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Thermochemical behavior of dissolved carboxylic acid solutes: part 4 - mathematical correlation of 4-nitrobenzoic acid solubilities with the abraham solvation parameter model

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THERMOCHEMICAL BEHAVIOR OF DISSOLVED CARBOXYLIC ACID SOLUTES: PART 4 – MATHEMATICAL CORRELATION OF 4-NITROBENZOIC ACID SOLUBILITIES WITH THE ABRAHAM SOLVATION PARAMETER MODEL

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The Abraham general solvation model is used to calculate the numerical values of the solute descriptors for 4-nitrobenzoic acid from experimental solubilities in organic solvents. The mathematical correlations take the form of

$$\begin{aligned}\log(C_S/C_W) &= c + r \cdot R_2 + s \cdot \pi_2^H + a \cdot \Sigma\alpha_2^H + b \cdot \Sigma\beta_2^H + v \cdot V_x \\ \log(C_S/C_G) &= c + r \cdot R_2 + s \cdot \pi_2^H + a \cdot \Sigma\alpha_2^H + b \cdot \Sigma\beta_2^H + l \cdot \log L^{(16)}\end{aligned}$$

where C_S and C_W refer to the solute solubility in the organic solvent and water, respectively, C_G is a gas phase concentration, R_2 is the solute excess molar refraction, V_x is the McGowan volume of the solute, $\Sigma\alpha_2^H$ and $\Sigma\beta_2^H$ are measures of the solute hydrogen-bond acidity and hydrogen-bond basicity, π_2^H denotes the solute dipolarity/polarizability descriptor, and $L^{(16)}$ is the solute gas phase dimensionless Ostwald partition coefficient into hexadecane at 298 K. The remaining symbols in the above expressions are known solvent coefficients, which have been determined previously for a large number of gas/solvent and water/solvent systems. We estimate R_2 as 0.9900, set $\Sigma\alpha_2^H = 0.6800$ and calculate V_x as 1.1059, and then solve a total of 51 equations to yield $\pi_2^H = 1.5200$, $\Sigma\beta_2^H = 0.4000$, and $\log L^{(16)} = 5.7699$. These descriptors reproduce the observed $\log(C_S/C_W)$ and $\log(C_S/C_G)$ values with a standard deviation of only 0.076 log units.

Keywords: 4-Nitrobenzoic acid solubilities; Alcohol solvents; Partition coefficients; Molecular solute descriptors; Solubility predictions

INTRODUCTION

Free energy of partition is an important thermodynamic variable that quantifies the Gibbs energy difference between a molecule in a given phase and the molecule dissolved

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in a second phase. Free energies of partition provide valuable information regarding molecular interactions between dissolved solute and surrounding solvent molecules, and can be used to calculate numerical values of partition coefficients that describe the equilibrium of a solute between two immiscible liquid phases. The partitioning process plays an important role in determining whether or not a given chemical is able to cross biological membranes. Mathematical correlations have been derived to describe the partitioning behavior of various chemicals between specific animal tissues and air (i.e., liver/air, kidney/air partition coefficients, etc.) based upon the substance's known organic solvent/air partition coefficients. Expressions can also be found in the environmental literature relating the partitioning behavior of known organic pollutants between the gas phase and a variety of natural substrates in soil, atmosphere, and foliage to the pollutant's measured organic solvent/air partition coefficient. Experimental studies have further shown that the mass transfer coefficient of a solute across the interface of two immiscible liquid phases depends both upon the solute concentration in each phase and the partition coefficient.

The general solvation parameter model of Abraham [1–8] is one of the most useful approaches for the analysis and prediction of free energies of partition in chemical and biochemical systems. The method relies on two linear free-energy relationships, one for processes within condensed phases

$$\log SP = c + r \cdot R_2 + s \cdot \pi_2^H + a \cdot \Sigma\alpha_2^H + b \cdot \Sigma\beta_2^H + v \cdot V_x \quad (1)$$

and one for processes involving gas to condensed phase transfer

$$\log SP = c + r \cdot R_2 + s \cdot \pi_2^H + a \cdot \Sigma\alpha_2^H + b \cdot \Sigma\beta_2^H + l \cdot \log L^{(16)} \quad (2)$$

where the subscript 2 denotes the solute. The dependent variable, $\log SP$, is some property of a series of solutes in a fixed phase. The independent variables, or descriptors, are solute properties as follows: R_2 and π_2^H refer to the excess molar refraction and dipolarity/polarity descriptors of the solute, respectively, $\Sigma\alpha_2^H$ and $\Sigma\beta_2^H$ are measures of the solute hydrogen-bond acidity and hydrogen-bond basicity, V_x is the McGowan volume of the solute, and $\log L^{(16)}$ is the logarithm of the solute gas phase dimensionless Ostwald partition coefficient into hexadecane at 298 K. The first four descriptors can be regarded as measures of the tendency of the given solute to undergo various solute–solvent interactions. The latter two descriptors, V_x and $\log L^{(16)}$, are both measures of solute size, and so will be measures of the solvent cavity term that will accommodate the dissolved solute. General dispersion interactions are also related to solute size, hence, both V_x and $\log L^{(16)}$ will also describe the general solute–solvent interactions. The regression coefficients and constants (c , r , s , a , b , v , and l) are obtained by regression analysis of experimental data for a specific process (i.e., a given partitioning process, a given stationary phase, and mobile phase combination, etc.). In the case of partition coefficients, where two solvent phases are involved, the c , r , s , a , b , v , and l coefficients represent differences in the solvent phase properties.

Presently, we are in the process of developing/updating correlation equations for additional/existing solvent systems [7–10], and in developing new computational methodologies for calculating solute descriptors from available experimental data and/or structural information [11–15]. Of particular interest are the carboxylic acid solutes

that possess large numerical values of their hydrogen-bonding acidity descriptor. The existing values that we have for the molecular descriptors of many of the carboxylic acids were derived almost entirely from "practical" partitioning data. For some solutes, there was only very limited experimental data of marginal quality, and one or two incorrect data points could lead to the calculation of incorrect values for the molecular descriptors as was the case in a recently completed solubility study involving acetylsalicylic acid [16]. For other carboxylic acid solutes there is no sufficient experimental data to even calculate the solute descriptor values. For this reason solubilities of 4-nitrobenzoic acid were measured in numerous organic solvents of varying polarity and hydrogen-bonding characteristics. 4-Nitrobenzoic acid is expected to exist almost exclusively in monomeric form in each of the solvent studied. Results of these measurements are interpreted using the Abraham solvation parameter equations (1) and (2).

MATERIALS AND METHODS

4-Nitrobenzoic acid was purchased from commercial source (Acros, 99+%) and was used as received. The purity of the commercial sample was 99.8% ($\pm 0.3\%$), as determined by nonaqueous titration with freshly standardized sodium methoxide solution to the thymol blue endpoint according to the method of Fritz and Lisicki [17], except toluene was substituted for benzene. Ethanol (Aaper Alcohol and Chemical Company, absolute), methanol (Aldrich, 99.8%, anhydrous), 1-propanol (Aldrich, 99+%, anhydrous), 1-butanol (Aldrich, HPLC, 99.8+%), 1-pentanol (Aldrich, 99+%), 1-hexanol (Alfa Aesar, 99+%), 1-heptanol (Alfa Aesar, 99+%), 1-octanol (Aldrich, 99+%, anhydrous), 2-propanol (Aldrich, 99+%, anhydrous), 2-butanol (Aldrich, 99+%, anhydrous), 2-methyl-1-propanol (Aldrich, 99+%, anhydrous), 2-methyl-2-propanol (Arco Chemical Company, 99+%), 2-methyl-1-butanol (Aldrich, 99%), 3-methyl-1-butanol (Aldrich, 99%, anhydrous), 1-decanol (Alfa Aesar, 99+%), 4-methyl-2-pentanol (Acros, 99+%), 2-pentanol (Acros, 99+%), 2-methyl-1-pentanol (Aldrich, 99%), 2-methyl-2-butanol (Aldrich, 99%), methyl acetate (Aldrich, 99.5%, anhydrous), ethyl acetate (Aldrich, HPLC, 99.9%), butyl acetate (Aldrich, HPLC, 99.7%), diethyl ether (Aldrich, 99+%, anhydrous), diisopropyl ether (Aldrich, 99%, anhydrous), dibutyl ether (Aldrich, 99.3%, anhydrous), tetrahydrofuran (Aldrich, 99.9%, anhydrous), 1,4-dioxane (Aldrich, 99.8%, anhydrous), pentyl acetate (Aldrich, 99%), and propylene carbonate (Aldrich, 99.7%, anhydrous) were stored over molecular sieves and distilled shortly before use. Gas chromatographic analysis showed solvent purities to be 99.7 mole percent or better.

Excess solute and solvent were placed in amber glass bottles and allowed to equilibrate in a constant temperature water bath at $25.0 \pm 0.1^\circ\text{C}$ for at least 24 h (often longer) with periodic agitation. After equilibration, the samples stood unagitated for several hours in the constant temperature bath to allow any finely dispersed solid particles to settle. Attainment of equilibrium was verified both by repetitive measurements the following day (or sometimes after two days) and by approaching equilibrium from supersaturation by preequilibrating the solutions at a slightly higher temperature. Aliquots of saturated 4-nitrobenzoic acid solutions were transferred through a coarse filter into a tared volumetric flask to determine the amount of sample and diluted quantitatively with methanol for spectrophotometric analysis at 272 nm on a Bausch and Lomb Spectronic 2000. Concentrations of the dilute solutions were determined from

a Beer–Lambert law absorbance *versus* concentration working curve for nine standard solutions. The calculated molar absorptivity varied systematically with concentration, and ranged from approximately $\epsilon \approx 10\,000$ to $9250\text{ L mol}^{-1}\text{ cm}^{-1}$ for 4-nitrobenzoic acid concentrations from 4.52×10^{-5} to 1.51×10^{-4} Molar. Identical molar absorptivities were obtained for select 4-nitrobenzoic acid solutions that contained up to 2 vol% of the neat alcohol, ether, and acylacetate solvents.

Experimental molar concentrations were converted to (mass/mass) solubility fractions by multiplying by the molar mass of 4-nitrobenzoic acid, volume(s) of volumetric flask(s) used, and any dilutions required to place the measured absorbances on the Beer–Lambert law absorbance *versus* concentration working curve, and then dividing by the mass of the saturated solution analyzed. Mole fraction solubilities were computed from solubility mass fractions using the molar masses of the solute and solvent. Experimental 4-nitrobenzoic acid solubilities, X_S , in the 26 organic solvents studied are listed in Table I. Numerical values represent the average of between four and eight independent determinations. Reproducibility ranged from $\pm 1.5\%$ for solvents having the lower mole fraction solubilities to $\pm 2.0\%$ for solvents having the larger 4-nitrobenzoic acid solubilities, where an extra dilution was necessary to keep the measured absorbances within the Beer–Lambert law region. Our measured value for the solubility of 4-nitrobenzoic acid in ethanol is in good agreement with the published data of Thuairé [18] as shown in Table I

TABLE I Experimental 4-nitrobenzoic acid mole fraction solubilities, X_S , in select organic solvents at 25°C

<i>Organic solvent</i>	X_S (<i>This work</i>)	X_S (<i>Literature</i>)
Methanol	0.007881	
Ethanol	0.008544	0.008675 [18]
1-Propanol	0.007990	
1-Butanol	0.007973	
1-Pentanol	0.009317	
1-Hexanol	0.01051	
1-Heptanol	0.01071	
1-Octanol	0.009758	
1-Decanol	0.01022	
2-Propanol	0.008550	
2-Butanol	0.008898	
2-Methyl-1-propanol	0.006093	
2-Methyl-2-propanol	0.01430	
2-Methyl-1-butanol	0.005897	
3-Methyl-1-butanol	0.007285	
2-Pentanol	0.008967	
4-Methyl-2-pentanol	0.008513	
2-Methyl-1-pentanol	0.006460	
2-Methyl-2-butanol	0.01814	
Diethyl ether	0.009861	
Diisopropyl ether	0.003621	
Dibutyl ether	0.002806	
Tetrahydrofuran	0.06393	
1,4-Dioxane	0.04203	
Methyl acetate	0.01168	
Ethyl acetate	0.01237	
Butyl acetate	0.01007	
Pentyl acetate	0.007469	
Propylene carbonate	0.004850	

RESULTS AND DISCUSSION

Equation (1) predicts partition coefficients, and for select solvents both “dry” and “wet” equation coefficients have been reported. For solvents that are partially miscible with water, such as 1-butanol and ethyl acetate, partition coefficients calculated as the ratio of the molar solute solubilities in the organic solvent and water are not the same as those obtained from direct partition between water (saturated with the organic solvent) and organic solvent (saturated with water). Care must be taken not to confuse the two sets of partitions. In the case of solvents that are fully miscible with water, such as methanol, no confusion is possible. Only one set of equation coefficients have been reported, and the calculated $\log P$ value must refer to the hypothetical partition between the two pure solvents. And for solvents that are “almost” completely immiscible with water, such as alkanes, cyclohexane, dichloromethane, trichloromethane, tetrachloromethane, and most aromatic solvents, there should be no confusion because indirect partition (see Eq. (3)) will be nearly identical to direct partition.

The predictive applicability of the Abraham solvation parameter model is relatively straightforward. We start with the set of equations that we have constructed for the partition of solutes between water and a given solvent. Table II gives the coefficients in Eq. (1) for the water–solvent partitions we shall consider. The actual numerical values may differ slightly from values reported in earlier publications. Coefficients are periodically revised when additional experimental data becomes available. Note that many of these are “hypothetical partitions” between pure water and the pure dry solvent; these are shown as “dry” in Table II. Although “hypothetical,” these partitions are very useful; as we show later, they can be used to predict solubilities (and activity coefficients) in the pure dry solvent. The partition coefficient of a solid between water and a solvent phase, P , is related to

$$SP = P = C_S/C_W \quad \text{or} \quad \log SP = \log P = \log C_S - \log C_W \quad (3)$$

the molar solubility of the solid in water, C_W , and in the solvent, C_S . Hence, if C_W is known, predicted $\log P$ values based upon Eq. (1) will lead to predicted molar solubilities through Eq. (3). Three specific conditions must be met in order to use the Abraham solvation parameter model to predict saturation solubilities. First, the same solid phase must be in equilibrium with the saturation solutions in the organic solvent and in water (i.e., there should be no solvate or hydrate formation). Second, the secondary medium activity coefficient of the solid in the saturated solutions must be unity (or near unity). This condition generally restricts the method to those solutes that are sparingly soluble in water and nonaqueous solvents. Finally, for solutes that are ionized in aqueous solution, C_W , refers to the solubility of the neutral form. For many carboxylic acids the correction should be fairly small, provided that the solute is not highly insoluble nor has a large acid dissociation constant. We use the solubility of 4-nitrobenzoic acid in water, $\log C_W = -2.98$ [18] (corrected for ionization), to convert the predicted partition coefficients to saturation solubilities, which can then be compared to the experimentally determined values. Ionization is not a concern in the organic solvents that have dielectric constants much smaller than water.

The second restriction may not be as important as initially believed. The Abraham solvation parameter model has shown remarkable success in correlating the solubility of several very soluble crystalline solutes. For example, Eqs. (1) and (2) described the molar solubility of benzil in 24 organic solvents to within overall standard deviations

TABLE II Coefficients in Eqs. (1) and (2) for various processes^a

Process/solvent	<i>c</i>	<i>r</i>	<i>s</i>	<i>a</i>	<i>b</i>	<i>v/l</i>
<i>A. Water-to-solvent: Eq. (1)</i>						
1-Octanol (wet)	0.088	0.562	-1.054	0.034	-3.460	3.814
Diethyl ether (wet)	0.248	0.561	-1.016	-0.226	-4.553	4.075
Diethyl ether (dry)	0.330	0.401	-0.814	-0.457	-4.959	4.320
1,4-Dioxane (dry)	0.098	0.350	-0.083	-0.556	-4.826	4.172
Tetrahydrofuran (dry)	0.207	0.372	-0.392	-0.236	-4.934	4.447
Methanol (dry)	0.329	0.299	-0.671	0.080	-3.389	3.512
Ethanol (dry)	0.208	0.409	-0.959	0.186	-3.645	3.928
1-Propanol (dry)	0.147	0.494	-1.195	0.495	-3.907	4.048
2-Propanol (dry)	0.063	0.320	-1.024	0.445	-3.824	4.067
1-Butanol (dry)	0.152	0.437	-1.175	0.098	-3.914	4.119
1-Pentanol (dry)	0.080	0.521	-1.294	0.208	-3.908	4.208
1-Hexanol (dry)	0.044	0.470	-1.153	0.083	-4.057	4.249
1-Heptanol (dry)	-0.026	0.491	-1.258	0.035	-4.155	4.415
1-Octanol (dry)	-0.034	0.490	-1.048	-0.028	-4.229	4.219
1-Decanol (dry)	-0.062	0.754	-1.461	0.063	-4.053	4.293
2-Butanol (dry)	0.106	0.272	-0.988	0.196	-3.805	4.110
2-Methyl-1-propanol (dry)	0.177	0.355	-1.099	0.069	-3.570	3.990
2-Methyl-2-propanol (dry)	0.197	0.136	-0.916	0.318	-4.031	4.113
Ethyl acetate (dry)	0.358	0.362	-0.449	-0.668	-5.016	4.155
Chloroform	0.327	0.157	-0.391	-3.191	-3.437	4.191
Toluene	0.143	0.527	-0.720	-3.010	-4.824	4.545
SDS	1.201	0.542	-0.400	-0.133	-1.580	2.793
HPLC-MKMA-N (k)	-1.216	0.495	-0.438	0.025	-2.757	2.671
HPLC-MKMB-N (k)	-1.082	0.574	-0.500	-0.009	-2.591	2.240
HPLC-ANNA (k)	-0.010	0.709	-0.934	-0.119	-3.401	3.784
HPLC-HAF-60 (k)	-0.789	0.095	-0.487	-0.337	-1.994	2.181
HPLC-HAF-75 (k)	-0.993	0.041	-0.397	-0.364	-1.629	1.757
HPLC-HAF-90 (k)	-1.176	0.079	-0.417	-0.306	-1.140	1.296
HPLC-TOM-50 (k)	-0.669	0.181	-0.687	-0.252	-1.872	2.491
HPLC-TOM-75 (k)	-0.919	0.096	-0.479	-0.336	-1.266	1.617
(Gas-to-water)	-0.994	0.577	2.549	3.813	4.841	-0.869
<i>B. Gas-to-solvent: Eq. (2)</i>						
1-Octanol (wet)	-0.198	0.002	0.709	3.519	1.429	0.858
Diethyl ether (wet)	0.206	-0.169	0.873	3.402	0.000	0.882
Diethyl ether (dry)	0.288	-0.347	0.775	2.985	0.000	0.973
Tetrahydrofuran (dry)	0.189	-0.347	1.238	3.289	0.000	0.982
1,4-Dioxane (dry)	-0.034	-0.354	1.674	3.021	0.000	0.919
Methanol (dry)	-0.004	-0.215	1.173	3.701	1.432	0.769
Ethanol (dry)	0.012	-0.206	0.789	3.635	1.311	0.853
1-Propanol (dry)	-0.028	-0.185	0.648	4.022	1.043	0.869
2-Propanol (dry)	-0.060	-0.335	0.702	4.017	1.040	0.893
1-Butanol (dry)	-0.039	-0.276	0.539	3.781	0.995	0.934
1-Pentanol (dry)	-0.042	-0.277	0.526	3.779	0.983	0.932
1-Hexanol (dry)	-0.035	-0.298	0.626	3.726	0.729	0.936
1-Heptanol (dry)	-0.062	-0.168	0.429	3.541	1.181	0.927
1-Octanol (dry)	-0.119	-0.203	0.560	3.576	0.702	0.940
1-Decanol (dry)	-0.136	-0.038	0.325	3.674	0.767	0.947
2-Butanol (dry)	-0.013	-0.456	0.780	3.753	1.064	0.906
2-Methyl-1-propanol (dry)	-0.012	-0.407	0.670	3.645	1.283	0.895
2-Methyl-2-propanol (dry)	0.071	-0.538	0.818	3.951	0.823	0.905
Ethyl acetate (dry)	0.203	-0.335	1.251	2.949	0.000	0.917
Chloroform	0.116	-0.467	1.203	0.138	1.432	0.994
Toluene	0.121	-0.222	0.938	0.467	0.099	1.012
Heptane	0.275	-0.162	0.000	0.000	0.000	0.983
(Gas-to-water)	-1.271	0.822	2.743	3.904	4.814	-0.213

^aThe solvents denoted as "dry" are those for which partitions refer to transfer to the pure dry solvent. The other partitions are from water (more correctly water saturated with solvent) to the solvent saturated with water (see text).

of 0.124 and 0.109 log units, respectively. Standard deviations for acetylsalicylic acid dissolved in 13 alcohols, 4 ethers and ethyl acetate were 0.123 and 0.138 log units. Benzil [15] and acetylsalicylic acid [16] exhibited solubilities exceeding 1 Molar in several of the organic solvents studied. In the case of acetylsalicylic acid it could be argued that the model's success relates back to when the equation coefficients were originally calculated for the dry solvents. The databases used in the regression analyses contained very few carboxylic acid solutes (benzoic acid, 2-hydroxybenzoic acid and 4-hydroxybenzoic acid). Most of the experimental data for carboxylic acids and other very acidic solutes was in the form of saturation solubilities, which were also in the 1–3 Molar range. Such arguments do not explain why Eqs. (1) and (2) described the measured benzil solubility data. The benzil solubilities were measured after most of the equation coefficients were determined.

For partition of solutes between the gas phase and solvents, Eq. (2) is used. (Equation coefficients are given in Table II for several organic solvents.) Predicted log L values can also be converted to saturation molar solubilities, provided that the solid saturated vapor pressure at 298.15 K, VP° , is available. VP° can be transformed into the gas phase concentration, C_G , and the gas–water and gas–solvent partitions, L_W and L_S , can be obtained through

$$SP = LW = C_W/C_G \quad \text{or} \quad \log SP = \log L_W = \log C_W - \log C_G \quad (4)$$

$$SP = L_S = C_S/C_G \quad \text{or} \quad \log SP = \log L_S = \log C_S - \log C_G \quad (5)$$

Eqs. (4) and (5), respectively. As before, the computational method will be valid if conditions discussed above are met. If one cannot find an experimental vapor pressure for the solute at 298.15 K in the published literature, one can assume an estimated value in the preliminary calculations. The value can be adjusted if necessary in order to reduce the log L deviations, and to make the log P and log L predictions internally consistent.

To determine the solute descriptors for 4-nitrobenzoic acid, we first convert the experimental mole fraction solubilities of 4-nitrobenzoic acid into molar solubilities by dividing X_S , by the ideal molar volume of the saturated solution (i.e., $C_S \approx X_S/[X_S V_{\text{Solute}} + (1 - X_S)V_{\text{Solvent}}]$). A value of $V = 117.7 \text{ cm}^3 \text{ mol}^{-1}$ was used for the molar volume of the hypothetical subcooled liquid 4-nitrobenzoic acid. Dibutyl ether was excluded from the solubility analysis because we felt that dimerization of 4-nitrobenzoic acid was inevitable in this larger ether solvent. Carboxylic acids are known to dimerize in saturated hydrocarbon and aromatic hydrocarbon solvents. It was noted when the equation coefficients for dibutyl ether were calculated that the derived equations did not describe the solubility behavior of several carboxylic acids (benzoic acid, 2-hydroxybenzoic acid, 4-hydroxybenzoic acid, and 3-nitrobenzoic acid) [10]. The calculated log P values were always less than observed log P values by the solubility method, as would be expected if dimerization did occur in dibutyl ether. Solubility measurements determine the total carboxylic acid concentration in the organic solvent, and unlike in the case of “practical” partition measurements, there is no convenient experimental means to correct the measured value for dimerization effects. Correlation equations for diethyl ether, tetrahydrofuran and 1,4-dioxane did describe the solubility behavior of the benzoic acid, 2-hydroxybenzoic acid, and 4-hydroxybenzoic acid [9]. The latter three ether solvents are included in the solubility analysis.

Available practical partition coefficient data for 4-nitrobenzoic acid is then retrieved from the published literature [19–21], along with three sets of chromatographic

retention data [22–25]. Combining the two sets of linear free-energy relationships we have a total of 51 equations for which partition data and equation coefficients are available. Not all of the solubility data can be used at the present time because we are missing equation coefficients for several of the organic solvents. The unused solubility data will be used in subsequent studies when we derive correlation equations for additional organic solvents. The characteristic McGowan volume of 4-nitrobenzoic acid ($V_x = 1.1059$) is calculated from the individual atomic sizes and number of bonds in the molecule [26], R_2 is estimated as 0.990, and $\Sigma\alpha_2^H$ is set at 0.680, which is a typical value that has been found for the hydrogen-bond acidity descriptor for similar aromatic carboxylic acid solutes. The set of 51 equations were then solved using Microsoft “Solver” to yield the values of the three unknown solute descriptors that best described the combined $\log P$ and $\log L$ experimental partitioning data. The final set of molecular descriptors were: $\pi_2^H = 1.520$, $\Sigma\beta_2^H = 0.400$, and $\log L^{(16)} = 5.7699$; and the vapor phase concentration was $\log C_G = -9.88$. The vapor phase concentration corresponds to a gas-to-water partition of $\log L_W = 6.90$, which is in good agreement with the calculated values based upon Eqs. (1) and (2) (the last numerical entry in Table III).

TABLE III Comparison between observed and back-calculated partitions and molar solubilities of 4-nitrobenzoic acid based upon Eqs. (1) and (2) and calculated molecular solute descriptors^a

Solvent	Equation (1)			Equation (2)			
	$\log C_S$	$\log P^{exp}$	$\log P^{calc}$	$\log C_S^{calc}$	$\log L^{exp}$	$\log L^{calc}$	$\log C_S^{calc}$
1-Octanol (wet)		1.890	1.899		8.790	8.797	
Chloroform		0.870	0.978		7.770	7.884	
Toluene		0.505	0.620		7.405	7.523	
SDS		3.490	3.496				
Diethyl ether (wet)		1.800	1.791		8.700	8.768	
Diethyl ether (dry)	-0.902	2.078	1.965	-1.015	8.978	8.766	-1.114
Tetrahydrofuran (dry)	-0.117	2.863	2.763	-0.217	9.763	9.630	-0.250
1,4-Dioxane (dry)	-0.317	2.663	2.624	-0.356	9.563	9.517	-0.363
Methanol (dry)	-0.719	2.261	2.188	-0.792	9.161	9.093	-0.787
Ethanol (dry)	-0.841	2.139	2.168	-0.812	9.039	8.925	-0.955
1-Propanol (dry)	-0.975	2.005	2.081	-0.899	8.905	8.940	-0.940
2-Propanol (dry)	-0.956	2.024	2.094	-0.886	8.924	8.976	-0.904
1-Butanol (dry)	-1.063	1.917	1.853	-1.127	8.819	8.868	-1.012
1-Pentanol (dry)	-1.067	1.913	1.861	-1.119	8.813	8.824	-1.056
1-Hexanol (dry)	-1.076	1.904	1.889	-1.091	8.804	8.847	-1.033
1-Heptanol (dry)	-1.121	1.859	1.792	-1.188	8.759	8.653	-1.227
1-Octanol (dry)	-1.209	1.771	1.813	-1.167	8.671	8.661	-1.219
1-Decanol (dry)	-1.271	1.709	1.633	-1.347	8.609	8.590	-1.290
2-Butanol (dry)	-1.017	1.963	2.030	-0.950	8.863	8.926	-0.954
2-Methyl-1-propanol (dry)	-1.183	1.797	1.870	-1.110	8.697	8.783	-1.097
2-Methyl-2-propanol (dry)	-0.821	2.159	2.091	-0.889	9.059	9.019	-0.861
Ethyl acetate (dry)	-0.902	2.078	2.168	-0.812	8.978	9.069	
HPLC MKMA-N (k)		0.360 ^b	0.476				
HPLC MKMB-N (k)		0.160 ^b	0.161				
HPLC ANNA (k)		1.953 ^c	2.016				
HPLC-TOM-50 (k)		0.334 ^d	0.301				
HPLC-TOM-75 (k)		-0.450 ^d	-0.499				
HPLC-HAF-60 (k)		0.013 ^e	-0.050				
HPLC-HAF-75 (k)		-0.462 ^e	-0.512				
HPLC-HAF-90 (k)		-0.987 ^e	-0.969				
Gas-to-Water		6.900	7.020			6.900	7.063

^aNumerical values of the descriptors used in these calculations are: $R_2 = 0.990$, $\pi_2^H = 1.520$, $\Sigma\alpha_2^H = 0.680$, $\Sigma\beta_2^H = 0.400$, $V_x = 1.1059$, and $\text{Log } L^{(16)} = 5.7699$. ^bExperimental value is taken from [23]. ^cExperimental value is taken from [24]. ^dExperimental value is taken from [22]. ^eExperimental value is taken from [25].

The final set of molecular descriptors reproduce the 51 experimental $\log P$ and $\log L$ values to within an overall standard deviation of 0.076 log units as shown in Table III. Individual standard deviations are 0.058 and 0.088 for the 30 calculated and observed $\log P$ values and 21 calculated and observed $\log L$ values, respectively. Statistically there is no difference between the set of 30 $\log P$ values and the total set of 51 $\log P$ and $\log L$ values, thus suggesting that the value of $\log C_G = -9.88$ is a feasible value for 4-nitrobenzoic acid. Whether or not the assumed value is in accord with future experimental vapor pressures, we can regard our value of $\log C_G$ simply as a constant that leads to calculations and predictions via Eq. (2). Our past experience in using different solution models has been that the better solution models will generally give back-calculated values that fall within 0.200 log units of the observed solute solubilities. The Abraham general solvation model meets this criterion.

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