquid phase, rather than chemical-water interactions as is usually assumed. The results indicate that improvements of quantitative structure-aqueous solubility relationships may be achieved by modelling chemical-chemical interactions in the pure (subcooled) liquid phase, rather than merely chemical-water interaction, and that within congeneric series of non-polar organic substances, an increase in octanol-water and environmental partition coefficients with increasing congener size is due to an increase in the congener's lipophilicity, not hydrophobicity.

INTRODUCTION

Hydrophobic interactions are generally considered to play a crucial role in the physical chemistry, biochemistry and environmental chemistry of non-polar organic chemicals in aqueous systems [1]. As a result, various processes including the dissolution of non-polar organic chemicals in water [2], the environmental fate [3] and toxicity [4] of persistent hydrophobic organic chemicals in aquatic ecosystems have been described and explained in terms of the unfavourable (i.e. phobic) interactions of these substances with water molecules. The origin of this hydrophobic effect was first explained by Frank and Evans [5]. Based on observations that the unfavourable free energy of solvation for gaseous solutes is largely due to a loss of entropy, they concluded that the presence of apolar solute molecules in water causes an increase in the order of the water molecules surrounding the solute and hence a loss of entropy, that is proportional to the solute's contact surface area with the water.

Since then the solute-water interfacial area based explanation of the entropy of solvation in water has been somewhat indiscriminately applied as the theoretical basis for the correlations between molecular structure and free energy-related properties such as aqueous solubility [6,7] and partition coefficients [7] of hydrophobic organic chemicals. Some excellent correlations between the aqueous solubility and molecular surface area or volume appear to justify this approach [7-9]. This has led to the popular belief that the decrease of the aqueous solubility and the increase of organic phase-water partition coefficients with increasing molecular size is the result of the solute's greater interfacial area with water [10] and hence the chemical's hydrophobicity. Consequently, there has been a considerable effort to determine and calculate the interfacial area of organic solutes with water molecules [11] to improve methods for estimating aqueous solubilities and partition coefficients.

However, this approach appears to have overlooked the following facts. First, it is true that, for a hydrophobic solute, the unfavorable free energy of aqueous solvation is mainly a result of a large negative entropy of solvation, and that this negative entropy of solvation is closely related to the interfacial area between solute and water or the molecular size of solute. However, this does not imply that the observed relationship between the free energy of solvation and solute size is also dominated by the dependence of the entropy of solvation on the solute size. The relationship between the free energy of solvation and solute size is a function of both the entropy's relationship and the enthalpy's relationship with solute size. It is therefore possible that, despite the fact that the absolute value of the enthalpy of solvation is small compared to the entropy of solvation, the relationship between the enthalpy of solvation and molecular size has a significant effect on the relationship between free energy of solvation and molecular size. Secondly, the thermodynamic data examined by Frank and Evans in their classic analysis of the behavior of solutes in water [5] are those for *gas*-to-water transfer or solvation, and not solution process. For a dissolving *solid* or *liquid* solute, solvation is only one step in the solution process. As is further illustrated in Figure 2, aqueous solution can therefore be viewed as the combined sum of vaporization, i.e., transfer of the solid or liquid chemical into the gas phase, and solvation, i.e., transfer of the gaseous solute into solution. The relationship between the free energy of vaporization and solute size therefore also has an effect on the relationship between the aqueous solubility and solute size, and thus should not be ignored.

In other words, the fact that the low aqueous solubility of a hydrophobic solute is predominantly the result of the unfavorable "hydrophobic interaction" between solute and water does not necessarily imply that the progressive drop of the aqueous solubility with the increasing solute size within a congeneric series is also due to the greater "hydrophobicity" of large solute.

In this study, we will present an analysis of the role of thermodynamic properties involved in the aqueous solution process of some environmentally relevant classes of organic chemicals, including chlorodibenzo-*p*-dioxins (PCDDs), alkylbenzenes (ABs), Polychlorinated Biphenyls (PCBs) and several Polynuclear Aromatic Hydrocarbons (PAHs), as well as alkanes and linear alcohols. We will present results which show that, within each congeneric series, the free energy of solvation, which reflects the contribution of the hydrophobic interaction to the aqueous solution process, is virtually independent on the congener's molecular size, and that the drop in aqueous solubility from one congener to another with a larger molar volume is not due to the increased interfacial area between the solute and the water molecules. The implications of these findings for modeling and the conceptual understanding of structure-property and structure-fate relationships are discussed.

THEORETICAL

The objective of this work is to investigate the thermodynamic properties of vaporization, solvation and solution and their relationships with molecular size for selected hydrophobic chemicals. As state functions, the three basic standard thermodynamic properties for the solution process (ΔG_s, ΔH_s, ΔS_s) of a liquid chemical or subcooled liquid chemical (for solids) in water can be subdivided into those for the vaporization process (ΔG_v, ΔH_v, ΔS_v), where the chemical leaves the pure (subcooled) liquid phase to enter the gas phase, and those for the solvation process (ΔG_{sv}, ΔH_{sv}, ΔS_{sv}), where the gaseous solute is incorporated into the water matrix, as is illustrated by the thermodynamic cycle in Figure 1. That is, ΔG_s equals $\Delta G_v + \Delta G_{sv}$. In a similar fashion, the enthalpy (ΔH_s) and entropy (ΔS_s) of solution are related to respectively the enthalpy (ΔH_v) and entropy (ΔS_v) of vaporization and the enthalpy (ΔH_{sv}) and entropy (ΔS_{sv}) of solvation: ΔH_s equals $\Delta H_v + \Delta H_{sv}$ and ΔS_s equals $\Delta S_v + \Delta S_{sv}$.

The interpretation and the numerical values of standard thermodynamic properties generally depend on the choice of standard states. By selecting the standard states of solute in each phase as shown in Figure 1, it is possible to interpret the thermodynamic properties of vaporization (ΔG_v, ΔH_v and ΔS_v) and solvation (ΔG_{sv}, ΔH_{sv} and ΔS_{sv}) in terms of respectively solute-solute interactions in the pure (subcooled) liquid phase and solute-water interactions at infinite dilute aqueous solution (see Figure 2). The thermodynamic cycle thus provides a means to quantitatively explore the contributions of solute-solute and solute-water interactions in the aqueous solution process.

Enthalpies, entropies and free energies of solution, vaporization and solvation can be derived from calorimetric experiments and/or measurements of aqueous solubility and vapor pressure as a function of temperature. The expressions that were used to calculate the standard thermodynamic properties (in Figure 1) from experimental data are summarized in Table 1. It was assumed in Table 1 that the effects of non-ideality of saturated vapour of chemicals are negligible. The saturated vapor pressure of the pure solute was thus equivalent to the fugacity. It was further assumed that the Henry's Law based activity coefficient of hydrophobic solute in dilute aqueous solution is 1.0. In addition, the effect of water dissolution in the pure solute phase was ignored. These are reasonable and

Table 1. Summary of expressions used to derive standard thermodynamic properties from experimental data*.

Solution Process

$$\Delta G_{s,i} = -RT\ln X_i - \Delta G_{f,i} \tag{1}$$

$$\Delta H_{s,i} = -R\left[\frac{\partial \ln X_i}{\partial(1/T)}\right]_P - \Delta H_{f,i} \tag{2}$$

$$\Delta S_{s,i} = \frac{\Delta H_{s,i} - \Delta G_{s,i}}{T} \tag{3}$$

Vaporization Process

$$\Delta G_{v,i} = -RT\ln p_i^o - \Delta G_{f,i} \tag{4}$$

$$\Delta H_{v,i} = -R\left[\frac{\partial \ln p_i^o}{\partial(1/T)}\right]_P - \Delta H_{f,i} \tag{5}$$

$$\Delta S_{v,i} = \frac{\Delta H_{v,i} - \Delta G_{v,i}}{T} \tag{6}$$

Solvation Process

$$\Delta G_{sv,i} = \Delta G_{s,i} - \Delta G_{v,i} \tag{7}$$

$$\Delta H_{sv,i} = \Delta H_{s,i} - \Delta H_{v,i} \tag{8}$$

$$\Delta S_{sv,i} = \Delta S_{s,i} - \Delta S_{v,i} \tag{9}$$

Fusion Process

$$\Delta G_{f,i} = \Delta H_{f,i} - T\Delta S_{f,i} \tag{10}$$

$$\Delta H_{f,i} = \Delta H_{f,i}(T_m) + \int_T^{T_m} \Delta c_p \, dT \tag{11}$$

$$\Delta S_{f,i} = \frac{\Delta H_{f,i}(T_m)}{T_m} + \int_T^{T_m} \frac{\Delta c_p}{T} \, dT \tag{12}$$

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* X_i is the mole fraction solubility of solute i in water. p_i^o is the saturated vapor pressure of the pure solute i. ΔC_p is the difference in the heat capacities of the solid and subcooled liquid state of the solute i. ΔG_f, ΔH_f and ΔS_f are respectively the free energy, enthalpy and entropy of fusion. For chemicals which are liquids at room temperature, ΔG_f is zero.

frequently made assumptions for many simple hydrophobic organic chemicals.

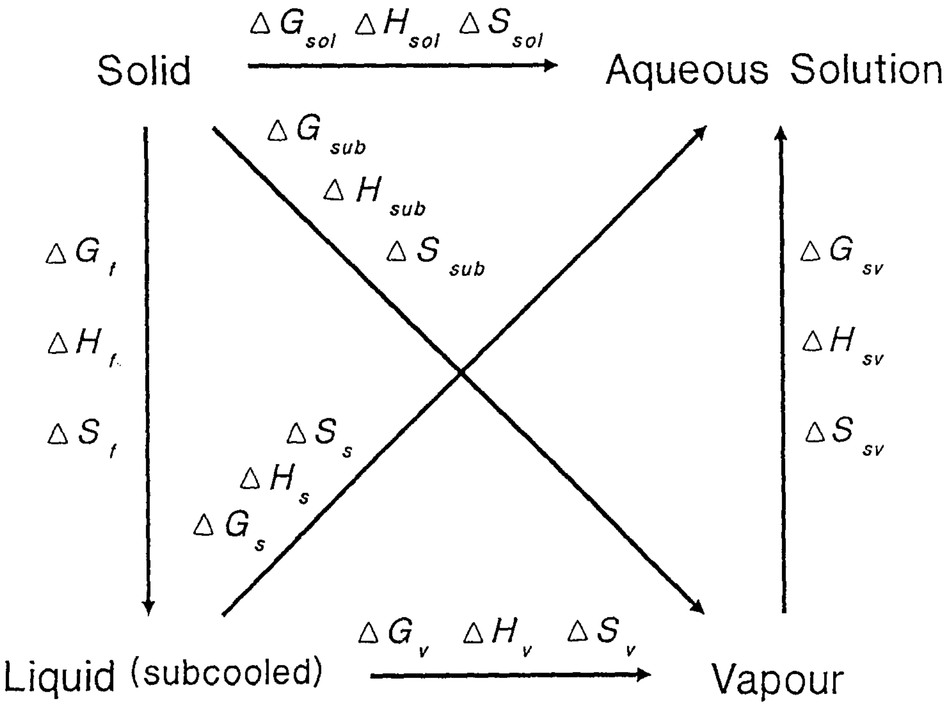

Figure 1: Thermodynamic cycle for the aqueous solution process, illustrating the thermodynamic contributions of vaporization (ΔG_v, ΔH_v, ΔS_v), solvation (ΔG_{sv}, ΔH_{sv}, ΔS_{sv}), solution of the (subcooled) liquid solute (ΔG_s, ΔH_s, ΔS_s), sublimation (ΔG_{sub}, ΔH_{sub}, ΔS_{sub}) and solution of the solid solute (ΔG_{sol}, ΔH_{sol}, ΔS_{sol}). The standard states are infinite dilution for aqueous solution, the ideal gas phase at 1 atmosphere for the vapour phase and the pure solid or (subcooled) liquid at 1 atmosphere and 298 K.

EXPERIMENTAL DATA

Molar Gibbs free energies, enthalpies and entropies of solution, vaporization and solvation processes at 298 K for PCDDs, PCBs, ABs, PAHs, alkanes, and linear alcohols were calculated or compiled from various sources, and, when necessary, were corrected to express them in terms of the same standard states. These properties along with the molar volumes of chemicals are presented in Table 2. Molar volume was chosen as an appropriate descriptor of molecular size because for the congeneric series in this study it is directly proportional to the molecular surface area, and it can easily be calculated for all substances by the Le Bas method [12]. Other methods for assessing molar volumes (e.g. densities) were not applied because of a lack of a consistent set of data for the substances in our study and the need for additional assumption for substances that are not liquids. In Figures 3a to 3d, the thermodynamic properties are plotted versus the molar volume of the solutes. Linear regressions between the

Table 2: Molar volumes (V) in cm^3/mol and enthalpies, entropies and free energies of aqueous solution (ΔH_S , $-T{\cdot}\Delta S_S$, ΔG_S), vaporization (ΔH_V , $-T{\cdot}\Delta S_V$, ΔG_V) and solvation (ΔH_{SV} , $-T{\cdot}\Delta S_{SV}$, ΔG_{SV}) processes of some (subcooled) liquid organic chemicals at 25°C (in kJ/mol).

Chemicals	Volume	ΔH_S	$-T{\cdot}\Delta S_S$	ΔG_S	ΔH_V	$-T{\cdot}\Delta S_V$	ΔG_V	ΔH_{SV}	$-T{\cdot}\Delta S_{SV}$	ΔG_{SV}
DD*	192.0	27.96^{a}	6.68^{b}	34.64^{c}	70.05^{bb}	-39.59^{cc}	30.46^{dd}	-41.69^{kk}	46.14^{ll}	4.45^{mm}
1-MCDD*	212.9	19.40^{a}	18.40^{b}	37.80^{c}	75.65^{bb}	-40.76^{cc}	34.89^{dd}	-57.75^{kk}	60.70^{ll}	2.95^{mm}
2-MCDD*	212.9	35.05^{a}	5.08^{b}	40.13^{c}	74.26^{bb}	-39.57^{cc}	34.69^{dd}	-43.61^{kk}	48.37^{ll}	4.76^{mm}
2,3-DCDD*	233.8	24.58^{a}	18.01^{b}	42.59^{c}	77.02^{bb}	-37.98^{cc}	39.04^{dd}	-55.04^{kk}	57.99^{ll}	2.95^{mm}
2,7-DCDD*	233.8	19.48^{a}	24.59^{b}	44.07^{c}	69.51^{bb}	-32.28^{cc}	37.23^{dd}	-59.23^{kk}	62.79^{ll}	3.56^{mm}
2,8-DCDD*	233.8	21.38^{a}	22.71^{b}	44.09^{c}	80.71^{bb}	-38.45^{cc}	42.26^{dd}	-64.33^{kk}	64.73^{ll}	0.40^{mm}
1,2,4-T_3CDD*	254.7	12.93^{a}	31.04^{b}	43.97^{c}	92.39^{bb}	-47.75^{cc}	44.64^{dd}	-71.96^{kk}	73.49^{ll}	1.53^{mm}
1,2,3,4-T_4CDD*	275.6	1.89^{a}	46.32^{b}	48.21^{c}	90.13^{bb}	-41.96^{cc}	48.17^{dd}	-85.44^{kk}	86.31^{ll}	0.87^{mm}
1,2,3,7-T_4CDD*	275.6	3.20^{a}	44.14^{b}	47.34^{c}	100.82^{bb}	-49.81^{cc}	51.01^{dd}	-83.52^{kk}	84.57^{ll}	1.05^{mm}
1,3,6,8-T_4CDD*	275.6				87.21^{bb}	-40.42^{cc}	46.78^{dd}			
2,3,7,8-T_4CDD*	275.6				85.10^{bb}	-37.09^{cc}	48.01^{dd}			
1,2,3,4,7-P_5CDD*	296.5	5.10^{a}	42.72^{b}	47.82^{c}	85.25^{bb}	-35.58^{cc}	49.67^{dd}	-74.15^{kk}	74.77^{ll}	0.62^{mm}
1,2,3,4,7,8-H_6CDD*	317.4	-2.60^{a}	51.92^{b}	49.32^{c}	96.99^{bb}	-41.12^{cc}	55.87^{dd}	-92.09^{kk}	88.95^{ll}	-3.14^{mm}
1,2,3,4,6,7,8-H_7CDD*	338.3	-11.70^{a}	61.80^{b}	50.10^{c}	112.84^{bb}	-48.76^{cc}	64.08^{dd}	-97.94^{kk}	95.78^{ll}	-2.16^{mm}
OCDD	359.2				108.92^{bb}	-44.20^{cc}	64.72^{dd}			
Benzene-D_6	96.5	1.99^{j}			33.74^{j}			-31.75^{j}		
Benzene	96.5	2.10^{d}	17.21^{e}	19.31^{d}	33.89^{h}	-28.74^{ee}	5.15^{h}	-31.92^{nn}	46.18^{oo}	14.25^{nn}
		2.09^{f}	17.15^{e}	19.25^{g}	34.02^{ff}	-28.97^{gg}	5.06^{hh}			14.23^{h}
				19.37^{h}	34.10^{ff}			-31.63^{i}		
		2.47^{i}			34.02^{ff}			-31.59^{pp}		
		2.43^{g}								
Toluene	122.4	2.51^{i}			38.28^{ff}			-36.18^{qq}	50.37^{oo}	14.18^{qq}
		2.68^{g}			41.92^{ff}			-35.77^{i}		
		1.73^{j}	20.95^{e}	22.68^{h}	37.99^{j}	-29.75^{ee}	8.24^{h}	-39.25^{pp}		
								-36.26^{j}	50.69^{oo}	14.43^{h}
EthylBenzene	144.6	2.02^{j}	24.05^{e}	26.07^{h}	42.26^{j}	-31.38^{ee}	10.88^{h}	-40.24^{j}	55.43^{oo}	15.19^{h}
		1.63^{g}			42.26^{ff}			-40.63^{pp}		
		1.59^{i}			42.72^{ff}			-41.13^{pp}		
		1.30^{k}	24.30^{e}	25.60^{k}	42.24^{ff}	-31.50^{gg}	10.74^{hh}	-40.10^{qq}	54.67^{oo}	14.57^{qq}

Table 2. (Continued)

Chemicals	Volume	ΔH_S	$-T\cdot\Delta S_S$	ΔG_S	ΔH_V	$-T\cdot\Delta S_V$	ΔG_V	ΔH_{SV}	$-T\cdot\Delta S_{SV}$	ΔG_{SV}
EthylBenzene	144.6							-40.94[rr]	55.80[rr]	14.86[rr]
n-PropylBenzene	166.8	3.70[k]	25.39[e]	29.09[k]	46.23[ff]	-32.88[gg]	13.35[hh]	-42.53[rr]	58.27[rr]	15.74[rr]
		2.30[j]	26.70[e]	29.00[h]	46.23[j]	-33.68[ee]	12.55[h]	-43.90[j]	60.34[oo]	16.44[h]
										15.65[ss]
n-ButylBenzene	189.0	6.60[k]	26.11[e]	32.71[k]	50.75[ff]	-34.50[gg]	16.25[hh]	-44.15[rr]	60.61[rr]	16.46[rr]
				32.97[h]			14.85[h]			18.12[h]
										16.22[ss]
n-PentylBenzene	211.2	6.50[k]	29.94[e]	36.44[k]	55.97[ff]	-36.74[gg]	19.23[hh]	-49.47[rr]	66.68[rr]	17.21[rr]
n-HexylBenzene	233.4	8.00[k]	31.93[e]	39.93[k]	60.34[ff]	-38.24[gg]	22.10[hh]	-52.34[rr]	70.17[rr]	17.83[rr]
		7.60[l]	32.10[e]	39.70[l]	60.30[ff]	-38.27[gg]	22.03[hh]	-52.70[rr]	70.37[rr]	17.67[rr]
Benzene-D_6	96.5	1.99[j]			33.74[j]					
Benzene	96.5	2.10[d]	17.21[e]	19.31[d]	34.02[ff]	-28.97[gg]	5.06[hh]	-31.92[nn]	46.18[oo]	14.25[nn]
		2.09[f]	17.15[e]	19.25[g]	33.89[h]	-28.74[ee]	5.15[h]	-31.59[pp]		
				19.37[h]	34.10[ff]			-31.63[i]		
		2.47[i]			34.02[ff]					14.13[h]
		2.43[g]								
Naphthalene	148.0	11.72[h]	15.65[h]	27.36[h]	53.93[h]	-34.35[ee]	19.58[h]	-46.86[qq]	54.75[oo]	7.89[qq]
		11.38[h]	15.98[h]	27.36[h]			19.54[hh]			7.82[h]
										7.87[tt]
Acenaphthene	173.0							-49.62[qq]	53.44[oo]	3.82[qq]
										4.71[tt]
Fluorene	188.0	13.10[m]	20.27[e]	33.37[m]	66.24[ff]	-36.47[gg]	29.77[hh]	-53.14[qq]	56.74[oo]	3.60[qq]
										3.47[tt]
Anthracene	197.0	15.06[h]	19.83[h]	34.89[h]	72.80[h]	-36.69[ee]	36.11[h]	-57.74[kk]	56.53[ll]	-1.21[mm]
	197.0	20.04[h]	14.85[h]	34.89[h]	78.18[ff]	-31.70[gg]	46.47[hh]	-58.58[qq]	48.99[oo]	-9.58[qq]
		19.60[m]	17.29[e]	36.89[m]						0.18[tt]
Phenanthrene	199.0	17.61[h]	17.99[h]	35.61[h]	72.13[h]	-38.03[ee]	34.10[h]	-54.52[r]	56.02[s]	1.51[t]
		27.28[h]	8.33[h]	35.61[h]	69.99[ff]	-35.94[gg]	34.05[hh]	-54.39[qq]	56.02[oo]	1.63[qq]
		15.60[m]	20.08[e]	35.68[m]						1.35[tt]
Pyrene	214.0	17.40[m]	20.49[e]	37.89[m]	81.00[ff]	-39.71[gg]	41.29[hh]	-63.60[qq]	60.20[oo]	-3.40[qq]

Table 2. (Continued)

Chemicals	Volume	ΔH_s	$-T\cdot\Delta S_s$	ΔG_s	ΔH_v	$-T\cdot\Delta S_v$	ΔG_v	ΔH_{sv}	$-T\cdot\Delta S_{sv}$	ΔG_{sv}
Pyrene	214.0	31.13[h]	8.83[h]	39.96[h]	78.83[h]	-37.49[ee]	41.34[h]	-47.70[h]	46.32[ee]	-1.38[h]
										-0.80[tt]
PCB 0[n]	178.0	15.50[o]	17.00[o]	32.50[o]	66.60[o]	-40.40[o]	26.20[o]	-51.10[o]	57.40[o]	6.30[o]
PCB 3	205.5	9.30[o]	26.90[o]	36.20[o]	71.60[o]	-41.60[o]	30.00[o]	-62.30[o]	68.50[o]	6.20[o]
PCB 77	268.2	25.90[o]	25.20[o]	51.10[o]						
PCB 101	289.1	13.10[o]	35.80[o]	48.90[o]						
PCB 136	310.0	24.50[o]	25.70[o]	50.20[o]						
PCB 202	351.8	27.90[o]	28.90[o]	56.80[o]	78.90[o]	-31.60[o]	47.30[o]	-51.00[o]	60.50[o]	9.50[o]
PCB 206	372.7	23.50[o]	35.10[o]	58.60[o]						
PCB 209	393.6	37.90[o]	26.00[o]	63.90[o]	93.10[o]	-36.90[o]	56.20[o]	-55.20[o]	62.90[o]	7.70[o]
Methanol	42.5	-7.34[p]			37.92[ff]			-44.52[uu]		-3.52[vv]
		-7.32[q]			37.95[ff]			-45.17[r]		
		-7.25[r]						-45.19[s]		
		-7.24[s]								
Ethanol	64.7	-10.17[p]	13.35[e]	3.18[p]	42.17[ii]	-35.69[ee]	6.49[ii]	-52.34[kk]	49.04[ll]	-3.31[mm]
		-10.10[r]			42.61[ff]			-52.71[r]		
		-10.00[q]			42.59[ff]			-52.40[uu]		-3.10[vv]
		-10.13[s]						-52.72[t]		
n-Propanol	81.8	-10.13[p]	16.74[e]	6.61[p]	47.03[ii]	-38.20[ee]	8.83[ii]	-57.15[kk]	54.94[ll]	-2.22[mm]
		-10.13[r]			47.56[ff]			-57.70[r]		
		-10.17[s]						-57.45[uu]		-2.31[vv]
		-9.20[q]								
n-Butanol	104.0	-9.41[p]	19.46[e]	10.04[p]	52.43[ii]	-40.71[ee]	11.72[ii]	-61.84[kk]	60.17[ll]	-1.67[mm]
		-9.28[r]			51.37[ff]			-60.65[r]		
		-8.16[q]			52.80[ff]			-61.58[uu]		-1.85[vv]
		-9.00[t]						-62.01[s]		
		-9.20[s]								
n-Pentanol	126.2	-7.82[p]	21.30[e]	13.47[p]	56.90[ii]	-42.68[ee]	14.23[ii]	-64.73[kk]	63.97[ll]	-0.75[mm]
		-7.66[s]			57.75[ff]			-64.75[uu]		-0.84[vv]

Table 2. (Continued)

Chemicals	Volume	ΔH_S	$-T\cdot\Delta S_S$	ΔG_S	ΔH_V	$-T\cdot\Delta S_V$	ΔG_V	ΔH_{SV}	$-T\cdot\Delta S_{SV}$	ΔG_{SV}
n-Pentanol	126.2	-6.36^{q}						-65.56^{p}		
		-8.08^{t}								
n-Hexanol	148.2	-6.02^{u}	22.89^{e}	16.86^{v}	61.92^{ii}	-45.19^{ee}	16.74^{ii}	-67.95^{kk}	68.07^{ll}	0.13^{mm}
		-4.64^{q}			61.63^{ff}			-66.27^{ww}		
		-5.77^{t}						-67.40^{ww}		
n-Hexanol	148.2	-6.57^{w}						-68.20^{w}		
		-6.40^{w}						-68.03^{w}		
								-66.20^{uu}		-0.38^{vv}
n-Heptanol	170.4	-5.36^{w}			66.32^{ff}			-71.67^{w}		
		-5.31^{w}						-71.63^{w}		0.12^{vv}
n-Octanol	192.6	-2.09^{x}			71.00^{ff}			-73.09^{x}		
		-0.42^{x}						-71.42^{x}		
		-3.77^{w}						-74.77^{w}		0.75^{vv}
n-Dodecanol	281.4	10.88^{x}			89.75^{ff}			-78.87^{x}		
Methane	37.7							-13.52^{qq}	39.87^{oo}	26.35^{qq}
								-12.76^{xx}		
								-13.79^{yy}	40.04^{oo}	26.25^{yy}
								-13.35^{ww}		
								-13.46^{zz}		
Ethane	59.9	-10.46^{h}	26.78^{e}	16.32^{h}	6.48^{hh}	-15.93^{gg}	-9.45^{hh}	-16.94^{zz}	42.71^{oo}	25.77^{qq}
								-16.65^{xx}		
								-19.76^{yy}	45.30^{oo}	25.54^{yy}
								-16.99^{ww}		
Propane	74.5	-7.11^{y}	27.61^{e}	20.50^{y}	14.26^{hh}	-19.86^{gg}	-5.60^{hh}	-21.38^{aaa}	47.48^{oo}	26.10^{aaa}
								-23.85^{xx}		
								-22.50^{yy}	48.56^{oo}	26.06^{yy}
Propane	74.5							-21.17^{ww}		
								-21.31^{zz}		
n-Butane	96.7	-3.35^{y}	28.03^{e}	24.69^{y}	21.34^{jj}	23.51^{ee}	-2.18^{jj}	-24.01^{aaa}	50.73^{oo}	26.72^{aaa}
								-24.06^{ww}		
								-25.97^{yy}	52.55^{oo}	26.58^{yy}

Table 2.(Continued)

Chemicals	Volume	ΔH_S	$-T\cdot\Delta S_S$	ΔG_S	ΔH_V	$-T\cdot\Delta S_V$	ΔG_V	ΔH_{SV}	$-T\cdot\Delta S_{SV}$	ΔG_{SV}
n-Butane	96.7							-25.10^{xx}		
n-Pentane	118.9	-2.09^{j} -1.26^{z}	30.54^{e}	28.45^{j} 26.74^{j} 26.78^{ff}	26.78^{jj}	-25.69^{ee}	1.09^{jj}	-28.87^{kk} -28.74^{j} -28.03^{z}	56.23^{ll}	27.36^{mm} 27.64^{ss}
n-Hexane	141.1	0.00^{j} 2.51^{z} 0.47^{aa}	32.64^{e}	32.64^{j} 31.55^{j} 31.80^{ff} 31.47^{ff}	31.59^{jj}	-27.49^{ee}	4.10^{jj}	-31.59^{kk} -31.60^{j} -29.29^{z} -31.00^{aa}	60.12^{ll}	28.53^{mm} 28.28^{tt}
n-Heptane	162.0	2.51^{z}	33.47^{e}	35.98^{h}	36.40^{h}	-29.41^{e}	6.99^{h}	-33.89^{z}	62.89^{oo}	29.00^{h} 28.84^{ss}
n-Octane	184.2	1.67^{z}	38.07^{e}	39.75^{h}	41.42^{h}	-31.51^{e}	9.92^{h}	-39.75^{z}	69.58^{oo}	29.83^{h} 29.98^{ss}

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*) DD is Dibenzo-*p*-dioxin, MCDD is MonoChloroDibenzo-*p*-dioxin, DCDD is DichloroDibenzo-*p*-dioxin, T_3CDD is TrichloroDibenzo-*p*-dioxin, T_4CDD is TetrachloroDibenzo-*p*-dioxin, P_5CDD is PentaChloroDibenzo-*p*-Dioxin, H_6CDD is HexaChloroDibenzo-*p*-Dioxin, H_7CDD is HeptaChloroDibenzo-*p*-Dioxin. a) calculated from (ΔH_{sol}-ΔH_f); ΔH_{sol} from refs. 15 and 16, ΔH_f from ref. 17. b) calculated as (ΔG_S-ΔH_S). c) calculated from (ΔG_{sol}-ΔG_f); ΔG_{sol} from refs. 15 and 16, ΔG_f from ref. 17. d) from ref. 18. e) calculated as (ΔG_S-ΔH_S). f) from ref. 19. g) from ref. 20. h) from ref. 21. i) from ref. 22. j) from ref. 23. k) determined from aqueous solubilities reported in ref. 24 following equation 1. l) from ref. 18. m) from ref. 18 calculated as (ΔG_{sol}-ΔG_f) and (ΔH_{sol}-ΔH_f). n) PCBs characterized by their IUPAC number. o) from ref. 25. p) from ref. 26. q) from ref. 27. r) from ref. 28. s) from ref. 29. t) from ref. 30. u) from ref. 31. v) from ref. 32. w) from ref. 33. x) from ref. 34. y) from ref. 35. z) from ref. 36. aa) from ref. 37. bb) calculated from (ΔH_{sub}-ΔH_f); ΔH_{sub}, ΔH_f from ref. 17. cc) calculated from ($-T.\Delta S_{sub}$-($-T.\Delta S_f$)); ΔS_{sub}, ΔS_f from ref. 17. dd) from (ΔH_V-$T.\Delta S_V$). ee) calculated as (ΔG_V-ΔH_V). ff) from (ΔH_S-ΔH_{SV}). gg) from ($-T.\Delta S_S$-($-T.\Delta S_{SV}$)). hh) from (ΔG_S-ΔG_{SV}). ii) from ref. 38. jj) from ref. 39. kk) from (ΔH_S-ΔH_V). ll) from ($-T.\Delta S_S$-($-T.\Delta S_V$)). mm) from (ΔG_S-ΔG_V). nn) from ref. 40. oo) calculated as (ΔG_{SV}-ΔH_{SV}). pp) from ref. 41. qq) from ref. 39. rr) from ref. 23, corrected for change in the standard state convention. ss) from ref. 42. tt) from ref. 43, corrected for change in the standard state convention. uu) from ref. 44. vv) from ref. 45. ww) from ref. 13. xx) from ref. 46. yy) from ref. 47. zz) from ref. 48. aaa) from ref. 49.

molar volume and thermodynamic properties are summarized in Table 3.

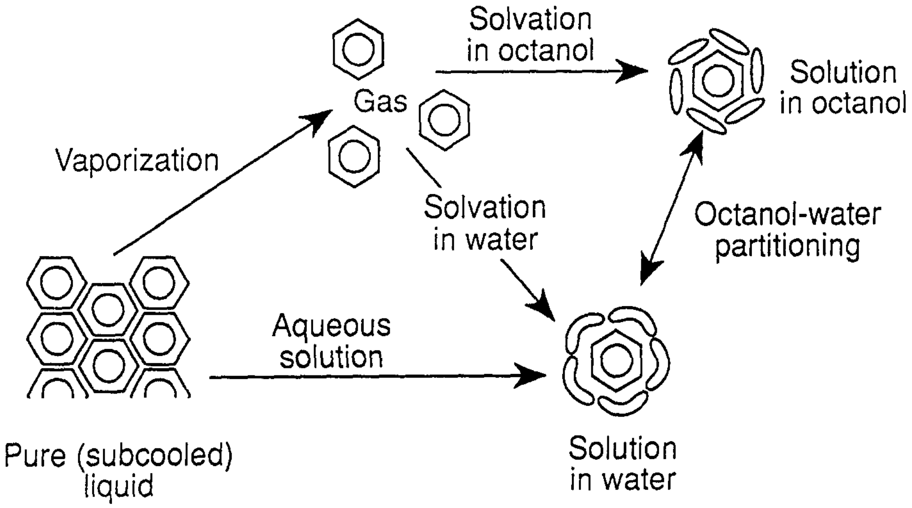

Figure 2: Schematic diagram of the inter-molecular interactions involved the aqueous solution and octanol-water partitioning processes.

RESULTS

Vaporization: Figure 3a demonstrates that for all chemical substances in this study, the enthalpy of vaporization is positive, indicating that energy is required to break the intermolecular bonds in the pure (subcooled) liquid phase. In each congeneric series, the enthalpy of vaporization increases linearly with increasing molar volume at a rate of 0.19 to 0.39 kJ/mol per cm^3 (Table 3). Apparently, solute-solute interactions in the pure (subcooled) liquid phase become stronger with increasing volume or surface area of the congener.

The entropy of vaporization is positive, representing a gain of entropy when the molecules from the (subcooled) liquid phase enter the gas phase (at 1 atm). Within each congeneric series, the entropy of vaporization is also a linear function of the solute's molar volume, but the change in the entropy term ($-T\cdot\Delta S_V$) with molar volume is smaller than the corresponding increase in enthalpy (Table 3). In fact, for PCDDs, there is no statistically significant change ($P<0.05$) in the entropy of vaporization with increasing molar volume.

The free energy of vaporization is composed of the enthalpy of vaporization and the entropy of vaporization. Since enthalpy of vaporization is more dependent on the molar volume than the entropy of vaporization, the observed linear increase of the free energy of vaporization with increasing molar volume at 0.12 to 0.32 kJ/mol per cm^3 (Table 3) largely reflects the increase of the enthalpy of vaporization with increasing molar volume. This indicates that the relationship between the free energy of vaporization and molar volume is predominantly due to

Table 3. Observed linear relationships between thermodynamic properties and molar volume.*

	Linear Correlation with Volume	S	r^2	n	chemicals
Vaporization	$\Delta H = 0.25 (\pm 0.07) \cdot V + 20.45$	6.09	0.81	15	PCDDs
	$\Delta H = 0.19 (\pm 0.01) \cdot V + 15.55$	0.98	0.99	18	ABs
	$\Delta H = 0.39 (\pm 0.03) \cdot V - 3.25$	2.37	0.99	12	PAHs
	$\Delta H = 0.22 (\pm 0.00) \cdot V + 29.04$	0.56	1.00	23	Alcohols
	$\Delta H = 0.27 (\pm 0.03) \cdot V - 6.19$	1.47	0.98	12	Alkanes
	$-T\Delta S = -0.04 (\pm 0.05) \cdot V - 30.06$	4.65	0.16	15	PCDDs
	$-T\Delta S = -0.07 (\pm 0.01) \cdot V - 21.57$	0.42	0.99	11	ABs
	$-T\Delta S = -0.07 (\pm 0.03) \cdot V - 22.05$	2.00	0.75	10	PAHs
	$-T\Delta S = -0.11 (\pm 0.02) \cdot V + 28.88$	0.33	0.99	5	Alcohols
	$-T\Delta S = -0.12 (\pm 0.03) \cdot V - 10.79$	1.22	0.96	7	Alkanes
	$\Delta G = 0.21 (\pm 0.02) \cdot V - 9.62$	1.79	0.97	15	PCDDs
	$\Delta G = 0.12 (\pm 0.01) \cdot V - 6.98$	0.58	0.99	12	ABs
	$\Delta G = 0.32 (\pm 0.06) \cdot V - 25.93$	3.90	0.93	11	PAHs
	$\Delta G = 0.13 (\pm 0.04) \cdot V + 2.42$	1.70	0.99	4	PCBs
	$\Delta G = 0.12 (\pm 0.01) \cdot V - 1.24$	0.20	1.00	5	Alcohols
	$\Delta G = 0.15 (\pm 0.02) \cdot V - 17.32$	0.70	0.99	7	Alkanes
Solvation	$\Delta H = -0.39 (\pm 0.08) \cdot V + 29.91$	6.44	0.89	12	PCDDs
	$-T\Delta S = 0.34 (\pm 0.08) \cdot V - 15.88$	6.05	0.87	12	PCDDs
	$\Delta G = -0.05 (\pm 0.02) \cdot V + 14.03$	1.10	0.82	12	PCDDs
	$\Delta H = -0.15 (\pm 0.02) \cdot V - 18.41$	1.15	0.97	19	ABs
	$-T\Delta S = 0.17 (\pm 0.02) \cdot V + 29.70$	0.93	0.99	12	ABs
	$\Delta G = 0.03 (\pm 0.01) \cdot V + 10.96$	0.57	0.86	14	ABs
	$\Delta H = -0.15 (\pm 0.02) \cdot V - 44.00$	2.78	0.91	23	Alcohols
	$-T\Delta S = 0.22 (\pm 0.06) \cdot V + 35.98$	1.18	0.98	5	Alcohols
	$\Delta G = 0.04 (\pm 0.01) \cdot V - 5.68$	0.18	0.99	5	Alcohols
	$\Delta H = -0.17 (\pm 0.02) \cdot V - 7.54$	1.24	0.97	23	Alkanes
	$-T\Delta S = 0.20 (\pm 0.03) \cdot V + 31.80$	0.94	0.99	8	Alkanes
	$\Delta G = 0.03 (\pm 0.01) \cdot V + 24.42$	0.49	0.91	8	Alkanes
	$\Delta H = -0.22 (\pm 0.06) \cdot V - 11.16$	4.22	0.87	12	PAHs
	$-T\Delta S = -0.06 (\pm 0.08) \cdot V + 43.31$	4.58	0.18	10	PAHs
	$\Delta G = -0.15 (\pm 0.04) \cdot V + 29.27$	3.28	0.80	12	PAHs
Solution	$\Delta G = 0.17 (\pm 0.02) \cdot V + 3.17$	1.86	0.95	12	PCDDs
	$\Delta G = 0.15 (\pm 0.01) \cdot V + 4.47$	0.37	1.00	13	ABs
	$\Delta G = 0.16 (\pm 0.01) \cdot V + 3.44$	0.73	0.99	14	PAHs
	$\Delta G = 0.14 (\pm 0.02) \cdot V + 9.33$	2.41	0.96	8	PCBs
	$\Delta G = 0.16 (\pm 0.01) \cdot V - 6.92$	0.30	1.00	5	Alcohols
	$\Delta G = 0.18 (\pm 0.01) \cdot V + 6.34$	0.64	1.00	7	Alkanes

* The 95% confidence intervals are given in brackets. S is the standard error of regression, r is the correlation coefficient and n is sample size.

breaking solute-solute interactions, which requires more energy when the congener's molar volume increases.

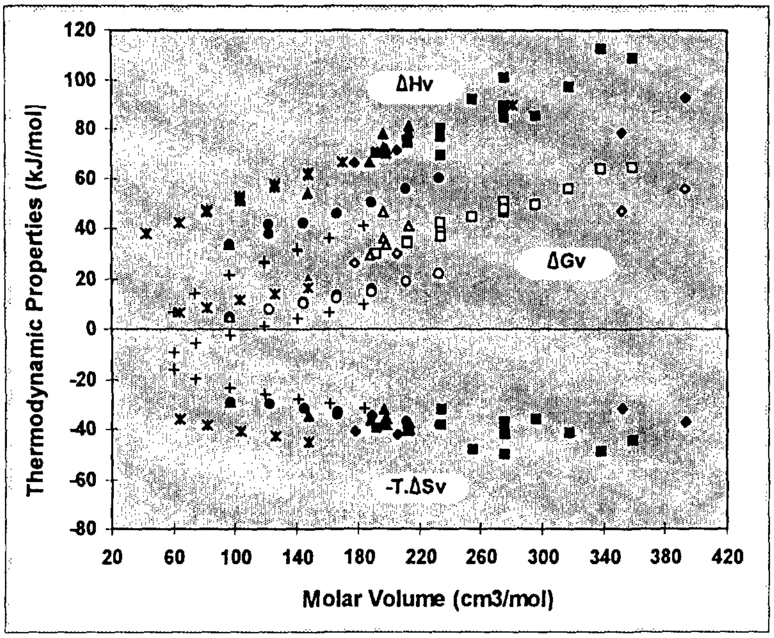

Figure 3a: Molar enthalpies i.e. ΔH_V (positive values, closed symbols), entropies, i.e. $-T\cdot\Delta S_V$ (negative values, closed symbols) and free energies i.e. ΔG_V (open symbols) of vaporization of chlorodibenzo-*p*-dioxins (■,□), alkylbenzenes (●,O), Polynuclear Aromatic Hydrocarbons (▲,Δ), Polychlorinated Biphenyls (◆,◇), Alcohols (✱,⊠), and Alkanes (+,⊞) in kJ/mol versus molar volume V (cm^3/mol).

Solvation: Figure 3b shows that the transfer of the solute from the ideal gas phase to the infinitely dilute aqueous solution (i.e. solvation), is accompanied by a negative enthalpy and entropy, which both decrease with increasing molar volume at approximately the same rate for a given congeneric series (Table 3). However, the free energy of solvation varies only slightly (i.e. between -0.15 to 0.04 kJ/mol per cm^3) among the congeners. This is due to the fact, that within each congeneric series, an increase in molar volume is always associated with an unfavourable decrease in the entropy contribution (i.e. $-T\cdot\Delta S_{SV}$) and an equally large favorable increase in enthalpy (ΔH_{SV}), which is an widely observed phenomenon often referred to as "enthalpy-entropy compensation"[50]. And, despite the large differences in molecular size among congeners, the free energy of solvation is almost identical. Apparently, the strong dependence and correlation of entropy of solvation on the molar volume within congeneric series is hardly reflected in the relationship between the free energy of solvation and molecular size. In fact, for PCDDs and PAHs, a statistically significant drop of the free energy of solvation is observed with increasing molar volume, indicating that congeners of PCDDs and PAHs actually become less hydrophobic (or their gas phase (1 atm) aqueous solubilities actually increase) with increasing molar volume. This effect can also be observed in terms of the small drop in the Henry's Law constants of these substances with increasing molecular size [12,15]. The

Henry's Law constant reflects the contribution of pure hydrophobic interaction or solvation, although it is derived, by its own definition, from the ratio of two properties-solubility and vapor pressure representing different molecular interactions. A similar finding has been reported before: The aqueous solubility of inert gases (at 1 atm) increases with increasing solute size [51].

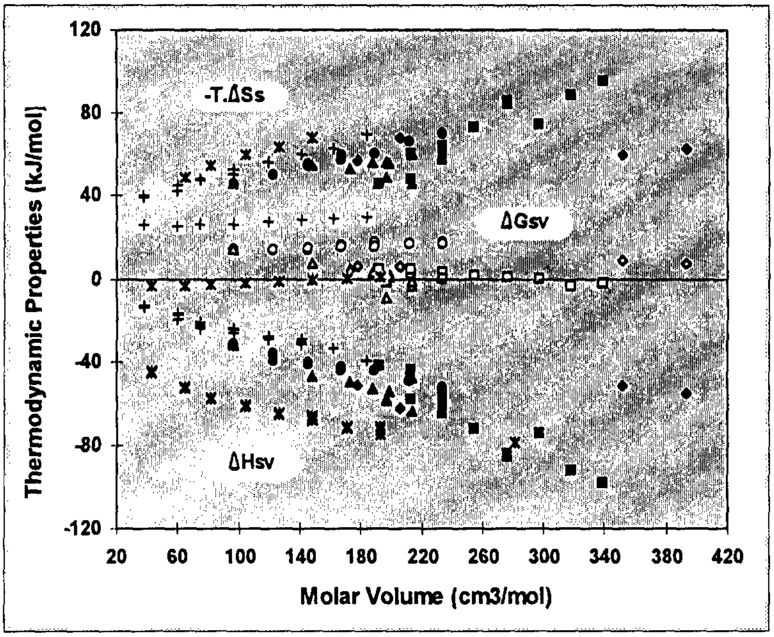

Figure 3b: Molar enthalpies i.e. ΔH_{sv} (negative values and closed symbols), entropies i.e. $-T\cdot\Delta S_{sv}$ (positive values and closed symbols) and free energies i.e. ΔG_{sv} (open symbols) of salvation of chlorodibenzo-*p*-dioxins (■,□), alkylbenzenes (●,O), Polynuclear Aromatic Hydrocarbons (▲,Δ), Polychlorinated Biphenyls (◆,◇), Alcohols (✱,☒), and Alkanes (+,⊞) in kJ/mol versus molar volume V (cm^3/mol).

Aqueous Solution: For the congeneric series tested in this study, there appear to he no consistent trends in the relationship between molar volume and the enthalpy and entropy of solution. For example, ΔH_s of PCDDs drops with increasing molar volume, while it increases with molar volume for PAHs (see Figure 3c). However, the free energies of solution of all homologous series increase with molar volume at approximately the same rate of 0.14 to 0.18 kJ/mol per cm^3 (see Figure 3d and Table 3). Since the contribution to the free energy of solution from free energy of solvation is virtually independent on molar volume, this increase of the free energy of solution with increasing molar volume largely reflects the increase of the free energy of vaporization with molar volume, which in turn reflects the relationship between the enthalpy of vaporization and molar volume. This indicates that the drop of the aqueous solubility with increasing molecular size is primarily due to the phenomenon that larger size molecules require more energy to leave the pure (subcooled) liquid phase. The relationship between the aqueous (subcooled liquid) solubility and molecular size descriptors thus reflects largely solute-solute interactions in the pure liquid phase and not solute-water interactions.

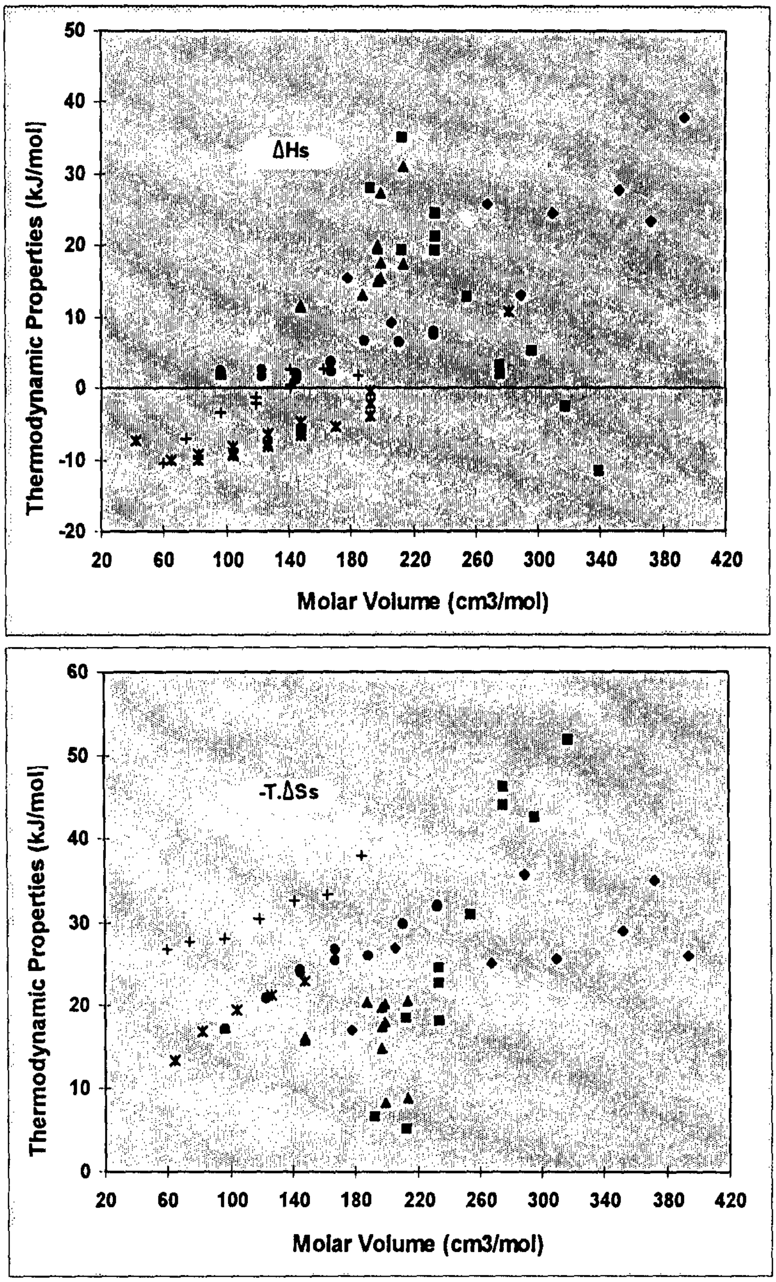

Figure 3c: Molar enthalpies and entropies of solution of the (subcooled) liquid solute, i.e. ΔH_S and $-T{\cdot}\Delta S_S$ of chlorodibenzo-*p*-dioxins (■), alkylbenzenes (●), Polynuclear Aromatic Hydrocarbons (▲), Polychlorinated Biphenyls (◆), Alcohols (✶), and Alkanes (+) in kJ/mol versus molar volume V (cm^3/mol).

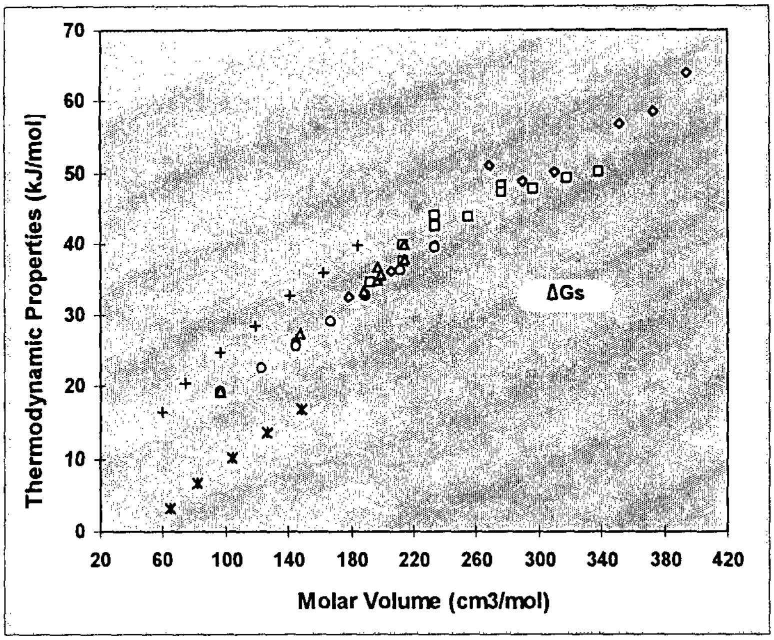

Figure 3d: Molar free energies of solution of the (subcooled) liquid solute, i.e. ΔG_S of chlorodibenzo-*p*-dioxins (□), alkylbenzenes (O), Polynuclear Aromatic Hydrocarbons (Δ), Polychlorinated Biphenyls (◇), Alcohols (✱), and Alkanes (+) in kJ/mol versus molar volume V (cm^3/mol).

DISCUSSION

The thermodynamic analysis, carried out for selected congeneric series, presents a picture of how the thermodynamic properties associated with the two contributing steps in the aqueous solution process are related to the molecular size within each congeneric series. It rejects the general viewpoint that, within congeneric series, the reduction of the aqueous solubility with increasing molar volume is due to an increase in the loss of entropy of solvation resulting from the larger contact surface area of the solute with the water. Our results indicate that due to enthalpy-entropy compensation in the aqueous solvation process, a loss of entropy of solvation resulting from an increase in the congener's molar volume is associated with an equally large favorable gain in the enthalpy of solvation, thus resulting in virtually no change in the free energy of solvation from one congener to another. The relationship between the aqueous solubility (or free energy of solution) of hydrophobic organic chemicals and molar volume or surface area within congeneric series appears to reflect the increase in the free energy of vaporization, rather than solvation, with increasing molar volume. It can then be concluded that, within a congeneric series, the relationship between the aqueous solubility of liquid (or subcooled liquid) hydrophobic chemicals and molar volume or surface area predominantly reflects interactions of the solute with other solute molecules in the (subcooled) liquid phase and that the contributions from solute-water (hydrophobic) interactions are relatively unimportant to the observed dependence of aqueous solubility on solute size, This implies that there is no sound physical-chemical basis for selecting solute-water surface areas as the basis for structure-solubility relationships for congeneric series of non-polar organic substances. Molecular descriptors expressing solute-solute interactions are likely to be a better basis for structure-solubility relationships within congeneric series. Considering the success of molar volumes and surface areas in correlating aqueous solubilities within congeneric series, it is likely that these molecular descriptors are also appropriate descriptors in characterizing chemical-chemical interactions in the pure (subcooled) liquid phase.

It might be worthwhile to emphasize here that, in this study, our discussion has mainly focused on the variations of thermodynamic properties with the congener's molar volume. The results presented here do therefore not imply that hydrophobic interactions related to the solute's surface area with the water, are unimportant in terms of controlling the low aqueous solubility of many hydrophobic solutes. Clearly, for some of the hydrophobic solutes, the unfavorable free energy of solvation, which is largely due to the large negative entropy of solvation, is an important contribution to the unfavorable free energy of solution and hence, the low aqueous solubility. However, for the congeneric series of hydrophobic compounds that were investigated, the reduction in the aqueous solubility with increasing molecular size is not due to a greater hydrophobicity of the larger congeners resulting from a larger surface area with the water. The reason for this is that, within each of the congeneric series investigated in this study, an increase in molecular size is associated with an unfavorable change in the entropy of solvation and a favorable change in enthalpy of solvation that are of similar magnitude, causing the free energy of solvation to be virtually independent on molecular size. A good example is alkanes. The unfavorable free energy of solvation of alkanes of 26 to 30 kJ/mol, which is largely due to the large negative entropy of solvation ($-T\cdot\Delta S_{sv}$) of 40 to 70 kJ/mol, is an important contribution to the unfavorable free energy of solution of 16 to 40 kJ/mol and, hence, the low aqueous solubility of this series of congeners. The contribution of the free energy of vaporization to the free energy of solution is small and even favorable for the lower molecular weight congeners (see Table 2). However, with increasing congener size (i.e. from methane to octane), the free energy of solvation increases only 4 kJ/mol (i.e. from 26 to 30 kJ/mol), which contributes little to the overall increase in the free energy of solution of 24 kJ/mol. The contribution of the increase in the free energy of vaporization of 20 kJ/mol to the increase in the free energy of solution of 24 kJ/mol is more important than the increase in the free energy of solvation of 4 kJ/mol. In other words, the decline in aqueous solubility from methane to octane is mainly caused by solute-solute in the pure (subcooled) liquid phase rather than solute-water interactions. It is further interesting to note that for the PCDDs and PAHs the contribution of the free energy of solvation to the free energy of solution (and hence the solubility) is much smaller than the free energy of vaporization and even favourable for some of the most "hydrophobic" congeners (Table 2), indicating that solute-water interactions contribute little to the very low aqueous solubilities of these substances.

Our findings have some interesting implications for modeling and understanding of the environmental fate of organic substances in aqueous systems. First, further improvements of quantitative structure- aqueous solubility relationships may be achieved by modeling solute-solute rather than solute-water interactions alone. Secondly, the traditional viewpoint that the increase in octanol-water and other organic phase-water partition coefficients with increasing molar volume or size is a reflection of the greater hydrophobicity of the larger size congeners should be reexamined. For example, the increase in octanol-water partition coefficients (K_{ow}) with increasing molar volume within hydrophobic congeneric series is often viewed as a result of the reduction of the aqueous solubility with increasing congener size while the solubility in octanol is relatively constant among congeners [14]. Hence, an increase in unfavourable solute-water interactions or hydrophobicity is believed to be the origin of the larger partition coefficients. This is incorrect because, as the data presented in this study indicate, an increase in unfavorable solute-water interactions is not responsible for the reduction of the aqueous solubility with increasing congener size. A better explanation for the dependence of K_{ow} on molar volume can be obtained by viewing octanol-water partitioning as a process where the solute is engaged in octanol and water "solvation" processes, rather than in octanol and water "dissolution" processes (see Figure 2). The apparent constant-like solubility of congeners in octanol is actually the result of the fact that the drop in free energy of octanol "solvation" with increasing molar volume is counter-balanced by the increase in the free energy of "vaporization", resulting in a free energy of octanol-solution that is virtually independent on molar volume within congeneric series. Since the free energy of solvation in water is approximately the same for congeners, it follows that the increase of K_{ow} with increasing molar volume is due to the drop in the free energy of solvation in octanol with increasing molar volume of the solute and is thus a reflection of the greater "lipophilicity" in octanol of the larger size congeners. Solute-octanol interactions are therefore responsible for the increase in K_{ow} within congeneric series of PCBs, PCDDs, alkanes and others. In terms of environmentally relevant partitioning processes such as bioconcentration in fish and sediment-water partitioning, which are related to the octanol-water partition coefficient [3,4], this means that differences in environmental partition coefficients within congeneric series of hydrophobic organic chemicals are largely controlled by interactions of the chemical with the non-aqueous phase (e.g. lipids or organic carbon). An increase in environmental partition coefficients between organic phases and water among congeners of hydrophobic organic chemicals thus reflects the congener's greater lipophilicity, not hydrophobicity.

ACKNOWLEDGMENT

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