

Three-Dimensional Quantitative Structure–Property Relationship (3D-QSPR) Models for Prediction of Thermodynamic Properties of Polychlorinated Biphenyls (PCBs): Enthalpies of Fusion and Their Application to Estimates of Enthalpies of Sublimation and Aqueous Solubilities

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Comparative Molecular Field Analysis (CoMFA) has been used to develop three-dimensional quantitative structure–property relationship (3D-QSPR) models for the fusion enthalpy at the melting point ($\Delta_{\text{fus}}H_{\text{m}}(T_{\text{fus}})$) of a representative set of polychlorinated biphenyls (PCBs). Various alignment schemes, such as *inertial*, *as is*, *atom fit*, and *field fit*, were used in this study to evaluate the predictive capabilities of the models. The CoMFA models have also been derived using partial atomic charges calculated from the electrostatic potential (ESP) and Gasteiger–Marsili (GM) methods. The combination of *atom fit* alignment and GM charges yielded the greatest self-consistency ($r^2 = 0.955$) and internal predictive ability ($r_{\text{cv}}^2 = 0.783$). This CoMFA model was used to predict $\Delta_{\text{fus}}H_{\text{m}}(T_{\text{fus}})$ of the entire set of 209 PCB congeners, including 193 PCB congeners for which experimental values are unavailable. The CoMFA-predicted values, combined with previous estimations of vaporization and sublimation enthalpies, were used to construct a thermodynamic cycle that validated the internal self-consistency of the predictions for these three thermodynamic properties. The CoMFA-predicted values of fusion enthalpy were also used to calculate aqueous solubilities of PCBs using Mobile Order and Disorder Theory. The agreement between calculated and experimental values of solubility at 298.15 K, characterized by a standard deviation of ± 0.41 log units, demonstrates the utility of CoMFA-predicted values of fusion enthalpies to calculate aqueous solubilities of PCBs.

INTRODUCTION

Although the manufacture and use of polychlorinated biphenyls (PCBs) have been banned since 1979,¹ these persistent organic pollutants remain widely distributed in the environment due to their chemical stability. Among the environmental pollutants that may be able to disrupt the endocrine system of humans and animals, PCBs have attracted particular attention.^{2,3}

The ability of PCBs to mimic natural hormones may reflect a close relationship between the physicochemical properties encoded in the molecular structure of these compounds and the toxic responses they elicit in biological systems. The aryl hydrocarbon receptor (AhR), an intracellular protein that mediates the induction of hepatic cytochrome P450IA1 and related enzymes, such as aryl hydrocarbon hydroxylase (AHH) and 7-ethoxyresorufin-*O*-deethylase (EROD), is also an important target for the biological and toxicological responses evoked by PCBs.^{4,5}

Fusion enthalpy, an important physical property of the solid state, reflects the molecular packing in the crystalline states of PCBs. The coplanarity of the phenyl rings is strongly influenced by the degree of ortho-substitution, and this is an important feature that facilitates the binding of PCBs to biological receptors such as AhR. The number and position

of Cl atoms on the biphenyl ring also affects the thermodynamic properties of PCBs.

Quantitative structure–property relationships (QSPRs) are quantitative models that correlate the variation in thermodynamic properties of a series of PCBs to the variation in chemical structure of the compounds in the series.⁶ Comparative molecular field analysis (CoMFA) has emerged as a powerful tool to construct three-dimensional QSPR models.⁷ In previous studies, we have employed similar computational techniques to predict vaporization enthalpies ($\Delta_{\text{vap}}H_{\text{m}}(298.15 \text{ K})$)⁸ and sublimation enthalpies ($\Delta_{\text{sub}}H_{\text{m}}(298.15 \text{ K})$)⁹ of PCBs.

The aim of the present study was to develop simple and predictive models that correlate the fusion enthalpies of PCBs at their melting point ($\Delta_{\text{fus}}H_{\text{m}}(T_{\text{fus}})$) and the CoMFA-generated steric and electrostatic fields surrounding the PCB molecules. This study shows that CoMFA and 3D-QSPR models permit the estimation of thermodynamic properties of 209 PCB congeners using the data from a limited set of measurements of a representative set of PCBs. Hence, these models provide a numerical value that can be used in cases when experimental data are unavailable.

METHODOLOGY

The molecular modeling and CoMFA computations were performed on a Silicon Graphics Inc. (SGI) Indy workstation and IRIX (version 6.2) operating system. The molecules in the data set were constructed using SYBYL (Version 6.7,

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Table 1. Enthalpies of Fusion ($\Delta_{\text{fus}}H_m(T_{\text{fus}})$ in kJ/mol) of 17 PCBs at the Melting Point (K)

| IUPAC no. | compounds | $\Delta_{\text{fus}}H_m$ (T_{fus}) | melting point |
|-----------|---|---|--------------------|
| | biphenyl | 18.7 ^a | 341.5 ^a |
| 1 | 2-monochlorobiphenyl | 14.5 ^b | 304.9 ^b |
| 3 | 4-monochlorobiphenyl | 13.3 ^c | 348.6 ^c |
| 10 | 2,6-dichlorobiphenyl | 12.6 ^d | 307.9 ^d |
| 29 | 2,4,5-trichlorobiphenyl | 22.8 ^c | 349.5 ^c |
| 30 | 2,4,6-trichlorobiphenyl | 16.5 ^c | 334.3 ^c |
| 49 | 2,2',4,5'-tetrachlorobiphenyl | 23.4 ^c | 339.1 ^c |
| 61 | 2,3,4,5-tetrachlorobiphenyl | 25.2 ^c | 363.9 ^c |
| 101 | 2,2',4,5,5'-pentachlorobiphenyl | 18.8 ^c | 350.1 ^c |
| 116 | 2,3,4,5,6-pentachlorobiphenyl | 21.8 ^c | 397.6 ^c |
| 128 | 2,2',3,3',4,4'-pentachlorobiphenyl | 29.2 ^c | 424.9 ^c |
| 136 | 2,2',3,3',6,6'-hexachlorobiphenyl | 21.1 ^c | 385.2 ^c |
| 155 | 2,2',4,4',6,6'-hexachlorobiphenyl | 17.5 ^c | 386.7 ^c |
| 171 | 2,2',3,3',4,4',6-heptachlorobiphenyl | 20.3 ^c | 395.4 ^c |
| 202 | 2,2',3,3',5,5',6,6'-octachlorobiphenyl | 22.8 ^c | 433.8 ^c |
| 208 | 2,2',3,3',4,5,5',6,6'-nonachlorobiphenyl | 22.6 ^c | 455.8 ^c |
| 209 | 2,2',3,3',4,4',5,5',6,6'-decachlorobiphenyl | 28.7 ^d | 578.9 ^d |

^a Reported in ref 16. ^b Reported in ref 17. ^c Reported in ref 18. ^d Reported in ref 15.

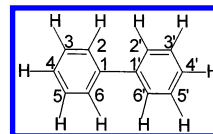
Tripes, Inc., St. Louis, MO). All molecules were geometry optimized by implementing the Merck Molecular Force Field (MMFF94)¹⁰ with a distance dependent dielectric function ($\epsilon = \epsilon_0 r$, with $\epsilon_0 = 1$) until the convergence criterion of 0.004184 kJ/mol (0.001 kcal/mol) change in energy between successive iterations was achieved.

Mulholland et al.¹¹ have reviewed three semiempirical methods, namely, MNDO (modified neglect of diatomic overlap),¹² PM3 (parametric method 3),¹³ and AM1 (Austin Model 1),¹⁴ for the rotational barriers and preferred conformations of biphenyl. It was observed in the study by Mulholland¹¹ that AM1 was the most accurate method to estimate the optimum dihedral angle and rotational energy barriers, with results comparable to experimental observations and ab initio calculations. Consequently, the optimized structures from SYBYL were used as initial coordinates for AM1 geometry optimization in SPARTAN (Version 5.0.1, Wavefunction, Inc., Irvine, CA). The conformational space about the twist bond connecting the two ring systems was systematically explored from 0° to 360° in 25 steps (or 14.4° increments). The lowest energy conformer obtained from this search was subjected to AM1 geometry optimization.

Data Set. The data set of 17 compounds consisted of the biphenyl molecule and 16 PCBs. Differential scanning calorimetry (DSC) is an experimental technique that has been used to determine melting points and enthalpies of fusion.¹⁵ The fusion enthalpies of PCBs at the melting point ($\Delta_{\text{fus}}H_m(T_{\text{fus}})$), presented in Table 1, have been reported in the literature.^{15–18} Isomers 116 (2,3,4,5,6-pentachlorobiphenyl) and 136 (2,2',3,3',6,6'-hexachlorobiphenyl) were selected as the test set since these compounds are representative of the pentachlorobiphenyl and hexachlorobiphenyl homologues.

Alignment Schemes. This study investigated various alignment schemes and partial charge formalisms to evaluate the predictive capabilities of the 3D-QSPR models constructed for $\Delta_{\text{fus}}H_m(T_{\text{fus}})$. Biphenyl was selected as the template molecule for the alignment schemes in this study.

Atom fit alignment aims to find the relative orientation of two molecules in which the root-mean-square-distance (RMSD) between pairs of atoms is minimized. PCB mol-

**Figure 1.** Atoms C1, C2, C4, and C5 of the biphenyl template were selected for *atom fit* alignment of PCB molecules.

ecules were aligned via RMSD fit of atoms C1, C2, C4, and C5 to the corresponding atoms on the biphenyl ring (Figure 1). These atoms were selected to consider the *ortho* (C2), *meta* (C5), and *para* (C4) positions on the benzene ring and the atom (C1) connected to the carbon atom of the second benzene ring.

Field fit, *inertial*, and *as is* alignment schemes have also been used to align PCBs to the biphenyl template. *Atom fit* alignment was used to study the effect of partial atomic charges on the fusion enthalpy of PCBs. The partial atomic charges derived from the calculated electrostatic potential (ESP)¹⁹ were imported from SPARTAN and Gasteiger–Marsili (GM)²⁰ charges were computed in SYBYL.

After the alignment of the compounds in the data set, each PCB molecule was placed in the center of a regularly spaced grid of 2.0 Å dimensions in x, y, and z directions. The steric (van der Waals/Lennard-Jones 12–6 function) and electrostatic (Coulombic) potential energy fields were calculated separately at each grid point of the three-dimensional lattice by summing the individual energy interactions between each atom of the PCB molecule and a probe consisting of a sp³ hybridized carbon atom with +1 charge. A distance-dependent dielectric function was applied and values of the steric and electrostatic energies were truncated at 125 kJ/mol.

Partial Least Squares (PLS) Analysis. Partial least squares (PLS),²¹ an extension of multiple linear regression technique, expresses the $\Delta_{\text{fus}}H_m(T_{\text{fus}})$ in terms of linear combinations of the CoMFA-generated steric and electrostatic fields. All statistical analyses were performed using the QSPR module in SYBYL. The QSPR table was constructed with rows containing values of $\Delta_{\text{fus}}H_m(T_{\text{fus}})$ of each compound in the training set as the dependent variable. The columns contained the steric and electrostatic fields as the independent variables.

The predictive ability of the CoMFA models was determined using “leave-one-out” cross-validation procedure, in which each compound is systematically excluded from the data set and its property predicted by a model that is derived from the remaining compounds. This analysis yields an optimum number of PLS components (or latent variables), which are associated with the highest cross-validated r^2 (r_{cv}^2) value. The PLS analysis was repeated without cross-validation using the optimum number of components. This procedure yielded a predictive model and associated conventional r^2 values.

RESULTS AND DISCUSSION

The statistical results of the CoMFA analysis using different alignment schemes and partial charge formalisms are summarized in Table 2. There are two models that demonstrate excellent predictive ability for the fusion enthalpies of PCBs at the melting point: *atom fit* alignment with ESP charges and *atom fit* alignment with GM charges.

Table 2. Summary of Statistical Results from CoMFA-PLS Analysis of Fusion Enthalpies ($\Delta_{\text{fus}}H_m(T_{\text{fus}})$) of 15 PCBs in the Training Set Using Different Alignment Schemes and Partial Charge Formalisms

| alignment scheme partial charge formalism | atom fit ESP ^a | atom fit GM ^b | field fit ESP ^a | inertial ESP ^a | as is ESP ^a |
|---|---------------------------|--------------------------|----------------------------|---------------------------|------------------------|
| cross-validated r^2 (r_{cv}^2) | 0.747 (0.702) | 0.807 (0.783) | 0.294 (0.248) | 0.089 (0.156) | 0.282 (0.205) |
| conventional r^2 | 0.941 (0.938) | 0.969 (0.955) | 0.733 (0.717) | 0.731 (0.740) | 0.888 (0.849) |
| standard error of estimate | 1.41 (1.34) | 1.13 (1.18) | 2.76 (2.64) | 2.88 (2.62) | 2.04 (2.16) |
| PLS components | 3 (3) | 5 (4) | 1 (1) | 2 (2) | 4 (4) |
| F values | 58.0 (65.1) | 56.2 (64.0) | 35.6 (38.1) | 16.3 (20.0) | 19.7 (16.9) |

^a Electrostatic potential. ^b Gasteiger–Marsili. ^c The values in parentheses represent the statistical results for the original data set of 17 PCBs.

Table 3. Comparison of Experimental and CoMFA-Predicted Values (*Atom Fit* Alignment, GM Charges) of Fusion Enthalpy ($\Delta_{\text{fus}}H_m(T_{\text{fus}})$ in kJ/mol) for the Model Constructed Using the Original Data Set of 17 PCBs

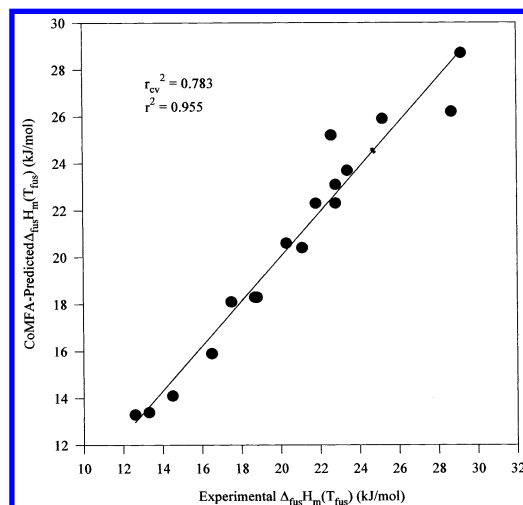
| IUPAC no. | compounds | exptl | pred | residual ^a |
|-----------|---|-------|------|-----------------------|
| | biphenyl | 18.7 | 18.3 | 0.4 |
| 1 | 2-monochlorobiphenyl | 14.5 | 14.1 | 0.4 |
| 3 | 4-monochlorobiphenyl | 13.3 | 13.4 | -0.1 |
| 10 | 2,6-dichlorobiphenyl | 12.6 | 13.3 | -0.7 |
| 29 | 2,4,5-trichlorobiphenyl | 22.8 | 22.3 | 0.5 |
| 30 | 2,4,6-trichlorobiphenyl | 16.5 | 15.9 | 0.6 |
| 49 | 2,2',4,5'-tetrachlorobiphenyl | 23.4 | 23.7 | -0.3 |
| 61 | 2,3,4,5-tetrachlorobiphenyl | 25.2 | 25.9 | -0.7 |
| 101 | 2,2',4,5,5'-pentachlorobiphenyl | 18.8 | 18.3 | 0.5 |
| 116 | 2,3,4,5,6-pentachlorobiphenyl | 21.8 | 22.3 | -0.5 |
| 128 | 2,2',3,3',4,4'-pentachlorobiphenyl | 29.2 | 28.7 | 0.5 |
| 136 | 2,2',3,3',6,6'-hexachlorobiphenyl | 21.1 | 20.4 | 0.7 |
| 155 | 2,2',4,4',6,6'-hexachlorobiphenyl | 17.5 | 18.1 | -0.6 |
| 171 | 2,2',3,3',4,4',6-heptachlorobiphenyl | 20.3 | 20.6 | -0.3 |
| 202 | 2,2',3,3',5,5',6,6'-octachlorobiphenyl | 22.8 | 23.1 | -0.3 |
| 208 | 2,2',3,3',4,5,5',6,6'-nonachlorobiphenyl | 22.6 | 25.2 | -2.6 |
| 209 | 2,2',3,3',4,4',5,5',6,6'-decachlorobiphenyl | 28.7 | 26.2 | 2.5 |

^a The residual is the difference between experimental and CoMFA-predicted values of fusion enthalpy ($\Delta_{\text{fus}}H_m(T_{\text{fus}})$).

The model constructed with *atom fit* alignment and GM charges demonstrated excellent self-consistency ($r^2 = 0.969$) and internal predictive ability ($r_{\text{cv}}^2 = 0.807$). This model, which consists of 15 PCBs in the training set, required only five PCs to explain the variation in $\Delta_{\text{fus}}H_m(T_{\text{fus}})$. The model was used to predict $\Delta_{\text{fus}}H_m(T_{\text{fus}})$ of the two compounds in the test set. The CoMFA-predicted value of $\Delta_{\text{fus}}H_m(T_{\text{fus}})$ was 22.4 kJ/mol (experimental value = 21.8 kJ/mol) for isomer 116 and 18.9 kJ/mol (experimental value = 21.1 kJ/mol) for isomer 136.

The two test-set compounds were combined with the training set of 15 compounds, and the PLS analysis was repeated to construct CoMFA models for the original data set consisting of 17 PCBs. The corresponding values of the experimental and CoMFA-predicted $\Delta_{\text{fus}}H_m(T_{\text{fus}})$, using *atom fit* alignment and GM charges, for this data set are listed in Table 3 and plotted in Figure 2. This model, which exhibited good statistical self-consistency ($r^2 = 0.955$) and predictive ability ($r_{\text{cv}}^2 = 0.783$), was used to predict the values of $\Delta_{\text{fus}}H_m(T_{\text{fus}})$ for the remaining 193 PCB isomers for which experimental values of fusion enthalpies are not available in the literature to the best of our knowledge (Table 4).

The magnitude of the fusion enthalpy is influenced by certain characteristic properties of PCBs, namely, the number and position of Cl atoms on the biphenyl ring. The values of $\Delta_{\text{fus}}H_m(T_{\text{fus}})$ generally increase as the total number of chlorine atoms increases yet decrease as the number of ortho-chlorine atoms increases (Table 5). In a study by Anderson,²² the internal barrier of rotation (E_{rot}) was calculated

**Figure 2.** A plot of CoMFA-predicted (*atom fit* alignment, GM charges) versus experimental values of $\Delta_{\text{fus}}H_m(T_{\text{fus}})$ for the 17 PCBs in the original data set.

for 209 PCBs using AM1 Hamiltonian. The internal barrier of rotation was defined as the difference in total energy between a forced planar conformation and the corresponding geometry-optimized twisted conformation. The values of E_{rot} were in the range of 8–483 kJ/mol and increased significantly with an increase in the number of chlorine atoms at the *ortho* position. Since chlorine has greater steric bulk than hydrogen, it forces the biphenyl ring to adopt a more twisted, noncoplanar structure when it occupies the *ortho* positions. This hinders close packing in the crystalline state and decreases the enthalpy of fusion. For example, within the hexachlorobiphenyl homolog, isomer 128 (2,2',3,3',4,4'-hexachlorobiphenyl) has a higher melting point (424.9 K) and fusion enthalpy (29.2 kJ/mol) than isomer 136 (2,2',3,3',6,6'-hexachlorobiphenyl, melting point = 385.2 K, fusion enthalpy = 21.1 kJ/mol) and isomer 155 (2,2',4,4',6,6'-hexachlorobiphenyl, melting point = 386.7 K, fusion enthalpy = 17.5 kJ/mol). Isomer 128 has only two *ortho*-chlorine atoms compared to four *ortho*-chlorine atoms on isomers 136 and 155.

Prediction of Aqueous Solubility of PCBs. In light of the probable carcinogenic activity of these compounds,^{23,24} and their tendency to sorb and bioaccumulate in aquatic environment, the aqueous solubility of PCBs has been measured by a variety of investigators.^{25–28} The magnitude of the fusion enthalpy influences the solubility of a solute in both an absolute manner as well as in its temperature dependence.²⁹ In view of the limited amount of experimental fusion enthalpy data available to us, we decided to test the reliability of the CoMFA-predicted values of fusion enthalpy by using these values to predict aqueous solubilities of PCBs.

Table 4. CoMFA-Predicted Values of Fusion Enthalpy ($\delta_{\text{fus}}H_m(T_{\text{fus}})$) in kJ/mol for 193 PCBs in the Test Set, Using the Model (Atom Fit Alignment, GM Charges) Constructed from the Original Data Set of 17 PCBs

| IUPAC no. | compounds | no. of atoms | | CoMFA pred values | IUPAC no. | compounds | no. of atoms | | CoMFA pred values |
|--------------|-------------------------------|--------------|----------|-------------------------|--------------|-----------------------------------|--------------|----------|-------------------------|
| | | Cl | ortho Cl | | | | Cl | ortho Cl | |
| 2 | 3-monochlorobiphenyl | 1 | 0 | 19.8 | 78 | 3,3',4,5-tetrachlorobiphenyl | 4 | 0 | 24.9 |
| 4 | 2,2'-dichlorobiphenyl | 2 | 2 | 17.8 | 79 | 3,3',4,5'-tetrachlorobiphenyl | 4 | 0 | 24.3 |
| 5 | 2,3-dichlorobiphenyl | 2 | 1 | 22.0 | 80 | 3,3',5,5'-tetrachlorobiphenyl | 4 | 0 | 24.7 |
| 6 | 2,3'-dichlorobiphenyl | 2 | 1 | 21.5 | 81 | 3,4,4',5-tetrachlorobiphenyl | 4 | 0 | 25.4 |
| 7 | 2,4-dichlorobiphenyl | 2 | 1 | 23.0 | 82 | 2,2',3,3',4-pentachlorobiphenyl | 5 | 2 | 19.5 |
| 8 | 2,4'-dichlorobiphenyl | 2 | 1 | 21.4 | 83 | 2,2',3,3',5-pentachlorobiphenyl | 5 | 2 | 20.2 |
| 9 | 2,5-dichlorobiphenyl | 2 | 1 | 22.0 | 84 | 2,2',3,3',6-pentachlorobiphenyl | 5 | 3 | 18.6 |
| 11 | 3,3'-dichlorobiphenyl | 2 | 0 | 21.2 | 85 | 2,2',3,4,4'-pentachlorobiphenyl | 5 | 2 | 25.3 |
| 12 | 3,4-dichlorobiphenyl | 2 | 0 | 20.4 | 86 | 2,2',3,4,5-pentachlorobiphenyl | 5 | 2 | 17.7 |
| 13 | 3,4'-dichlorobiphenyl | 2 | 0 | 21.7 | 87 | 2,2',3,4,5'-pentachlorobiphenyl | 5 | 2 | 25.4 |
| 14 | 3,5-dichlorobiphenyl | 2 | 0 | 20.6 | 88 | 2,2',3,4,6-pentachlorobiphenyl | 5 | 3 | 23.8 |
| 15 | 4,4'-dichlorobiphenyl | 2 | 0 | 21.3 | 89 | 2,2',3,4,6'-pentachlorobiphenyl | 5 | 3 | 17.6 |
| 16 | 2,2',3-trichlorobiphenyl | 3 | 2 | 15.4 | 90 | 2,2',3,4',5-pentachlorobiphenyl | 5 | 2 | 25.7 |
| 17 | 2,2',4-trichlorobiphenyl | 3 | 2 | 20.2 | 91 | 2,2',3,4',6-pentachlorobiphenyl | 5 | 3 | 25.2 |
| 18 | 2,2',5-trichlorobiphenyl | 3 | 2 | 14.7 | 92 | 2,2',3,5,5'-pentachlorobiphenyl | 5 | 2 | 27.2 |
| 19 | 2,2',6-trichlorobiphenyl | 3 | 3 | 15.1 | 93 | 2,2',3,5,6-pentachlorobiphenyl | 5 | 3 | 24.1 |
| 20 | 2,3,3'-trichlorobiphenyl | 3 | 1 | 23.6 | 94 | 2,2',3,5,6'-pentachlorobiphenyl | 5 | 3 | 16.9 |
| 21 | 2,3,4-trichlorobiphenyl | 3 | 1 | 17.0 | 95 | 2,2',3,5',6-pentachlorobiphenyl | 5 | 3 | 20.4 |
| 22 | 2,3,4'-trichlorobiphenyl | 3 | 1 | 23.3 | 96 | 2,2',3,6,6'-pentachlorobiphenyl | 5 | 4 | 19.0 |
| 23 | 2,3,5-trichlorobiphenyl | 3 | 1 | 16.9 | 97 | 2,2',3',4,5-pentachlorobiphenyl | 5 | 2 | 20.0 |
| 24 | 2,3,6-trichlorobiphenyl | 3 | 2 | 15.2 | 98 | 2,2',3',4,6-pentachlorobiphenyl | 5 | 3 | 23.6 |
| 25 | 2,3',4-trichlorobiphenyl | 3 | 1 | 23.2 | 99 | 2,2',4,4',5-pentachlorobiphenyl | 5 | 2 | 27.8 |
| 26 | 2,3',5-trichlorobiphenyl | 3 | 1 | 23.7 | 100 | 2,2',4,4',6-pentachlorobiphenyl | 5 | 3 | 16.4 |
| 27 | 2,3',6-trichlorobiphenyl | 3 | 2 | 21.8 | 102 | 2,2',4,5,6'-pentachlorobiphenyl | 5 | 3 | 16.6 |
| 28 | 2,4,4'-trichlorobiphenyl | 3 | 1 | 24.3 | 103 | 2,2',4,5',6-pentachlorobiphenyl | 5 | 3 | 18.4 |
| 31 | 2,4',5-trichlorobiphenyl | 3 | 1 | 17.0 | 104 | 2,2',4,6,6'-pentachlorobiphenyl | 5 | 4 | 16.0 |
| 32 | 2,4',6-trichlorobiphenyl | 3 | 2 | 19.5 | 105 | 2,3,3',4,4'-pentachlorobiphenyl | 5 | 1 | 20.8 |
| 33 | 2',3,4-trichlorobiphenyl | 3 | 1 | 24.2 | 106 | 2,3,3',4,5-pentachlorobiphenyl | 5 | 1 | 27.2 |
| 34 | 2',3,5-trichlorobiphenyl | 3 | 1 | 24.6 | 107 | 2,3,3',4',5-pentachlorobiphenyl | 5 | 1 | 28.4 |
| 35 | 3,3',4-trichlorobiphenyl | 3 | 0 | 22.8 | 108 | 2,3,3',4,5'-pentachlorobiphenyl | 5 | 1 | 26.7 |
| 36 | 3,3',5-trichlorobiphenyl | 3 | 0 | 23.2 | 109 | 2,3,3',4,6-pentachlorobiphenyl | 5 | 2 | 25.6 |
| 37 | 3,4,4'-trichlorobiphenyl | 3 | 0 | 23.4 | 110 | 2,3,3',4',6-pentachlorobiphenyl | 5 | 2 | 26.2 |
| 38 | 3,4,5-trichlorobiphenyl | 3 | 0 | 21.8 | 111 | 2,3,3',5,5'-pentachlorobiphenyl | 5 | 1 | 27.0 |
| 39 | 3,4',5-trichlorobiphenyl | 3 | 0 | 23.8 | 112 | 2,3,3',5,6-pentachlorobiphenyl | 5 | 2 | 26.0 |
| 40 | 2,2',3,3'-tetrachlorobiphenyl | 4 | 2 | 22.7 | 113 | 2,3,3',5',6-pentachlorobiphenyl | 5 | 2 | 25.7 |
| 41 | 2,2',3,4-tetrachlorobiphenyl | 4 | 2 | 22.6 | 114 | 2,3,4,4',5-pentachlorobiphenyl | 5 | 1 | 19.9 |
| 42 | 2,2',3,4'-tetrachlorobiphenyl | 4 | 2 | 22.3 | 115 | 2,3,4,4',6-pentachlorobiphenyl | 5 | 2 | 23.5 |
| 43 | 2,2',3,5-tetrachlorobiphenyl | 4 | 2 | 16.8 | 117 | 2,3,4',5,6-pentachlorobiphenyl | 5 | 2 | 23.8 |
| 44 | 2,2',3,5'-tetrachlorobiphenyl | 4 | 2 | 16.7 | 118 | 2,3',4,4',5-pentachlorobiphenyl | 5 | 1 | 20.4 |
| 45 | 2,2',3,6-tetrachlorobiphenyl | 4 | 3 | 15.0 | 119 | 2,3',4,4',6-pentachlorobiphenyl | 5 | 2 | 25.9 |
| 46 | 2,2',3,6'-tetrachlorobiphenyl | 4 | 3 | 15.6 | 120 | 2,3',4,5,5'-pentachlorobiphenyl | 5 | 1 | 26.7 |
| 47 | 2,2',4,4'-tetrachlorobiphenyl | 4 | 2 | 16.8 | 121 | 2,3',4,5',6-pentachlorobiphenyl | 5 | 2 | 25.5 |
| 48 | 2,2',4,5-tetrachlorobiphenyl | 4 | 2 | 15.4 | 122 | 2',3,3',4,5-pentachlorobiphenyl | 5 | 1 | 21.3 |
| 50 | 2,2',4,6-tetrachlorobiphenyl | 4 | 3 | 14.7 | 123 | 2',3,4,4',5-pentachlorobiphenyl | 5 | 1 | 26.0 |
| 51 | 2,2',4,6'-tetrachlorobiphenyl | 4 | 3 | 15.3 | 124 | 2',3,4,5,5'-pentachlorobiphenyl | 5 | 1 | 21.0 |
| 52 | 2,2',5,5'-tetrachlorobiphenyl | 4 | 2 | 15.8 | 125 | 2',3,4,5,6'-pentachlorobiphenyl | 5 | 2 | 17.8 |
| 53 | 2,2',5,6-tetrachlorobiphenyl | 4 | 3 | 24.0 | 126 | 3,3',4,4',5-pentachlorobiphenyl | 5 | 0 | 25.6 |
| 54 | 2,2',6,6'-tetrachlorobiphenyl | 4 | 4 | 15.0 | 127 | 3,3',4,5,5'-pentachlorobiphenyl | 5 | 0 | 26.3 |
| 55 | 2,3,3',4-tetrachlorobiphenyl | 4 | 1 | 25.2 | 129 | 2,2',3,3',4,5-hexachlorobiphenyl | 6 | 2 | 20.4 |
| 56 | 2,3,3',4'-tetrachlorobiphenyl | 4 | 1 | 25.8 | 130 | 2,2',3,3',4,5'-hexachlorobiphenyl | 6 | 2 | 28.8 |
| 57 | 2,3,3',5-tetrachlorobiphenyl | 4 | 1 | 26.2 | 131 | 2,2',3,3',4,6-hexachlorobiphenyl | 6 | 3 | 19.5 |
| 58 | 2,3,3',5'-tetrachlorobiphenyl | 4 | 1 | 25.4 | 132 | 2,2',3,3',4,6'-hexachlorobiphenyl | 6 | 3 | 18.0 |
| 59 | 2,3,3',6-tetrachlorobiphenyl | 4 | 2 | 24.0 | 133 | 2,2',3,3',5,5'-hexachlorobiphenyl | 6 | 2 | 21.2 |
| 60 | 2,3,4,4'-tetrachlorobiphenyl | 4 | 1 | 26.2 | 134 | 2,2',3,3',5,6-hexachlorobiphenyl | 6 | 3 | 19.7 |
| 62 | 2,3,4,6-tetrachlorobiphenyl | 4 | 2 | 18.5 | 135 | 2,2',3,3',5,6'-hexachlorobiphenyl | 6 | 3 | 21.3 |
| 63 | 2,3,4',5-tetrachlorobiphenyl | 4 | 1 | 26.6 | 137 | 2,2',3,4,4',5-hexachlorobiphenyl | 6 | 2 | 27.6 |
| 64 | 2,3,4',6-tetrachlorobiphenyl | 4 | 2 | 21.6 | 138 | 2,2',3,4,4',5'-hexachlorobiphenyl | 6 | 2 | 21.0 |
| 65 | 2,3,5,6-tetrachlorobiphenyl | 4 | 2 | 19.9 | 139 | 2,2',3,4,4',6-hexachlorobiphenyl | 6 | 3 | 26.9 |
| 66 | 2,3',4,4'-tetrachlorobiphenyl | 4 | 1 | 26.6 | 140 | 2,2',3,4,4',6'-hexachlorobiphenyl | 6 | 3 | 19.3 |
| 67 | 2,3',4,5-tetrachlorobiphenyl | 4 | 1 | 25.8 | 141 | 2,2',3,4,5,5'-hexachlorobiphenyl | 6 | 2 | 29.1 |
| 68 | 2,3',4,5'-tetrachlorobiphenyl | 4 | 1 | 25.1 | 142 | 2,2',3,4,5,6-hexachlorobiphenyl | 6 | 3 | 16.8 |
| 69 | 2,3',4,6-tetrachlorobiphenyl | 4 | 2 | 23.6 | 143 | 2,2',3,4,5,6'-hexachlorobiphenyl | 6 | 3 | 17.9 |
| 70 | 2,3',4',5-tetrachlorobiphenyl | 4 | 1 | 25.7 | 144 | 2,2',3,4,5',6-hexachlorobiphenyl | 6 | 3 | 17.1 |
| 71 | 2,3',4',6-tetrachlorobiphenyl | 4 | 2 | 24.0 | 145 | 2,2',3,4,6,6'-hexachlorobiphenyl | 6 | 4 | 17.3 |
| 72 | 2,3',5,5'-tetrachlorobiphenyl | 4 | 1 | 25.4 | 146 | 2,2',3,4',5,5'-hexachlorobiphenyl | 6 | 2 | 30.3 |
| 73 | 2,3',5,6-tetrachlorobiphenyl | 4 | 2 | 23.7 | 147 | 2,2',3,4',5,6-hexachlorobiphenyl | 6 | 3 | 27.3 |
| 74 | 2,4,4',5-tetrachlorobiphenyl | 4 | 1 | 26.4 | 148 | 2,2',3,4',5,6'-hexachlorobiphenyl | 6 | 3 | 19.6 |
| 75 | 2,4,4',6-tetrachlorobiphenyl | 4 | 2 | 21.4 | 149 | 2,2',3,4',5',6-hexachlorobiphenyl | 6 | 3 | 18.0 |
| 76 | 2',3,4,5-tetrachlorobiphenyl | 4 | 1 | 26.3 | 150 | 2,2',3,4',6,6'-hexachlorobiphenyl | 6 | 4 | 18.4 |
| 77 | 3,3',4,4'-tetrachlorobiphenyl | 4 | 0 | 25.3 | 151 | 2,2',3,5,5',6-hexachlorobiphenyl | 6 | 3 | 17.4 |

Table 4. (Continued)

| IUPAC no. | compounds | no. of atoms | | CoMFA pred values | IUPAC no. | compounds | no. of atoms | | CoMFA pred values |
|--------------|--------------------------------------|--------------|----------|-------------------------|--------------|--|--------------|----------|-------------------------|
| | | Cl | ortho Cl | | | | Cl | ortho Cl | |
| 152 | 2,2',3,5,6,6'-hexachlorobiphenyl | 6 | 4 | 17.6 | 181 | 2,2',3,4,4',5,6-heptachlorobiphenyl | 7 | 3 | 18.7 |
| 153 | 2,2',4,4',5,5'-hexachlorobiphenyl | 6 | 2 | 19.2 | 182 | 2,2',3,4,4',5,6'-heptachlorobiphenyl | 7 | 3 | 20.6 |
| 154 | 2,2',4,4',5,6'-hexachlorobiphenyl | 6 | 3 | 19.3 | 183 | 2,2',3,4,4',5',6-heptachlorobiphenyl | 7 | 3 | 31.3 |
| 156 | 2,3,3',4,4',5-hexachlorobiphenyl | 6 | 1 | 29.6 | 184 | 2,2',3,4,4',6,6'-heptachlorobiphenyl | 7 | 4 | 19.4 |
| 157 | 2,3,3',4,4',5'-hexachlorobiphenyl | 6 | 1 | 29.1 | 185 | 2,2',3,4,5,5',6-heptachlorobiphenyl | 7 | 3 | 18.3 |
| 158 | 2,3,3',4,4',6-hexachlorobiphenyl | 6 | 2 | 26.3 | 186 | 2,2',3,4,5,6,6'-heptachlorobiphenyl | 7 | 4 | 18.6 |
| 159 | 2,3,3',4,5,5'-hexachlorobiphenyl | 6 | 1 | 22.3 | 187 | 2,2',3,4',5,5',6-heptachlorobiphenyl | 7 | 3 | 22.4 |
| 160 | 2,3,3',4,5,6-hexachlorobiphenyl | 6 | 2 | 25.3 | 188 | 2,2',3,4',5,6,6'-heptachlorobiphenyl | 7 | 4 | 19.7 |
| 161 | 2,3,3',4,5',6-hexachlorobiphenyl | 6 | 2 | 21.8 | 189 | 2,3,3',4,4',5,5'-heptachlorobiphenyl | 7 | 1 | 31.3 |
| 162 | 2,3,3',4',5,5'-hexachlorobiphenyl | 6 | 1 | 29.5 | 190 | 2,3,3',4,4',5,6-heptachlorobiphenyl | 7 | 2 | 30.1 |
| 163 | 2,3,3',4',5,6-hexachlorobiphenyl | 6 | 2 | 28.3 | 191 | 2,3,3',4,4',5',6-heptachlorobiphenyl | 7 | 2 | 29.5 |
| 164 | 2,3,3',4',5',6-hexachlorobiphenyl | 6 | 2 | 27.8 | 192 | 2,3,3',4,5,5',6-heptachlorobiphenyl | 7 | 2 | 29.7 |
| 165 | 2,3,3',5,5',6-hexachlorobiphenyl | 6 | 2 | 27.9 | 193 | 2,3,3',4',5,5',6-heptachlorobiphenyl | 7 | 2 | 24.2 |
| 166 | 2,3,4,4',5,6-hexachlorobiphenyl | 6 | 2 | 25.6 | 194 | 2,2',3,3',4,4',5,5'-octachlorobiphenyl | 8 | 2 | 35.3 |
| 167 | 2,3',4,4',5,5'-hexachlorobiphenyl | 6 | 1 | 22.5 | 195 | 2,2',3,3',4,4',5,6-octachlorobiphenyl | 8 | 3 | 30.9 |
| 168 | 2,3',4,4',5',6-hexachlorobiphenyl | 6 | 2 | 27.5 | 196 | 2,2',3,3',4,4',5,6'-octachlorobiphenyl | 8 | 3 | 21.9 |
| 169 | 3,3',4,4',5,5'-hexachlorobiphenyl | 6 | 0 | 27.6 | 197 | 2,2',3,3',4,4',6,6'-octachlorobiphenyl | 8 | 4 | 23.7 |
| 170 | 2,2',3,3',4,4',5-heptachlorobiphenyl | 7 | 2 | 23.1 | 198 | 2,2',3,3',4,5,5',6-octachlorobiphenyl | 8 | 3 | 22.0 |
| 172 | 2,2',3,3',4,5,5'-heptachlorobiphenyl | 7 | 2 | 31.0 | 199 | 2,2',3,3',4,5,5',6'-octachlorobiphenyl | 8 | 3 | 23.7 |
| 173 | 2,2',3,3',4,5,6-heptachlorobiphenyl | 7 | 3 | 20.5 | 200 | 2,2',3,3',4,5,6,6'-octachlorobiphenyl | 8 | 4 | 22.6 |
| 174 | 2,2',3,3',4,5,6'-heptachlorobiphenyl | 7 | 3 | 22.4 | 201 | 2,2',3,3',4,5',6,6'-octachlorobiphenyl | 8 | 4 | 22.9 |
| 175 | 2,2',3,3',4,5',6-heptachlorobiphenyl | 7 | 3 | 30.1 | 203 | 2,2',3,4,4',5,5',6-octachlorobiphenyl | 8 | 3 | 19.9 |
| 176 | 2,2',3,3',4,6,6'-heptachlorobiphenyl | 7 | 4 | 21.4 | 204 | 2,2',3,4,4',5,6,6'-octachlorobiphenyl | 8 | 4 | 20.8 |
| 177 | 2,2',3,3',4',5,6-heptachlorobiphenyl | 7 | 3 | 21.6 | 205 | 2,3,3',4,4',5,5',6-octachlorobiphenyl | 8 | 2 | 31.7 |
| 178 | 2,2',3,3',5,5',6-heptachlorobiphenyl | 7 | 3 | 22.7 | 206 | 2,2',3,3',4,4',5,5',6-nonachlorobiphenyl | 9 | 3 | 23.7 |
| 179 | 2,2',3,3',5,6,6'-heptachlorobiphenyl | 7 | 4 | 21.6 | 207 | 2,2',3,3',4,4',5,6,6'-nonachlorobiphenyl | 9 | 4 | 24.9 |
| 180 | 2,2',3,4,4',5,5'-heptachlorobiphenyl | 7 | 2 | 22.1 | | | | | |

Table 5. Average CoMFA-Predicted^a Values of $\delta_{\text{fus}}H_m(T_{\text{fus}})$ for the Entire Set of 209 PCBs Grouped by Homologue (Total Number of Chlorine Atoms) and Ortho-Chlorine Atoms

| total number of Cl atoms | number of ortho-Cl atoms | | | | |
|---|--------------------------|------|------|------|------|
| | 0 | 1 | 2 | 3 | 4 |
| Average $\Delta_{\text{fus}}H_m(T_{\text{fus}})$, kJ/mol | | | | | |
| 2 | 21.0 | 22.0 | 15.5 | | |
| 3 | 23.0 | 21.8 | 17.5 | 15.1 | |
| 4 | 24.9 | 25.9 | 20.6 | 16.9 | 15.0 |
| 5 | 25.9 | 24.1 | 23.7 | 20.1 | 17.5 |
| 6 | 27.6 | 26.6 | 25.5 | 19.9 | 18.4 |
| 7 | | 31.3 | 27.1 | 22.6 | 20.1 |
| 8 | | | 33.5 | 23.7 | 22.6 |

^a The CoMFA model (*atom fit* alignment, GM charges) corresponds to the original data set of 17 PCBs. Note that the fusion enthalpy generally tends to increase with increasing number of Cl atoms but tends to decrease with increasing number of ortho-Cl atoms.

Mobile order and disorder theory, developed by Ruelle and Kesselring, takes the form of eq 1, which has been used to predict aqueous solubility of a diverse set of environmentally significant compounds²⁵

$$\log_{10} S_B = \frac{A}{2.3} + \frac{O}{2.3} + 2.154 - 0.036V_B - 0.217(\ln V_B) \quad (1)$$

where S_B = solubility of a solute B in solvent S, V_B = molar volume of solute B (estimated from the addition of group contributions),²⁵ and O = hydrogen bond formation between proton-acceptor solutes and proton-donor solvents (1.69 for biphenyl, 0.977 for PCBs)²⁵

$$A = \text{fluidization of a solid solute} = \frac{-\Delta_{\text{fus}}H_m}{R} \left(\frac{1}{T} - \frac{1}{T_{\text{fus}}} \right) \quad (2)$$

The terms in eq 2 are defined as T equal to 298.15 K, T_{fus} represents the melting point of the solute, and R is the gas constant (8.314 J/K mol).

The aqueous solubilities of 61 PCBs have been reported in the literature.²⁵ The values of $\Delta_{\text{fus}}H_m(T_{\text{fus}})$ predicted by the 3D-QSPR model (*atom fit* alignment, GM charges) in this study were used to calculate the aqueous solubilities of these 61 PCBs using eq 1. The results are shown in Table 6. The good agreement between calculated and experimental values of solubility of PCBs at 298.15 K (standard deviation = ± 0.41 log units) demonstrates the utility and capability of CoMFA-predicted values of fusion enthalpies to calculate the aqueous solubilities of any PCB.

The present work is third in a series of studies aimed at estimating various thermochemical properties of PCBs. The CoMFA-predicted values of vaporization enthalpies ($\Delta_{\text{vap}}H_m(298.15 \text{ K})$ in kJ/mol)⁸ and sublimation enthalpies ($\Delta_{\text{sub}}H_m(298.15 \text{ K})$ in kJ/mol)⁹ of PCBs have been reported in previous work by the present authors. These studies also used a database of 17 compounds in the training set to predict the enthalpies of 209 PCBs. Although there is some overlap, many compounds in each of the training sets for these thermodynamic properties are different. The previous studies, combined with the present work, complete a thermodynamic cycle that can be used as an independent test of the internal self-consistency of the calculations. The thermodynamic cycle is given by eq 3:

$$\Delta_{\text{sub}}H_m(298.15 \text{ K}) = \Delta_{\text{vap}}H_m(298.15 \text{ K}) + \Delta_{\text{fus}}H_m(298.15 \text{ K}) \quad (3)$$

The values of fusion enthalpy at the melting point ($\Delta_{\text{fus}}H_m(T_{\text{fus}})$) of PCBs have been predicted in this study. These values were adjusted to 298.15 K using eq 4:³⁰

$$\Delta_{\text{fus}}H_m(298.15 \text{ K}) = \Delta_{\text{fus}}H_m(T_{\text{fus}}) + [0.75 + 0.15\{C_{p_{\text{cestd}}}(298.15 \text{ K})\}]\{T_{\text{fus}} - 298.15\} + [10.58 + 0.26\{C_{p_{\text{lestd}}}(298.15 \text{ K})\}]\{298.15 - T_{\text{fus}}\} \quad (4)$$

Table 6. Comparison of Experimental and Calculated Values of Aqueous Solubilities (at 298.15 K) of PCBs

| IUPAC no. | compounds | $\Delta_{\text{fus}}H_m(T_{\text{fus}})^a$ | T_{fus}/K | V_B^b | A^b | $\log S_B^b$ | $\log S_B^c$ |
|-----------|---|--|---------------------------|---------|--------|--------------|---------------------|
| | biphenyl | 18.3 | 341.5 ^d | 160.0 | -0.937 | -4.38 | -4.31 ^o |
| 1 | 2-monochlorobiphenyl | 14.1 | 304.9 ^e | 172.9 | -0.126 | -4.82 | -4.54 ^p |
| 3 | 4-monochlorobiphenyl | 13.4 | 348.6 ^f | 172.9 | -0.782 | -5.10 | -5.20 ^p |
| 4 | 2,2'-dichlorobiphenyl | 17.8 | 334.2 ^g | 185.8 | -0.773 | -5.58 | -5.27 ^p |
| 8 | 2,4'-dichlorobiphenyl | 21.4 | 319.2 ^h | 185.8 | -0.569 | -5.49 | -5.28 ^p |
| 10 | 2,6-dichlorobiphenyl | 13.3 | 307.9 ⁱ | 185.8 | -0.170 | -5.32 | -5.21 ^p |
| 11 | 3,3'-dichlorobiphenyl | 21.2 | 302.2 ^j | 185.8 | -0.113 | -5.29 | -5.80 ^p |
| 12 | 3,4-dichlorobiphenyl | 20.4 | 322.7 ^h | 185.8 | -0.626 | -5.52 | -6.39 ^q |
| 15 | 4,4'-dichlorobiphenyl | 21.3 | 422.2 ^g | 185.8 | -2.52 | -6.34 | -6.56 ^p |
| 18 | 2,2',5-trichlorobiphenyl | 14.7 | 317.2 ^j | 198.7 | -0.355 | -5.88 | -6.02 ^p |
| 22 | 2,3,4'-trichlorobiphenyl | 23.3 | 346.3 ^h | 198.7 | -1.31 | -6.29 | -6.26 ^p |
| 24 | 2,3,6-trichlorobiphenyl | 15.2 | 322.2 ^j | 198.7 | -0.457 | -5.92 | -6.29 ^p |
| 26 | 2,3',5-trichlorobiphenyl | 23.7 | 313.5 ^h | 198.7 | -0.468 | -5.93 | -6.01 ^p |
| 28 | 2,4,4'-trichlorobiphenyl | 24.3 | 330.7 ^h | 198.7 | -0.965 | -6.14 | -6.21 ^p |
| 29 | 2,4,5-trichlorobiphenyl | 22.3 | 349.5 ^f | 198.7 | -1.32 | -6.30 | -6.27 ^p |
| 30 | 2,4,6-trichlorobiphenyl | 15.9 | 334.3 ^f | 198.7 | -0.694 | -6.02 | -6.14 ^p |
| 31 | 2,4',5-trichlorobiphenyl | 17.0 | 340.2 ^h | 198.7 | -0.848 | -6.09 | -6.25 ^p |
| 33 | 2',3,4-trichlorobiphenyl | 24.2 | 333.2 ^j | 198.7 | -1.02 | -6.17 | -6.29 ^p |
| 37 | 3,4,4'-trichlorobiphenyl | 23.4 | 360.5 ^h | 198.7 | -1.63 | -6.43 | -7.06 ^q |
| 40 | 2,2',3,3'-tetrachlorobiphenyl | 22.7 | 393.7 ^h | 211.6 | -2.22 | -7.17 | -7.28 ^p |
| 44 | 2,2',3,5'-tetrachlorobiphenyl | 16.7 | 320.0 ^h | 211.6 | -0.460 | -6.40 | -6.47 ^p |
| 47 | 2,2',4,4'-tetrachlorobiphenyl | 16.8 | 314.2 ^h | 211.6 | -0.346 | -6.35 | -6.51 ^p |
| 49 | 2,2',4,5'-tetrachlorobiphenyl | 23.7 | 339.1 ^f | 211.6 | -1.16 | -6.70 | -6.57 ^p |
| 52 | 2,2',5,5'-tetrachlorobiphenyl | 15.8 | 360.2 ^g | 211.6 | -1.10 | -6.68 | -7.00 ^p |
| 53 | 2,2',5,6'-tetrachlorobiphenyl | 24.0 | 377.2 ^j | 211.6 | -2.03 | -7.08 | -6.80 ^p |
| 54 | 2,2',6,6'-tetrachlorobiphenyl | 15.0 | 471.2 ^h | 211.6 | -2.22 | -7.17 | -7.21 ^q |
| 61 | 2,3,4,5-tetrachlorobiphenyl | 25.9 | 363.9 ^f | 211.6 | -1.89 | -7.02 | -7.16 ^p |
| 66 | 2,3',4,4'-tetrachlorobiphenyl | 26.6 | 397.2 ^h | 211.6 | -2.68 | -7.36 | -6.68 ^q |
| 70 | 2,3',4',5-tetrachlorobiphenyl | 25.7 | 377.2 ^h | 211.6 | -2.17 | -7.15 | -7.25 ^p |
| 75 | 2,4,4',6-tetrachlorobiphenyl | 21.4 | 366.2 ^k | 211.6 | -1.60 | -6.90 | -6.94 ^q |
| 77 | 3,3',4,4'-tetrachlorobiphenyl | 25.3 | 446.2 ^h | 211.6 | -3.39 | -7.67 | -8.53 ^q |
| 80 | 3,3',5,5'-tetrachlorobiphenyl | 24.7 | 437.2 ^h | 211.6 | -3.17 | -7.58 | -8.54 ^q |
| 82 | 2,2',3,3',4-pentachlorobiphenyl | 19.5 | 393.0 ^h | 224.5 | -1.90 | -7.50 | -7.05 ^p |
| 83 | 2,2',3,3',5-pentachlorobiphenyl | 20.2 | 338.2 ^k | 224.5 | -0.965 | -7.10 | -6.96 ^q |
| 86 | 2,2',3,4,5-pentachlorobiphenyl | 17.7 | 373.2 ^l | 224.5 | -1.44 | -7.30 | -7.21 ^p |
| 87 | 2,2',3,4,5'-pentachlorobiphenyl | 25.4 | 385.5 ^h | 224.5 | -2.32 | -7.69 | -7.91 ^p |
| 88 | 2,2',3,4,6-pentachlorobiphenyl | 23.8 | 373.2 ^l | 224.5 | -1.93 | -7.52 | -7.43 ^p |
| 101 | 2,2',4,5,5'-pentachlorobiphenyl | 18.3 | 350.1 ^f | 224.5 | -1.10 | -7.15 | -7.33 ^p |
| 104 | 2,2',4,6,6'-pentachlorobiphenyl | 16.0 | 364.2 ^k | 224.5 | -1.17 | -7.19 | -7.32 ^p |
| 116 | 2,3,4,5,6-pentachlorobiphenyl | 22.3 | 397.6 ^f | 224.5 | -2.25 | -7.66 | -7.92 ^p |
| 118 | 2,3',4,4',5-pentachlorobiphenyl | 20.4 | 379.2 ^h | 224.5 | -1.76 | -7.44 | -7.39 ^p |
| 128 | 2,2',3,3',4,4'-hexachlorobiphenyl | 28.7 | 424.9 ^f | 224.5 | -3.45 | -8.18 | -9.01 ^p |
| 129 | 2,2',3,3',4,5-hexachlorobiphenyl | 20.4 | 358.2 ^m | 237.4 | -1.38 | -7.75 | -8.07 ^q |
| 134 | 2,2',3,3',5,6-hexachlorobiphenyl | 19.7 | 373.2 ⁿ | 237.4 | -1.60 | -7.85 | -8.60 ^p |
| 136 | 2,2',3,3',6,6'-hexachlorobiphenyl | 20.4 | 385.2 ^f | 237.4 | -1.86 | -7.96 | -8.65 ^p |
| 138 | 2,2',3,4,4',5'-hexachlorobiphenyl | 21.0 | 352.5 ^h | 237.4 | -1.31 | -7.72 | -8.32 ^p |
| 141 | 2,2',3,4,5,5'-hexachlorobiphenyl | 29.1 | 358.2 ^j | 237.4 | -1.97 | -8.01 | -7.68 ^p |
| 151 | 2,2',3,5,5',6-hexachlorobiphenyl | 17.4 | 373.7 ^h | 237.4 | -1.42 | -7.77 | -7.42 ^p |
| 153 | 2,2',4,4',5,5'-hexachlorobiphenyl | 19.2 | 376.2 ^g | 237.4 | -1.61 | -7.85 | -8.56 ^p |
| 155 | 2,2',4,4',6,6'-hexachlorobiphenyl | 18.1 | 386.7 ^f | 237.4 | -1.67 | -7.88 | -8.71 ^p |
| 156 | 2,3,3',4,4',5-hexachlorobiphenyl | 29.6 | 400.2 ^j | 237.4 | -3.04 | -8.48 | -7.82 ^p |
| 158 | 2,3,3',4,4',6-hexachlorobiphenyl | 26.3 | 380.2 ^j | 237.4 | -2.29 | -8.15 | -7.66 ^p |
| 171 | 2,2',3,3',4,4',6-heptachlorobiphenyl | 20.6 | 395.4 ^f | 250.3 | -2.04 | -8.52 | -8.30 ^p |
| 183 | 2,2',3,4,4',5',6-heptachlorobiphenyl | 31.3 | 356.2 ^j | 250.3 | -2.06 | -8.52 | -7.92 ^p |
| 185 | 2,2',3,4,5,5',6-heptachlorobiphenyl | 18.3 | 421.7 ^h | 250.3 | -2.16 | -8.57 | -8.46 ^j |
| 187 | 2,2',3,4',5,5',6-heptachlorobiphenyl | 22.4 | 422.2 ⁿ | 250.3 | -2.66 | -8.78 | -8.94 ^p |
| 194 | 2,2',3,3',4,4',5,5'-octachlorobiphenyl | 35.3 | 429.7 ^h | 263.2 | -4.36 | -10.00 | -9.16 ^p |
| 202 | 2,2',3,3',5,5',6,6'-octachlorobiphenyl | 23.1 | 433.8 ^f | 263.2 | -2.91 | -9.37 | -9.15 ^p |
| 206 | 2,2',3,3',4,4',5,5',6-nonachlorobiphenyl | 23.7 | 478.7 ^h | 276.1 | -3.61 | -10.15 | -10.26 ^p |
| 208 | 2,2',3,3',4,5,5',6,6'-nonachlorobiphenyl | 25.2 | 455.8 ^f | 276.1 | -3.52 | -10.11 | -10.41 ^p |
| 209 | 2,2',3,3',4,4',5,5',6,6'-decachlorobiphenyl | 26.2 | 578.9 ^j | 289.0 | -5.13 | -11.28 | -11.62 ^p |

^a CoMFA-predicted values of fusion enthalpy at the melting point ($\Delta_{\text{fus}}H_m(T_{\text{fus}})$ in kJ/mol) using the model (atom fit alignment, GM charges) constructed from the original data set of 17 PCBs. ^b Equation 1 developed by Ruelle and Kesseling²⁵ was used to calculate the aqueous solubilities of PCBs using CoMFA-predicted values of fusion enthalpy at the melting point. ^c The experimental values of aqueous solubility of PCBs at 298.15 K have been reported in the literature in refs 26–28. ^d From ref 16. ^e From ref 17. ^f From ref 18. ^g From ref 33. ^h From ref 34. ⁱ From ref 15. ^j From ref 25. ^k From ref 35. ^l From ref 36(a)–(c). ^m From ref 36(a)–(c) and ref 37. ⁿ From ref 36(a),(b). ^o From ref 26. ^p From ref 27. ^q From ref 28.

The values of the heat capacity of the solid and liquid phase, $C_{p,\text{cestd}}(298.15 \text{ K})$ and $C_{p,\text{lestd}}(298.15 \text{ K})$, respectively, were estimated using a group additivity method.³¹ The standard deviation for the difference between CoMFA-predicted $\{\Delta_{\text{fus}}H_m(298.15 \text{ K}), \text{this study} + \Delta_{\text{vap}}H_m(298.15 \text{ K})^8\}$ and CoMFA-predicted $\Delta_{\text{sub}}H_m(298.15 \text{ K})^9$ for 103 PCBs, for

which melting points have been reported in the literature, was $\pm 8.9 \text{ kJ/mol}$. The results, summarized in Table 1 in Supporting Information, are within two standard deviations of the typical reproducibility of experimental measurements of sublimation enthalpies.³² Hence, the CoMFA-predicted values of the thermodynamic properties (fusion, vaporization

and sublimation enthalpies) of PCBs in our study appear to be internally self-consistent.

CONCLUSIONS

In this study, the fusion enthalpies at the melting points ($\Delta_{\text{fus}}H_{\text{m}}(T_{\text{fus}})$) of 209 PCB congeners have been predicted by a three-dimensional quantitative structure–property relationship (3D-QSPR) model, constructed by correlating $\Delta_{\text{fus}}H_{\text{m}}(T_{\text{fus}})$ with CoMFA-generated steric and electrostatic fields. The combination of *atom fit* alignment and Gasteiger–Marsili charges yielded the greatest self-consistency ($r^2 = 0.955$) and internal predictive ability ($r_{\text{cv}}^2 = 0.783$). The thermodynamic cycle constructed from the CoMFA-predicted values of fusion, vaporization, and sublimation enthalpies shows that the values predicted in our study are internally self-consistent.

A measure of the general reliability of the various thermochemical properties of PCBs predicted by 3D-QSPR models has been independently assessed. These models can be used to examine quantitative structure–property relationships between solubility and solute properties that will enable the development of better predictive methods with applicability to a variety of compounds of environmental significance. These models provide a rapid estimation of the physicochemical properties of PCBs, and the estimated values appear to be reliable within acceptable limits. This study can be extended to other toxic compounds, such as polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans.

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Supporting Information Available: The thermodynamic cycle for the CoMFA-predicted values of fusion, vaporization and sublimation enthalpies of PCBs is presented in Table 1. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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