Octanol−Water Partition Coefficients of Non-*Ortho*- and Mono-*Ortho*-Substituted Polychlorinated Biphenyls

Mei-Fen Yeh[†] **and Chia-Swee Hong***[,‡]

School of Public Health, MPH Program, State University of New York at Albany, Albany, New York 12201-0509, and Wadsworth Center, New York State Department of Health, Albany, New York 12201-0509

The octanol/water partition coefficients (K_{ow}) at 25 °C were determined for 12 non-*ortho*- and mono-*ortho*-substituted polychlorinated biphenyls (PCBs). A generator-column/extractor-column technique was used, followed by off-line GC/ECD analysis. The relative standard deviations for the measurements ranged from 2.2 to 11.5%. The results were compared with both experimental and estimated literature values. Log K_{ow} values determined for 12 congeners ranged from 6.47 to 7.15 and generally increased with an increase in molecular weight. Within homologue groups, congeners with less *ortho*-substitution generally have greater K_{ow} values. The log K_{ow} values of 46 congeners measured by the generator-column method from the literature and from this study were compiled and used for evaluation of quantitative structure−property relationships (QSPRs) relating the chlorine substitution pattern to the K_{ow}. A useful equation to estimate log K_{ow} was derived on the basis of multiregression analysis, which employs easily calculable molecular descriptors. The validity of this equation is demonstrated by comparing the estimated values with experimental values. This newly developed model agrees well with other model predictions. The empirical data-fitting approach based on coefficients related to chlorine substitution patterns appears promising.

Introduction

Studies of structure−activity relationships of polychlorinated biphenyls (PCBs) have elucidated the profound effect of the chlorine substitution patterns on the toxic response and on induction of drug-metabolizing enzymes in mammalian and avian species.[1,2] The PCB congeners having no chlorines (coplanar) or one chlorine (semi-coplanar) substituted in the *ortho*-position of the phenyl rings are particularly toxic and are potent inducers of hepatic aryl hydroxylase (AHH).[3] PCB congeners with no *ortho*-, two *para*-, and two or more *meta*-chlorine substituents are approximate isostereomers of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), and their ability to induce mixed-function oxidase activity qualitatively resembles that observed in organisms exposed to TCDD.[4] There are an increasing number of reports indicating the widespread presence of toxic coplanar and semi-coplanar PCB congeners. Therefore, the evaluation of the environmental behavior of these toxic PCBs in terms of their physicochemical characteristics is very important.

The octanol−water partition coefficient has become a key parameter in studies of the environmental fate of organic chemicals. It has been found to be related to water solubility, soil/sediment adsorption coefficients, toxicities, and bioconcentration factors for aquatic life.[5−7] Because of its increasing use in the estimation of these other properties, K_{ow} is considered a required property in studies of new or problematic chemicals.

Values for K_{ow} are obtained by direct measurement or by using one of several estimation techniques. Direct experimental measurement of K_{ow} with traditional shake-flask methods may be inaccurate due to the formation of molecular aggregates and the analytical difficulties inherent in the measurement of the extremely low aqueous equilibrium concentrations. In the slow-stirring method the water and octanol phases are equilibrated under conditions of slow stirring which may take 2 to 4 days to achieve equilibration. Measurements and estimates based upon reverse-phase high-performance liquid chromatography and thin-layer chromatography (RP-HPLC and RP-TLC) have achieved moderate success for other groups of lipophilic compounds but require the use of empirical correction factors in the case of PCBs.[8,9] Another technique used is the generator-column method where log K_{ow} values up to 8.5 can be measured.[10] Reliable and consistent K_{ow} values for a number of PCB congeners have been obtained by the generator-column technique, which obviates problems such as colloidal suspensions and adsorption of the solute.[11−13]

Most of the reported prediction methods are based on the substituent constants approach,[14] thermodynamically oriented theories,[15,16] connectivity indexes,[11,17−19] characteristic root indexes,[20] and quantum chemical molecular properties.[21,22] It is highly desirable to have a reliable method to calculate *n*-octanol/water partition coefficients from information available in the structural formulas of the compounds.

Although non- and mono-*ortho*-substituted PCBs are widely recognized as serious environmental pollutants, there are only a limited number of K_{ow} values of these compounds available,[11,14] which limits the evaluation of their potential environmental behavior. The aims of this study were to experimentally determine K_{ow} values at 25 °C for 12 non- and mono-*ortho*-substituted PCBs using the generator-column method. The experimentally determined K_{ow} values from previous investigations and this study using the generator-column method were utilized in the

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* To whom correspondence should be addressed. Telephone: (518) 473-7299. Fax: (518) 473-7689. E-mail: hongc@wadsworth.org.
[†] State University of New York at Albany.
[‡] New York State Department of Health.

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development of QSPR (quantitative structure−property relationship) models. A useful equation is derived to estimate the log K_{ow} values of PCB congeners on the basis of the chlorine substitution pattern.

Experimental Section

Reagents and Materials. All PCB congeners used in this study were ≥99% pure and obtained from AccuStandard Inc. (New Haven, CT). The PCBs were used without further purification. Hexane and acetone were nanograde from Mallinckrodt, Inc. (St. Louis, MO). The water used was distilled water, which was passed through a Milli-Q Plus water purification system (Millipore Corporation, Bedford, MA). 1-Octanol was 99.9% pure from Adrich Chemical Inc. (Milwaukee, WI). Sodium sulfate (Fisher Scientific, Pittsburgh, PA) was washed with hexane in a Soxhlet system for 6 h and then dried at 80 °C under vacuum.

Apparatus. The generator-column method has been described by Woodburn et al.,[12] DeVoe et al.,[23] and Hong and Qiao.[24] The procedure was modified and described below.

The apparatus consisted of a water reservoir attached to the generator column, with the effluent going either to waste or to an extractor column controlled by a switching valve. All tubing or connections used were either Teflon or stainless steel. The generator column was a 30 cm × 0.4 cm HPLC stainless steel column (Waters Associates, Milford, MA) hand-packed with Chromosorb W 60/80 (Manville Products Corp., Denver, CO). Both the water reservoir and the generator column were contained in a water bath controlled at 25 ± 0.2 °C. An extractor column (HPLC guard column of 2 cm × 0.2 cm i.d.) was packed with 100 mg of 37−50 μm C18 Corasil (Waters Associates, Milford, MA) and fitted with a 5-μm stainless steel frit on both ends to extract PCB solutes from the effluent of the generator columns. An HPLC pump (Waters Associates, Milford, MA) was used to deliver the octanol-saturated water from a reservoir through the generator and extractor columns.

Procedure. Approximately 3 mg of individual PCB was dissolved in 15 mL of 1-octanol. This solution was then vigorously stirred with 120 mL of distilled water for 18 h. The concentration of PCB in the octanol phase was determined by GC/ECD. The octanol layer was then applied to the generator column and pulled through the dry support with gentle suction until the solid support was saturated, as evidenced by the appearance of the 1-octanol at the column base.

The water was presaturated with octanol prior to being pumped through the generator column. Octanol-saturated water was prepared by stirring the octanol with water in an Erlenmeyer flask for 12 to 30 h. After they were stirred, the saturated solutions were allowed to stand unagitated for at least 48 h to permit complete phase separation.[25] Before the first K_{ow} determination was made with a newly packed column, at least 500 mL of octanol-saturated water was pumped through the generator column to equilibrate the system. The C18 extractor column was then connected to the generator column. The octanol-saturated water was pumped from the reservoir through the generator and extractor columns at a flow rate of 1 mL/min. The effluent was collected in a tared weighing flask with the volume ranging from 0.1 to 1 L, depending on the test compounds and the measured K_{ow}. After an amount of PCB sufficient for analysis was collected on the extractor column, the extractor column was disconnected from the generator column.

Collected PCB on the extractor column was successively eluted in the reverse direction by injection of 1 mL of acetone, 5 mL of hexane, and 1 mL of acetone, to a 50 mL Erlenmeyer flask. About 15 mL of hexane was added to the Erlenmeyer flask. The collected extract was dried with sodium sulfate and was concentrated to the appropriate volume in a Kuderna-Danish (K−D) evaporator with a three-ball Snyder column on a steam bath. Acetone was excluded in the evaporation. The extractor columns were reused by backward washing with, in order, 1 mL of acetone, 5 mL of hexane, 1 mL of acetone, and 5 mL of water.

Instrumental Analysis. The concentration of individual PCBs in hexane was then determined with a Hewlett-Packard 6890 gas chromatograph equipped with a ^{63}Ni electron-capture detector (ECD). An HP-5 capillary column (30 m × 0.32 mm × 0.25 μm film thickness) was used in the analysis. The external standard, which was prepared in hexane with the concentration 10 ng/mL of each mono-*ortho*- and non-*ortho*-substituted PCB, was used in the GC analysis. The GC oven temperature was programmed as follows: initial temperature at 100 °C for 0.5 min, then programmed at 10 °C/min to 180 °C, and finally to 240 °C at a rate of 2 °C/min. A constant flow rate of helium at 2.6 mL/min was used in all measurements. The K_{ow} was calculated by dividing the PCB concentration in the octanol phase by that in the aqueous phase.

Development of Calculation Models. QSPRs were developed as linear additive multivariant models for calculation of log K_{ow}. The SAS (Statistical Analysis System) program was used to perform statistical analysis to determine the descriptors most important in reducing the error associated with each model. The descriptors determined to be of least importance or containing collinear relationships with other descriptors were removed from the model until a model was obtained which accurately described the experimental data and contained the least number of parameters possible. Both simple and multiple regression were performed. The goodness of fit for each model was evaluated on the basis of the residual sum of squares and the mean squared error (standard error of the model) by the F test, as well as visual observation of plots containing experimental versus calculated log K_{ow} values.

Results and Discussion

Evaluation of the Generator-Column Method. One experimental difficulty described by DeVoe et al.[23] is the eventual depletion of octanol from the generator column due to its slight solubility in water. To slow the depletion of octanol from the column, the water was presaturated with octanol prior to being pumped through the generator column. DeVoe et al.[23] demonstrated that the aqueous solute concentration exiting the generator column was independent of flow rate from 0.5 to 2.0 mL/min, of the volume of water passed through the column, and of the concentration of solute in octanol. In this study, the aqueous PCB concentration exiting the generator column was independent of flow rate between 0.6 and 1.8 mL/min at 25 °C. The efficiency of the C18 column in extracting PCBs from the aqueous solutions was found to be >97%. The extraction efficiency of the C18 column was also compared with that of a traditional liquid−liquid extraction for the PCB + octanol + water system, and they were found to be equivalent.

For direct measurements, the generator-column method has several advantages over the shake-flask or stir-flask method. The flow rate of pumping octanol-saturated water

Table 1. Mean log K_{ow} Values Measured by the Generator-Column Method: Comparison with Literature Values

				literature K_{ow} values			
PCB	IUPAC number	log K_{ow}[a]	RSD[b] (%)	gc[c]	ss[d]	RP-HPLC[e]	calculated[f]
3,3′,4,4′-tetra	77	6.48 (3)	2.2	6.21	6.63	6.11−6.40	−, 6.11
3,4,4′,5-tetra	81	6.53 (3)	4.2				6.64, 6.24
2,3,3′,4,4′-penta	105	6.61 (3)	5.9	5.82		6.41−7.14	7.00, 6.47
2,3,4,4′,5-penta	114	6.47 (3)	3.1			6.65, 6.78	7.00, 6.59
2,3′,4,4′,5-penta	118	6.49 (4)	3.3			6.57	7.00, 6.67
2,3′,4,4′,5′-penta	123	6.50 (3)	8.0				7.00, 6.48
3,3′,4,4′,5-penta	126	6.56 (3)	5.9				7.05, 6.67
2,3,3′,4,4′,5-hexa	156	6.75 (3)	4.7			7.13−7.84	7.37, 7.05
2,3,3′,4,4′,5′-hexa	157	6.73 (3)	5.0				7.37, 6.97
2,3′,4,4′,5,5′-hexa	167	6.82 (3)	5.0			7.29	7.37, 7.14
3,3′,4,4′,5,5′-hexa	169	7.01 (4)	11.5		7.41	7.42−7.62	−, 7.17
2,3,3′,4,4′,5,5′-hepta	189	7.15 (3)	8.3			7.72	7.67, 7.54

[a] Mean experimental log K_{ow} (number of measurements) from this study. [b] Relative standard deviation. [c] Direct generator-column method values from ref 11. [d] Direct slow-stirring method values from ref 14. [e] Indirect chromatographic estimation values from ref 8. [f] Calculated method; first value from ref 18 and second value from ref 21.

can be made slow enough to avoid colloidal dispersion, while the large interfacial area between the organic and aqueous phases allows rapid equilibration. When the column is part of a continuous and closed flow system, the system walls become equilibrated with the aqueous solution and errors from adsorption are avoided. Also, there is no exposure of the solution to the atmosphere, which avoids the problem of volatilization. Various authors have discussed the reliability and accuracy of the generator-column technique for determinations of partition coefficients.[11−13,23]

Mean experimental log K_{ow} values, relative standard deviations, and numbers of observations for 12 non- and mono-*ortho*-substituted PCBs are given in Table 1. In addition, log K_{ow} values determined by the generator-column method, slow stirring, HPLC, and calculation from the literature are presented in Table 1 for comparison purposes. The values range from 6.47 to 7.15. At least three replicate determinations were done for each compound in the study. The percent variation about the mean ranged from 2.2 to 11.5%, with an average variation of 5.6%. Of the experimentally determined log K_{ow} values, only those of 3,3′,4,4′-tetra-, 2,3,3′,4,4′-penta-, and 3,3′,4,4′,5,5′-hexachlorobiphenyl have been measured before. Although the number of log K_{ow} values for non- and mono-*ortho*-substituted PCBs determined by the generator-column or slow-stirring method from the literature are limited, data in Table 1 show that the values for 3,3′,4,4′-tetra- and 3,3′,4,4′,5,5′-hexachlorobiphenyl agree well with our experimental data. In the case of 2,3,3′,4,4′-pentachlorobiphenyl, there is a considerable difference between the data from ref 11 and our measurement: 5.82 against 6.61, respectively. No reasonable explanation can be given for this discrepancy.

Results of the indirect chromatographic estimation technique using RP-HPLC are also presented in Table 1 for 12 non- and mono-*ortho*-substituted PCBs. The HPLC literature values in Table 1 are taken from ref 8 and were determined on two different reversed-phase systems using methanol/water or acetonitrile/water as the mobile phase. Rapaport and Eisenreich[26] noticed a considerable relative reduction in capacity factors (retention factors) for *ortho*-substituted PCBs as compared with *meta*- and *para*-substituted congeners. This phenomenon was explained to be the result of a restricted rotation about the 1,1′ bond by the opposing *ortho*-positioned chlorine. The biphenyl moiety is pushed into a nonplanar configuration that might be less hydrophobic than planar congeners are. The fact that these nonplanar congeners behave differently in an RP-HPLC column as compared with an octanol/water two-phase system might be explained by the differences between the processes that lead to either retention on the HPLC column or partitioning in octanol/water. There are strong indications that the mechanism for C18 HPLC is adsorption rather than solvent/solute partitioning. A decrease in substrate−compound contact area might therefore lead to a relatively greater decrease in retention time on the HPLC column than the decrease in K_{ow} would indicate. Calculated values using RP-HPLC[8] are in fair agreement with our experimental values for the selected non- and mono-*ortho*-substituted PCBs. Woodburn et al.[12] indicated that the K_{ow} values estimated from the chromatographic technique deviate considerably from the generator-column measurements, especially for the more highly chlorinated PCBs or *ortho*-substituted congeners.

Sabljic et al.[18] evaluated the performance of 12 models for calculating PCB partition coefficients by comparing the log K_{ow} data calculated for each model with those measured by the slow-stirring method.[14] The molecular topology model as suggested by Sabljic et al.[18] seems to be the most reliable one, since it enables the log K_{ow} data of chlorinated biphenyls to be predicted within 0.10 log unit for 19 PCBs. Makino[21] predicted K_{ow} values by a multilinear regression analysis on the basis of six descriptors: molecular weight, heat of formation, solvent accessible surface area, ionization potential (I_p), electron affinity (E_A), and dipole moment (μ). The log K_{ow} values estimated by Sabljic et al.[18] and Makino[21] are compared to our measured values in Table 1. Agreement between our measurements and those of the molecular topology approach of Sabljic et al.[18] or the multilinear regression analysis of Makino[21] is within 0.62 and 0.40 log unit for 12 non- and mono-*ortho*-substituted PCBs, respectively.

Experimental log K_{ow} values, determined using the generator-column method, from various sources were compiled for PCBs. This resulted in a database of a total of 46 compounds containing 61 individual determinations. Most of these values are in fact not means but individual observations derived from a single reference. Table 2 contains the compiled data of log K_{ow} for 46 PCB congeners. A plot of experimentally derived log K_{ow} values in Table 2 against number of chlorines (N_{Cl}) is shown in Figure 1 for PCBs ranging from mono- to decachlorobiphenyl and containing all levels of *ortho* substitution.

$$\log K_{ow} = 0.395 N_{Cl} + 4.33 \tag{1}$$

$$r = 0.944, \quad s = 0.312, \quad n = 46$$

This equation demonstrates a highly significant relation-

Table 2. Data Compilation for the log K_{ow} Values of 46 PCBs Derived from the Generator-Column Method

IUPAC no.	substitution pattern	experimental[a] log K_{ow}	pred log K_{ow}
1	2	4.44 (4.50,[b] 4.38[c])	4.64
2	3	4.58[c]	4.80
3	4	4.43 (4.49,[c] 4.37[d])	4.80
4	2,2′	4.9[c]	4.93
8	2,4′	5.14[c]	5.09
9	2,5	5.16[b]	5.09
10	2,6	4.93[b]	4.93
12	3,4	5.29[c]	5.26
15	4,4′	5.33[c]	5.26
18	2,2′,5	5.60[c]	5.38
29	2,4,5	5.66 (5.51,[b] 5.81[c])	5.55
30	2,4,6	5.63 (5.47,[b] 5.57,[c] 5.75,[d] 5.71[e])	5.38
31	2,4′,5	5.79[c]	5.55
40	2,2′,3,3′	5.55[f]	5.83
49	2,2′,4,5′	5.73[b]	5.83
53	2,2′,5,6′	5.46[f]	5.67
54	2,2′,6,6′	5.48[f]	5.51
61	2,3,4,5	6.09 (5.72,[b] 6.38,[d] 6.18[f])	6.00
65	2,3,5,6	5.94[f]	5.83
66	2,3′,4,4′	6.31[f]	6.00
77	3,3′,4,4′	6.35 (6.21,[f] **6.48**)	6.16
81	3,4,4′,5	**6.53**	6.16
101	2,2′,4,5,5′	6.21 (5.92,[b] 6.50[c])	6.29
104	2,2′,4,6,6′	5.37[f]	5.96
105	2,3,3′,4,4′	6.22 (5.82,[f] **6.61**)	6.45
114	2,3,4,4′,5	**6.47**	6.45
116	2,3,4,5,6	6.30[b]	6.29
118	2,3′,4,4′,5	**6.49**	6.45
123	2,3,4,4′,5′	**6.50**	6.45
126	3,3′,4,4′,5	**6.56**	6.62
128	2,2′,3,3′,4,4′	6.98[b]	6.74
136	2,2′,3,3′,6,6′	6.40 (6.63,[b] 6.81,[c] 5.76[f])	6.41
153	2,2′,4,4′,5,5′	6.90[c]	6.74
155	2,2′,4,4′,6,6′	7.40 (7.55,[b] 7.24[d])	6.41
156	2,3,3′,4,4′,5	**6.75**	6.90
157	2,3,3′,4,4′,5′	**6.73**	6.90
167	2,3′,4,4′,5,5′	**6.82**	6.90
169	3,3′,4,4′,5,5′	**7.01**	7.07
171	2,2′,3,3′,4,4′,6	6.68[b]	7.03
189	2,3,3′,4,4′,5,5′	**7.15**	7.36
194	2,2′,3,3′,4,4′,5,5′	7.67[f]	7.65
201	2,2′,3,3′,4,5′,6,6′	7.21[f]	7.32
202	2,2′,3,3′,5,5′,6,6′	7.12 (7.11,[b] 7.12[c])	7.32
207	2,2′,3,3′,4,4′,5,6,6′	7.52[f]	7.77
208	2,2′,3,3′,4,5,5′,6,6′	8.16[b]	7.77
209	2,2′,3,3′,4,4′,5,5′,6,6′	8.23 (8.26,[b] 8.20[c])	8.22

[a] Mean generator-column-measured log K_{ow} values derived from various sources or individual value from a single source. Bold values are from this study. [b] Miller et al.[13] [c] Woodburn et al.[12] [d] Li and Doucette.[28] [e] Doucette and Anders.[29] [f] Hawker and Connell.[11]

ship between log K_{ow} and N_{Cl}, which indicated an increasing trend of log K_{ow} with increasing molecular weight. This equation does not account for variations in substitution patterns between isomers that have been observed to mark an effect on log K_{ow}. Values of log K_{ow} for individual congeners within a homologue group differed very much because of different substitution patterns and proximity effects that occur in the higher-chlorinated congeners. Substitution of a chlorine at the *ortho* position apparently leads to a much lower partition coefficient than substitutions at the *meta* or *para* positions, as a result of interference of the *ortho* chlorine with the opposite phenyl ring.

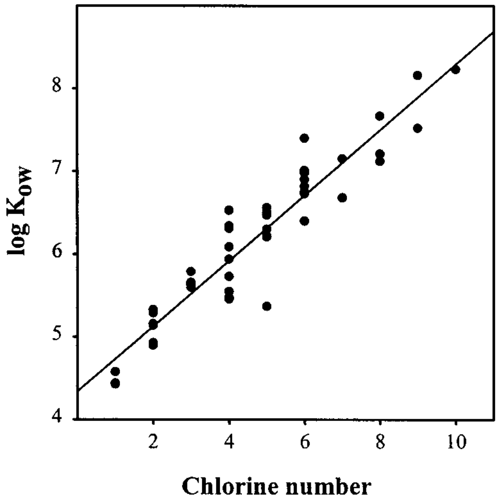

Figure 1. Log K_{ow} as a function of chlorine number for the 46 PCB congeners listed in Table 2.

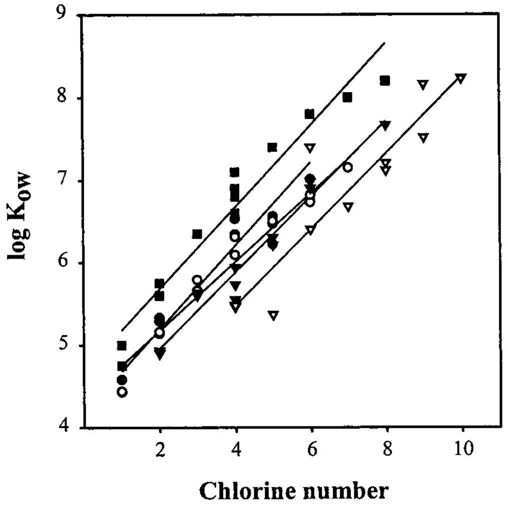

Figure 2. Log K_{ow} as a function of chlorine number for 46 PCB congeners grouped by number of *ortho* chlorine substitutions: (●) non-*ortho* PCB; (○) mono-*ortho* PCB; (▼) di-*ortho* PCB; (▽) multi-*ortho* PCB; (■) dioxin.

Table 3. Regression Equations and Correlation Coefficients for Each Line in Figure 2

congener group	regression equation	r[a]	s[b]	n[c]
non-*ortho* PCB	$\log K_{ow} = 0.507N_{Cl} + 4.173$	0.978	0.222	8
mono-*ortho* PCB	$\log K_{ow} = 0.417N_{Cl} + 4.336$	0.979	0.160	15
di-*ortho* PCB	$\log K_{ow} = 0.460N_{Cl} + 4.035$	0.981	0.167	12
multi-*ortho* PCB	$\log K_{ow} = 0.462N_{Cl} + 3.626$	0.922	0.424	11
dioxin	$\log K_{ow} = 0.497N_{Cl} + 4.680$	0.973	0.263	14

[a] Correlation coefficient. [b] Standard error of the estimate. [c] Number of data points.

A close examination of the log K_{ow} values in Table 2 showed that there are differences between the partition coefficients of the different congener classes. Figure 2, drawn from the data in Table 2, shows a group of linear plots of log K_{ow} versus chlorine number classified on the basis of the number of *ortho* chlorine atoms (N_{or}). Table 3 is a summary of the regression equations and correlation coefficients obtained for each line in Figure 2. The correlation coefficients between predicted and measured log K_{ow} values markedly increased by utilizing the classification. Significantly different correlations were obtained for PCBs containing chlorine atoms in the positions *ortho* to the phenyl−phenyl bond. This clearly indicates that the log K_{ow} values for PCBs within a homologue group increase as the molecule becomes more planar; that is, log K_{ow} for multi-*ortho*-substituted PCBs < log K_{ow} for di-*ortho*-substituted PCBs < log K_{ow} for mono-*ortho* substituted PCBs < log K_{ow} for non-*ortho*-substituted PCBs. Even more intriguing is

Table 4. List of Statistical Parameters Showing Progress in Developing the Regression Models for log K_{ow} Values of PCBs

model (descriptors)	r^a	s^b	F^c
N_{cl}	0.944	0.312	359
N_{cl}, N_{or}	0.963	0.256	278
N_{cl}, N_{or}, N_{ad}	0.966	0.248	199
N_{cl}, N_{or}, N_m	0.964	0.256	186
N_{cl}, N_{or}, N_m, N_{mp}	0.968	0.245	152
N_{cl}, N_{or}, N_m, N_{ad}	0.967	0.247	149
N_{cl}, N_{or}, N_m, N_{mp}, N_{ad}	0.968	0.248	120

[a] Correlation coefficient. [b] Standard error of the estimate. [c] Test of the null hypothesis (F-test).

how the log K_{ow} values of the coplanar PCBs approach that of a dioxin congener[27] with the same number of chlorines. Thus, real differences in the partitioning behavior of planar and nonplanar PCBs exist. Other structural features that control the magnitude of log K_{ow} data of PCBs are the crowding of chlorine substituents as well as specific substitution patterns, that is, the number of *meta*-chlorine substituents (N_m), the number of *meta*/*para* pairs of chlorine substituents (N_{mp}), and the number of adjacent chlorine atoms (N_{ad}).

To better estimate log K_{ow} values, the influence of an *ortho*-substituted chlorine and proximity effects on the activity coefficient should be taken into account. A stepwise multiregression procedure was used to select the best correlation for log K_{ow}. The following statistical parameters were used to test the quality of generated regression equations: the correlation coefficient (r), the standard error of the estimates (s), a test of the null hypothesis (F test), and the significant level (p). The suitability of chlorine numbers (N_{cl}) alone in log K_{ow} correlations was first examined, and six other models with different combinations of variables were also tested. The associated statistics are summarized in Table 4. N_{cl} explained 89.1% of the variation in log K_{ow} with 0.31 standard error. The correlation significantly improved and the error was reduced in the second model, which adds the variable N_{or}. Both N_{cl} and N_{or} were significant at the $p < 0.01$ level. The rest of the models, which add one or more variables of N_m, N_{mp}, and N_{ad}, did not significantly improve the correlation coefficient and standard error. Pr (probability) values of N_m, N_{mp}, and N_{ad} in the Student's t-test of the regression model are larger than 0.01, which indicates that the contribution of N_m, N_{mp}, and N_{ad} to log K_{ow} is insignificant. Therefore, only N_{cl} and N_{or} were entered into the model, with simply two variables, thus increasing the utility value of the predicting equation. By using the stepwise multiple-regression analysis, the best model for log K_{ow} was found to be

$$\log K_{ow} = 4.35 + 0.453N_{cl} - 0.164N_{or} \qquad (2)$$

$$n = 46, \quad r = 0.963, \quad s = 0.256, \quad F^{2,43} = 278$$

The average contributions of N_{cl} and N_{or} are 0.453 and −0.164, respectively.

The collinearities between N_{cl} and N_{or} for 46 congeners were analyzed. The correlation coefficient was 0.58, which indicates that there is only a limited relationship between N_{cl} and N_{or}. The predicted log K_{ow} values were calculated by the above equation and presented in the last column of Table 2.

Estimated versus Measured log K_{ow}. A comparison of literature data reveals considerable scatter among K_{ow} values for identical PCB congeners. Therefore, use of an internally consistent data set, obtained under similar conditions, is necessary in order to develop a QSPR model, which does not contain errors resulting from use of different analytical procedures. The goodness of fit for this model (eq 2) was tested by plotting predicted versus observed log K_{ow} values, as shown in Figure 3. The percent error ranged from 0 to 13% with an average error of 2.8% for 46 PCB congeners. This model resulted in a high correlation ($r = 0.963$) and a low standard error ($s = 0.243$), which are indicative of good model predictions. Equation 2 could be used to predict log K_{ow} for the remaining PCBs, since only knowledge of the chemical structure is required. Several models are currently available for predicting the log K_{ow} values of PCBs. Sabljic et al.[18] developed a model based on molecular topology using 19 log K_{ow} data points measured by the slow-stirring method. They compared their model with 12 different models previously used for calculating log K_{ow} values for 19 congeners with slow-stirring-measured values and showed that the molecular topology model was superior in accuracy to all other models. To judge the validity and predictive utility of our model, log K_{ow} values fitted to our model were plotted against those from Sabljic's model using the same data set of 19 slow-stirring-measured log K_{ow} values, as shown in Figure 4a. The regression results of correlation coefficient (r) 0.988, slope 0.971, and standard error 0.117 indicate that our model predicts log K_{ow} values of PCBs as well as Sabljic's model. The advantage of our model is the ease of use, since both the molecular descriptors (N_{cl}, N_{or}) used in this model can be easily figured out from the molecular structure, without any experimental inputs.

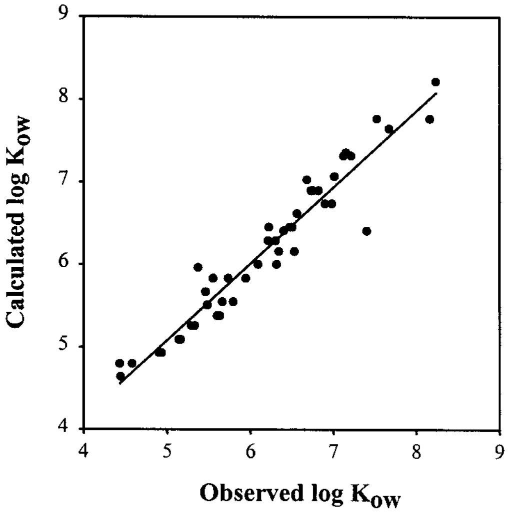

Figure 3. Calculated versus observed log K_{ow} values for the 46 PCB congeners listed in Table 2.

Our model using 46 generator-column-measured log K_{ow} values was also compared with Sabljic's model using 19 slow-stirring-measured log K_{ow} values, as shown in Figure 4b. The log K_{ow} values obtained from the generator-column method are consistently lower than those from the slow-stirring method, as shown in Table 2. The slope of 0.885 indicating that our estimated log K_{ow} values are lower than the estimated values from Sabljic's is not surprising. Therefore, the selection of an accurate data set for modeling is important and contributes significantly to the accuracy of the model.

To further compare our model with the total surface area (TSA)-based model, the regression analysis of log K_{ow} values (46 generator-column-measured data) from Table 2 against TSA values taken from ref 11 was performed. The relationship was used to predict unknown log K_{ow}

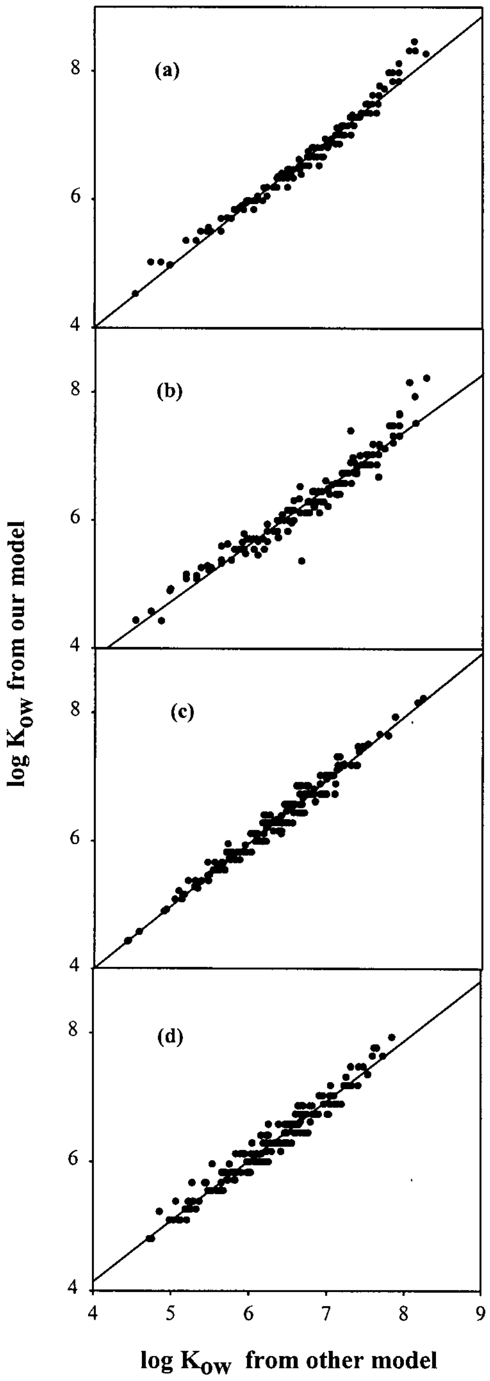

Figure 4. Log K_{ow} values based on our model versus log K_{ow} values based on other reported models: (a) our model and Sabljic's model both using the same data set of 19 slow-stirring-measured log K_{ow} values; (b) our model using 46 generator-column-measured log K_{ow} values and Sabljic's model using 19 slow-stirring-measured log K_{ow} values; (c) our model and TSA-based model both using 46 generator-column-measured log K_{ow} values; (d) our model using 46 generator-column-measured log K_{ow} values and Makino's model using 139 log K_{ow} values reported by Patil.[17]

values of PCBs. The comparison of our model based on N_{cl} and N_{or} with the model based on TSA using the same data set of 46 PCBs was shown in Figure 4c. The regression results of correlation coefficient (r) 0.987, slope 0.988, and standard error 0.110 indicate that our model correlates very well with the model based on TSA.

Makino[21] derived an equation to estimate the log K_{ow} values of PCBs on the basis of quantum chemical molecular properties such as I_p, E_A, and μ. Data for the observed log K_{ow} values of 139 PCB congeners, which were reported by Patil in 1991,[17] were analyzed. Our model using 46 generator-column-measured log K_{ow} values was compared with Makino's model using 139 observed log K_{ow} values, as shown in Figure 4d. The regression results of correlation coefficient (r) 0.977, slope 0.933, and standard error 0.147 indicate that our model correlates very well with the model based on quantum chemical molecular properties.

Congeners with less *ortho*-substitution generally have greater log K_{ow} values within homologue groups. On the basis of this, we expected that concentrations of these congeners might increase relative to those of their homologue group with increasing trophic level.

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