Aqueous Solubility of Chloroguaiacols

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The aqueous solubilities of guaiacol (2-methoxyphenol) and seven chlorinated guaiacols are reported at 25 °C, and for five of these over a temperature range from 5 to 45 °C, from which the enthalpies of solution are deduced. It is shown that the solubilities are well correlated with molar volume and that chlorinated phenols and guaiacols follow similar solubility–molar volume and vapor pressure–molar volume relationships. This does not, however, apply to 1-octanol–water partition coefficients. It is concluded that the equilibrium partitioning of the chlorinated and methoxylated phenols is more complex than has been generally assumed and that an improved understanding is required of the fundamental determinants of partitioning among water, air, octanol, and lipid phases of this important class of environmental contaminants.

Introduction

The chlorophenols, chlorocatechols, and chloroguaiacols (2-methoxyphenols) are of increasing environmental interest because of their formation during wood pulp bleaching by the forest industry (*1*). Their environmental fate and effects depend on their physical–chemical properties; thus, there is a need to determine these properties and develop predictive methods for use in situations when experimental values are unavailable or are suspect. Suntio et al. (*2*) have reviewed the presence of organochlorine compounds in pulp mill effluents and noted the lack of reported physical–chemical properties. Aqueous solubility is an important parameter for assessing environmental fate and effects because it influences evaporation rates and extent of sorption to biotic and abiotic phases as well as toxicity to aquatic organisms. In this work, the solubilities of chlorinated guaiacols in water over a range of temperature have been measured. In addition to expanding the experimentally determined data base for solubility, there is a need to gather and correlate other environmentally relevant physical–chemical properties such as the vapor pressure and 1-octanol–water partition coefficient, and establish quantitative structure–property relationships (QSPR) for these properties with appropriate molecular descriptors. We thus review such data, and in doing so explore how these properties relate to those of the structurally similar chlorophenols for which solubility measurements have been reported recently (*3*).

Ultimately there is also a need to relate these descriptors, and especially solubility, to toxicity data in order to assess the likelihood of adverse effects.

Kovacs et al. (*4*) have recently reviewed toxicity data for phenolic compounds and, by deducing toxicity equivalency factors, have demonstrated that water solubility, or the related 1-octanol–water partition coefficient, is a primary determinant of relative toxicity in this series of chemicals.

Experimental Section

Materials. Guaiacol (98% purity) was purchased from Aldrich Chemical Co. Chlorinated guaiacols (99+% purity) were obtained from Helix Biotech Corp. of Richmond BC. Water was doubly distilled. Methanol and hexane (both of HPLC grade) were obtained from Caledon Laboratories, Ontario. The guaiacols were used without further purification.

Preparation of Saturated Solutions. Excess amounts of chloroguaiacols were added to 50–250-mL Erlenmeyer flasks containing double-distilled water. They were stirred or shaken gently for 24 h and allowed to settle in a temperature bath at the desired temperature for at least 48 h before analysis. pH values were measured by a Radiometer Model PHM84 research pH meter before aqueous samples were taken for analysis. There was no pH adjustment or buffering. The pH of the doubly distilled water was measured to be 5.60, the low pH being attributable to dissolved CO_2.

To provide confirmation of the reliability of the results, concentrations were measured by two independent analytical methods, HPLC and GC.

HPLC Measurements. Analysis was performed by direct injection of an aqueous sample onto the column of a Waters' Associates (Millford, MA) liquid chromatograph (HPLC system) consisting of a Model 6000 solvent delivery system, a Model M45 solvent delivery system, a Model 440 UV absorbance detector with 254- and 280-nm kits, and a Model 720 system flow controller. The system was operated in isocratic mode with a methanol and water mixture (85:15 v/v) as the mobile phase. The analytical column was a Waters 3.9-mm-o.d. × 300-mm-long μBondapak C_{18} column. Calibration standards were prepared by dissolving known amounts of guaiacols in methanol. Peak areas were integrated and recorded by a Waters Model 730 data module.

Gas Chromatographic Measurements. The saturated aqueous solution was extracted with hexane and then injected onto the GC column of a Hewlett-Packard 5890 gas chromatograph equipped with a ^{63}Ni EC detector. Conditions were the following: capillary injector at 250 °C, oven in isothermal mode at 195 °C, and detector at 300 °C. The analytical column was a 0.32-mm-o. d. by 30-m-long J&W DB5.625 fused silica capillary column. The makeup and carrier gas was a 5:95 argon–methane mixture. The peak area was recorded on a Hewlett-Packard 3392A integrator.

Results

Table 1 gives the measured aqueous solubilities of eight guaiacols at their natural pH measured by both HPLC and GC at 25 °C, the values by both methods being in good agreement. In each case there were 20 determinations, the standard deviation of the results also being given. Selected solubilities and their estimated standard deviations are also given.

Table 2 gives the aqueous solubilities of the chloroguaiacols at various temperatures. The van't Hoff plot of the logarithm of mole fraction solubility versus reciprocal absolute tem-

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Table 1. Melting Points t_m, Dissociation Constant pK_a, LeBas Molar Volume V_L, Experimental Solubilities S by HPLC–UV and GC–ECD Methods at 25 °C, Selected Solubility S_{SEL} with Standard Deviations, Concentration of Nonionized Species Corresponding to the Selected Solubility S_{NI}, pH, and Previously Reported Values from the Literature

compound	t_m, °C	pK_a	V_L, cm^3/mol	S, g m^{-3} HPLC–UV	S, g m^{-3} GC–ECD	S_{SEL}, g m^{-3}	S_{NI}, g m^{-3}	pH	lit. value
guaiacol	28		125.6	24 800 ± 830		24 800 ± 830			16 000 (15 °C) (*8*)
4-guaiacol	liq		153.9	5140 ± 190	5604 ± 741	5370 ± 300		2.8	
5-guaiacol	34–35		153.9	3875 ± 70	4044 ± 585	3960 ± 300		5.4	
4,5-dichloroguaiacol	69–70	8.52 (*6*)	174.8	584 ± 20	565 ± 29	575 ± 25	574	5.6	
4,6-dichloroguaiacol	63–64		174.8	717 ± 16	700 ± 40	708 ± 30		4.0	
3,4,5-trichloroguaiacol	85–86	7.56 (*6*) 7.90 (*7*)	195.7	305 ± 18	313 ± 16	310 ± 18	303 307	5.9	
4,5,6-trichloroguaiacol	112–115	7.20 (*6*) 7.07 (*7*)	195.7	57 ± 6.4	50 ± 5	54 ± 6	52 51	5.8	
tetrachloroguaiacol	121–122	6.26 (*6*) 7.0 (*7*)	216.6	27 ± 2.0	25 ± 3.0	26 ± 3	26 26	4.2	

Table 2. Temperature Dependence of the Aqueous Solubility S of Chloroguaiacols Measured by GC–ECD, Enthalpy of Solution, and Its Standard Deviation

compound	S, g m^{-3} 5 °C	7 °C	15 °C	25 °C	35 °C	45 °C	ΔH, kJ mol^{-1}
4-chloroguaiacol				5604 ± 741			
5-chloroguaiacol				4044 ± 585			
4,5-dichloroguaiacol	166 ± 8		196 ± 10	565 ± 29	698 ± 40	1021 ± 76	35.0 ± 5.7
4,6-dichloroguaiacol	365 ± 17		422 ± 14	700 ± 40	1129 ± 42	1496 ± 79	27.9 ± 2.8
3,4,5-trichloroguaiacol	113 ± 11		176 ± 11	313 ± 16	363 ± 21	536 ± 23	28.3 ● 2.4
4,5,6-trichloroguaiacol		30 ± 1.0	42 ± 2.0	50 ± 5	81 ± 5	148 ± 8	29.6 ± 3.8
tetrachloroguaiacol		20 ± 2.0	16 ± 1.0	25 ± 3	26 ± 1.7	50 ± 3	17.9 ± 6.1

perature (K) is shown in Figure 2, and the enthalpies of solution calculated from the slopes by least-squares regression are given in Table 2.

No results are reported for the temperature dependence of the solubilities of the monochloroguaiacols since the results were judged insufficiently accurate for reporting.

Table 1also gives the melting point, pK_a, pH, and additive LeBas molar volume (*5*). The subcooled liquid solubilities were calculated from the fugacity ratio F, using an estimated entropy of fusion of 56 J mol^{-1} K^{-1} for rigid organic molecules as suggested by Yalkowsky (*9*),

$$F = C_S/C_L = \exp\{(\Delta S_{fus}/R)(1 - T_M/T)\}$$

where C_S and C_L (mol m^{-3}) are the solubilities of the solid and liquid of the solute, respectively, R is the ideal gas constant (8.314 J mol^{-1} K^{-1}), ΔS_{fus} is the entropy change of fusion, T_m is the melting point of the solute, and T is the system temperature. The plot of the hypothetical subcooled liquid solubility (C_L) versus LeBas molar volume (V_M) is shown in Figure 1, indicating the consistent logarithmic–linear behavior. Fugacity ratios are given in Table 3.

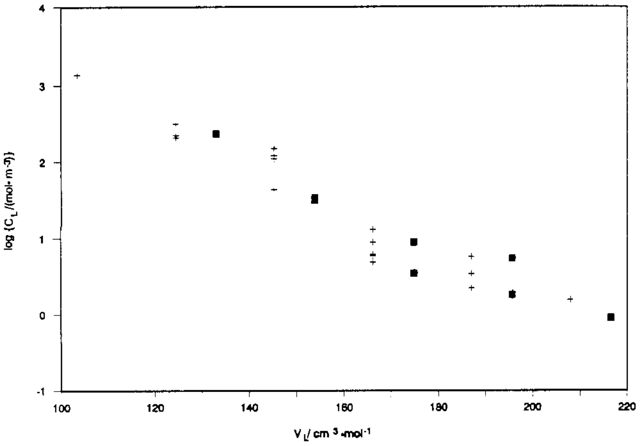

Figure 1. Subcooled liquid solubility C_L versus LeBas molar volume V_L for chloroguaiacols (■) and chlorophenols (+).

Other Properties

It is also of interest to tabulate and examine other physical–chemical properties which determine environmental fate. Table 3 gives reported literature data for liquid or solid vapor pressure ($P_L{}^S$) and the subcooled liquid vapor pressure ($P_L{}^S$), and log(1-octanol–water partition coefficients) (log K_{ow}). The quantitative structure–property relationship (QSPR) plots of the logarithms of vapor pressure and 1-octanol–water partition coefficient versus LeBas molar volume are presented in Figures 3 and 4. Figure 5 shows the inverse relationship between the 1-octanol–water partition coefficient and the subcooled liquid solubility. This QSPR approach is identical to that used in recent handbooks of environmentally relevant physical–chemical properties (*17, 18*). Also shown, in these figures are corresponding data for the chlorophenols (*3*).

Discussion

The possible dissociation of the chloroguaiacols affects the aqueous solubilities. Reported pK_a data are given in Table 1, there being some uncertainty about pK_a for the tetrachlo-

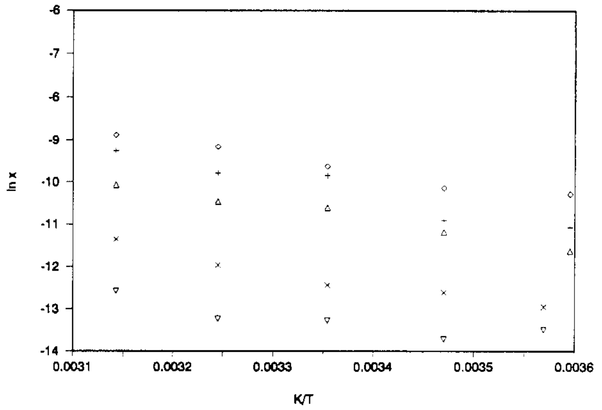

Figure 2. Dependence of mole fraction aqueous solubilities x on temperature for 4,5-dichloroguaiacol (+), 4,6-dichloroguaiacol (◇), 3,4,5-trichloroguaiacol (△), 4,5,6-trichloroguaiacol (×), and tetrachloroguaiacol (▽).

Table 3. Molecular Mass M_w, Fugacity Ratio F, Solid Vapor Pressures P^s, Liquid or Subcooled Liquid Vapor Pressures P_L, and 1-Octanol–Water Partition Coefficients K_{ow} of Some Chloroguaiacols at 25 °C

compound	M_w, g/mol	F	vapor pressure P^s, Pa	vapor pressure P_L, Pa	log K_{ow}
guaiacol	125.15	0.85		24.5 (*10*)	1.33 (*12*)
			13.73 (*8*)		2.53 (*8*)
4-chloroguaiacol	158.6	1			2.15 (*13*)
5-chloroguaiacol	158.6	0.796			
4,5-dichloroguaiacol	193.04	0.86		1.54 (*11*)	3.26 (*14*)
					3.18 (*15*)
					3.41 (*16*)
					2.86 (*13*)
					3.19 (*6*)
4,6-dichloroguaiacol	193.04	0.411			2.86 (*13*)
3,4,5-trichloroguaiacol	227.49	0.249		0.64 (*11*)	3.77 (*14*)
					4.11 (*15*)
					4.0 (*7*)
					3.57 (*13*)
					4.45 (*16*)
					4.13 (*6*)
4,5,6-trichloroguaiacol	227.49	0.129		0.25 (*11*)	3.74 (*15*)
					4.10 (*16*)
					3.69 (*7*)
					3.57 (*13*)
					3.72 (*6*)
tetrachloroguaiacol	261.93	0.11		0.14 (*11*)	4.45 (*15*)
					4.42 (*6*)
					4.29 (*14*)
					4.53 (*7*)
					5.14 (*16*)
					4.28 (*13*)

roguaiacol. The ratio of ionized to nonionized concentrations is given by

$$(\text{ionized})/(\text{nonionized}) = 10^{(\text{pH}-\text{p}K_a)}$$

The solubilities in Table 1 are "corrected" using this formula to give S_{NI}, the reduced concentration of the nonionized species. The effect is small or negligible for all the compounds.

As shown in Figure 1, the effect of substituting four chlorines for hydrogens is to reduce the subcooled liquid solubility by approximately 2.4 log units, or a factor in solubility of 4.0 per chlorine substituted. The vapor pressure data in Figure 3 show a similar trend but with a slightly lower slope corresponding to a factor of approximately 3.6 per chlorine substituted. The net effect is that Henry's law constant (H) when estimated as the ratio of vapor pressure to solubility is fairly constant, with most values lying in the range 0.10–0.44 (Pa·m^3)/mol, with 0.16 being typical. The dimensionless air–water partition coefficient H/RT or K_{AW} thus averages 6.5 × 10^{-5}; that is, equilibrium concentrations in air are a factor of approximately 15 000 lower than those in water. As a result the chloroguaiacols tend to evaporate very slowly from solution in water, and the rate of evaporation will be entirely gas phase resistance controlled (*19*). For example, a typical gas phase mass transfer coefficient k_G of 5 m/h will result in a half-time for evaporation of chloroguaiacols from water 1 m deep of approximately 0.693/($k_G K_{AW}$), or 2100 h or 90 days. It is very likely that some evaporation will take place especially in turbulent water, or in aeration basins used to treat effluents containing chlorinated guaiacols, but evaporation is unlikely to be a major environmental fate process, especially compared with biodegradation, photolysis, and sedimentation. It would be useful to measure H directly by a stripping technique (*20*) to confirm that this estimate is correct.

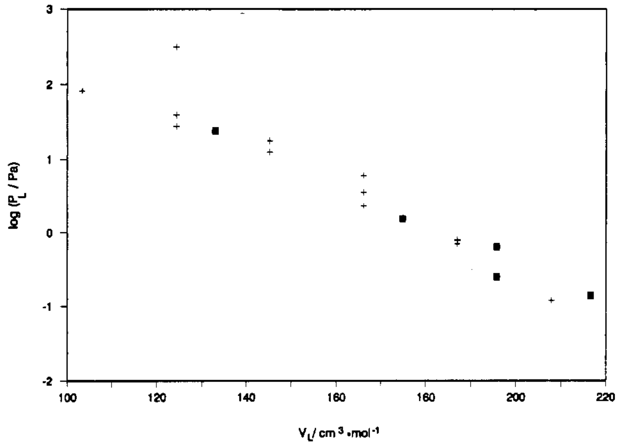

Figure 3. Subcooled vapor pressure P_L versus LeBas molar volume V_L for chloroguaiacols (■) and chlorophenols (+) (phenol to pentachlorophenol).

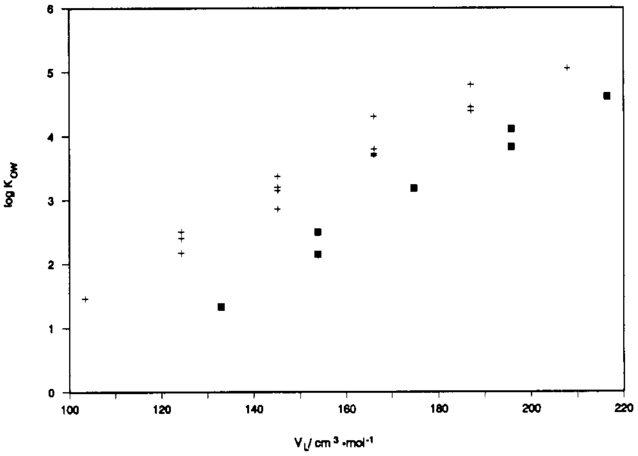

Figure 4. 1-Octanol–water partition coefficient K_{OW} versus LeBas molar volume V_L for chloroguaiacols (■) and chlorophenols (+) (phenol to pentachlorophenol).

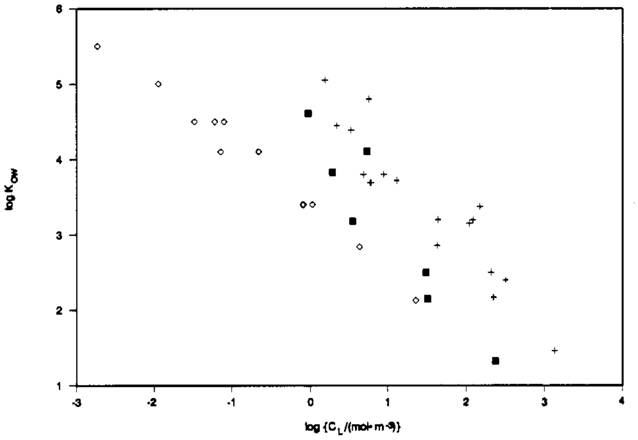

Figure 5. 1-Octanol–water partition coefficient K_{OW} versus subcooled liquid solubility C_L for chloroguaiacols (□), chlorophenols (+) (phenol to pentachlorophenol), and chlorobenzenes (◇) (benzene to hexachlorobenzene).

Figure 4 shows the trend of increasing log K_{OW}. The increase from guaiacol to tetrachloroguaiacol is about 3.0 log units, or a factor of 5.6 per chlorine substituted. This is a somewhat larger increase than the decrease in solubility. The net effect, as shown in Figure 5, is that the slope of the log K_{OW} versus log C^S_L line is about −1.45. Most correlations between log K_{OW} and log C^S_L have lower slopes of approximately −0.8 to −1.0 (*21*), but they are generally derived from data for more hydrophobic chemicals with solubilities less than 10 mol/m^3. To illustrate this, Figure 5 also contains data for benzene and chlorobenzenes showing the lower slope and generally lower values of K_{OW} at the same solubility. The implication is that the more chlorinated guaiacols, and especially the phenols, partition into octanol to a greater extent than is expected from their solubility, the magnitude being 0.5–1 log unit or a factor of 3–10. If this increased affinity for octanol is also manifested as an affinity for lipid phases in organisms, then phenolic substances may partition (bioconcentrate) into organisms more than is expected from their solubility.

The chlorophenol data plotted in Figures 1 and 3 suggest that to a first approximation chlorine and methoxy substituents have similar effects on solubility and vapor pressure when viewed in terms of the increase in molar volume. That is, molar volume is an adequate descriptor for chlorinated and methoxyphenols. It is not known if this extends to multiple methoxy groups. It is striking however that this similarity does not apply to K_{OW}. Figure 4 shows that K_{OW} values for chlorophenols are considerably greater than those of a chloroguaiacol of similar molar volume. Apparently, the chlorophenols tend to be more soluble in octanol, or have lower activity coefficients, than the chloroguaiacols. It is also possible that, for this class of chemicals, the usual assumption that octanol is a satisfactory partitioning surrogate for lipids is suspect. Clearly, there is a need to measure lipid–water and 1-octanol–water partition coefficients and interpret the results in terms of activity coefficients in the aqueous and these organic phases. Only then will the fundamental nature of the bioconcentration phenomena be determined. A subsequent step is obviously to measure organism–water partitioning, but this will probably be complicated by metabolism and toxicity. The use of tissue concentrations as a biomonitor to infer water concentrations for this class of chemicals is thus believed to be more complex than generally applies. A sound appreciation of the physical chemistry of the chloroguaiacols is clearly needed for environmental assessment purposes.

Literature Cited

(1) Canadian Environmental Protection Act. Priority substances list assessment report No. 2: effluents from pulp mills using bleaching, Catalogue No. En 40-215/2E; ISBN 0-662-18734-2; Ministry of Supply and Services Canada, 1991.

(2) Suntio, L. R.; Shiu, W. Y.; Mackay, D. *Chemosphere* **1988**, *17*, 1249–1290.

(3) Ma, K. C.; Shiu, W. Y.; Mackay, D. *J. Chem. Eng. Data* **1993**, *38*, 364–366.

(4) Kovacs, T. G.; Martel, P. H.; Voss, R. H.; Wrist, P. E.; Willes, R. F. *Environ. Tox. Chem.* **1993**, *12*, 281–289.

(5) Reid, R. C.; Prausnitz, J. M.; Poling, B. E. *The Properties of Gases and Liquids*, 4th ed.; McGraw-Hill Book Co.: New York, 1987.

(6) Xie, T. M.; Dryssen, D. *Anal. Chim. Acta* **1984**, *160*, 21–30.

(7) Leuenberger, C.; Giger, W.; Coney, R.; Graydon, J. W.; Molnar-Kubica, E. *Water Res.* **1985**, *19*, 885–894.

(8) Verschueren, K. *Handbook of Environmental Data on Organic Chemicals*, 2nd ed.; Van Nostrand Reinhold Co.: New York, 1984.

(9) Yalkowsky, S. H. *Ind. Eng. Chem. Fundam.* **1979**, *18*, 108–111.

(10) Stephenson, R. M.,;Malnowski, A. *Handbook of the Thermodynamics of Organic Compounds;* Elsevier: New York, 1987.

(11) Bidleman, T. F.; Renberg, L. *Chemosphere* **1985**, *14*, 1475–1481.

(12) Hansch, C.; Leo, A. J. *Substituent Constants for Correlation Analysis in Chemistry and Biology;* John Wiley & Sons: New York, 1979.

(13) Niimi, A. J.; Lee, H. B.; Kissoon, G. P. *Environ. Tox. Chem.* **1990**, *9*, 649–653.

(14) Saarikoski, J.; Wiluksela, M. *Ecotox. Environ. Safety* **1982**, *6*, 501–512.

(15) Xie, T. M.; Hulthe, B.; Folestad, S. *Chemosphere* **1984**, *13*, 445–459.

(16) Xie, T. M. *Chemosphere* **1983**, *12*, 1183–1191.

(17) Mackay, D.,;Shiu, W. Y.; Ma, K. C. *Illustrated Handbook of Physical-Chemical Properties and Environmental Fate for Organic Chemicals, Vol. I, Monoaromatic Hydrocarbons, Chlorobenzenes and PCBs;* Lewis Publishers Inc.: Chelsea, MI, 1992.

(18) Mackay, D.; Shiu, W. Y.; Ma, K. C. *Illustrated Handbook of Physical-Chemical Properties and Environmental Fate for Organic Chemicals, Vol. II, Polynuclear Aromatic Hydrocarbons, Polychlorinated Dioxins and Dibenzofurans;* Lewis Publishers Inc.: Chelsea, MI, 1992.

(19) Mackay, D.; Yuen, A. T. K. *Environ. Sci. Technol.* **1983**, *17*, 211–216.

(20) Mackay, D.; Shiu, W. Y.; Sutherland, R. P. *Environ. Sci. Technol.* **1979**, *13*, 333.

(21) Miller, M. M.; Wasik, S. P.; Huang, G. L.; Shiu, W. Y.; Mackay, D. *Environ. Sci. Technol.* **1985**, *19*, 522–529.

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