Thermochemical behavior of dissolved Carboxylic Acid solutes: Part 3 - Mathematical Correlation of 2-Methylbenzoic acid solubilities with the Abraham Solvation Parameter Model

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THERMOCHEMICAL BEHAVIOR OF DISSOLVED CARBOXYLIC ACID SOLUTES: PART 3 – MATHEMATICAL CORRELATION OF 2-METHYLBENZOIC 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 2-methylbenzoic acid from experimental solubilities in organic solvents. The mathematical correlations take the form of

$$\log(C_S/C_W) = c + r \cdot R_2 + s \cdot \pi_2^H + a \cdot \Sigma\alpha_2^H + b \cdot \Sigma\beta_2^H + v \cdot V_x$$
$$\log(C_S/C_G) = c + r \cdot R_2 + s \cdot \pi_2^H + a \cdot \Sigma\alpha_2^H + b \cdot \Sigma\beta_2^H + 1 \cdot \log L^{(16)}$$

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 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 0.7300 and calculate V_x as 1.0726, and then solve a total of 47 equations to yield $\pi_2^H = 0.8400$, $\Sigma\alpha_2^H = 0.4200$, $\Sigma\beta_2^H = 0.4400$ and $\log L^{(16)} = 4.6770$. 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: 2-Methylbenzoic acid solubilities; Alcohol solvents; Partition coefficients; Molecular solute descriptors

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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 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

$$\log SP = c + r \cdot R_2 + s \cdot \pi_2^H + a \cdot \Sigma\alpha_2^H + b \cdot \Sigma\beta_2^H + v \cdot V_x \tag{1}$$

and the other and for processes involving gas to condensed phase transfer

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

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 a 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 not sufficient experimental data to even calculate the solute descriptor values. For this reason solubilities of 2-methylbenzoic acid were measured in numerous organic solvents of varying polarity and hydrogen-bonding characteristics. 2-Methylbenzoic 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 Eqs. (1) and (2).

MATERIALS AND METHODS

2-Methylbenzoic acid was purchased from commercial source (Aldrich, 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), 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+%), 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 $25.0 \pm 0.1^{\circ}$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 pre-equilibrating the solutions at a slightly higher temperature.

Aliquots of saturated 2-methylbenzoic 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 279 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, which ranged in concentration from 2.95×10^{-4} to 1.48×10^{-3} M. The calculated molar absorptivity of $\varepsilon \approx 1110 \, \mathrm{L \, mol^{-1} cm^{-1}}$ was constant over the concentration range studied. Identical molar absorptivities were obtained for select 2-methylbenzoic acid solutions that contained up to 2 vol% of the neat alcohol, ether and alkylacetate solvents.

Experimental molar concentrations were converted to (mass/mass) solubility fractions by multiplying by the molar mass of 2-methylbenzoic 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 2-methylbenzoic 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 2-methylbenzoic acid solubilities, where an extra dilution was necessary to keep the measured absorbances within the Beer–Lambert law region.

TABLE I   Experimental 2-methylbenzoic acid mole fraction solubilities, X_S, in select organic solvents at 25°C

Organic solvent	X_S (*this work*)	X_S (*literature*)
Ethanol	0.1401	0.1460 [18], 0.1432 [19,20]
1-Propanol	0.1450	
1-Butanol	0.1551	
1-Pentanol	0.1646	
1-Hexanol	0.1707	
1-Heptanol	0.1755	
1-Octanol	0.1758	
1-Decanol	0.1853	
2-Propanol	0.1612	0.1580 [19,20]
2-Butanol	0.1700	
2-Methyl-1-propanol	0.1229	
2-Methyl-2-propanol	0.2138	
2-Methyl-1-butanol	0.1381	
3-Methyl-1-butanol	0.1473	
2-Pentanol	0.1856	
4-Methyl-2-pentanol	0.1735	
Diethyl ether	0.1718	
Diisopropyl ether	0.1148	
Dibutyl ether	0.0939	
Tetrahydrofuran	0.2629	
1,4-Dioxane	0.2534	
Methyl acetate	0.1306	
Ethyl acetate	0.1509	
Butyl acetate	0.1514	
Pentyl acetate	0.1494	
Propylene carbonate	0.04081	

Literature values do exist for the solubility of 2-methylbenzoic acid in both ethanol and 2-propanol. Our measured values are in good agreement with the published data of Thuaire [18], Domanska [19] and Domanska and Hofman [20] as shown in Table I. The latter authors reported the solubility of 2-methylbenzoic acid at several temperatures. The literature values at 298.15 K were obtained from a ln X *versus* $1/T$ graph.

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 the 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 I. 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

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

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

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

Process/solvent	c	r	s	a	b	v/l
A. Water to solvent: Eq. (1)						
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
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
Cyclohexane	0.159	0.784	−1.678	−3.740	−4.929	4.577
Thin layer (RM_w)	0.259	0.239	−0.662	−0.667	−3.006	3.603
HPLC BK-20/10 ($t'_R/10$)	1.184	0.027	−0.148	−0.556	−0.839	1.098
HPLC BK-40/10 ($t'_R/10$)	1.284	0.023	−0.381	−1.030	−1.734	2.417
(Gas to water)	−0.994	0.577	2.549	3.813	4.841	−0.869
B. Gas to solvent: Eq. (2)						
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
Cyclohexane	0.163	−0.110	0.000	0.000	0.000	1.013
(Gas to water)	−1.271	0.822	2.743	3.904	4.814	−0.213

[a]The 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).

2-methylbenzoic acid in water, $\log C_W = -2.06$ [21,22], 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 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 M 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 were in the form of saturation solubilities, which were also in the 1–3 M 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^{o}, is available. VP^{o} 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

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

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

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 2-methylbenzoic acid, we first convert the experimental mole fraction solubilities of 2-methylbenzoic acid into molar solubilities by dividing X_S, by the ideal molar volume of the saturated solution (i.e., $C_S \approx X_S/[X_S V_{\mathrm{Solute}} + (1 - X_S)V_{\mathrm{Solvent}}]$). A value of $V = 121.8\,\mathrm{cm^3\,mol^{-1}}$ was used for the molar volume of the hypothetical subcooled liquid 2-methylbenzoic acid. Dibutyl ether was excluded from the solubility analysis because we felt that dimerization of 2-methylbenzoic 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 benzoic acid, 2-hydroxybenzoic acid and 4-hydroxy-benzoic acid [9]. The latter three ether solvents are included in the solubility analysis.

Available practical partition coefficient data for 2-methylbenzoic acid is then retrieved from the published literature [4,23,24], along with three sets of chromato-graphic retention data [25,26] and the experimental aqueous solubility measurement. The published amended correlation of Abraham and Le [21]

$$(\log C_W)/5 = 0.104 - 0.201R_2 + 0.154\pi_2^H + 0.434\Sigma\alpha_2^H$$
$$+ 0.848\ \Sigma\beta_2^H - 0.672\Sigma\alpha_2^H \cdot \Sigma\beta_2^H - 0.797V_x \qquad (6)$$

and its updated version (unpublished)

$$(\log C_W)/5 = 0.079 - 0.191R_2 + 0.064\pi_2^H + 0.231\Sigma\alpha_2^H$$
$$+ 0.651\Sigma\beta_2^H - 0.157\Sigma\alpha_2^H \cdot \Sigma\beta_2^H - 0.666V_x \qquad (7)$$

are used for the aqueous solubilities. The cross $\Sigma\alpha_2^H \cdot \Sigma\beta_2^H$ term was added to the model to account for hydrogen-bond interactions between the acidic and basic sites in the pure liquid or solid solute. Such interactions are not normally included in partition coefficient correlations as the dissolved solute is surrounded by solvent molecules. In solubility determinations the equilibrium phase may be the pure crystalline solute, in which case, solute–solute interactions become significantly more important. Crystal lattice forces would have to be overcome in dissolving a crystalline material.

Combining the two sets of linear free energy relationships we have a total of 47 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 2-methylbenzoic acid ($V_x = 1.0726$) is calculated from the individual atomic sizes and number of bonds in the molecule [27], and R_2 is estimated as 0.730. The set of 47 equations were then solved using Microsoft "Solver" to yield the values of the four unknown solute descriptors that best described the combined $\log P$ and $\log L$ experimental partitioning data. The final set of molecular descriptors were: $\pi_2^H = 0.840$, $\Sigma\alpha_2^H = 0.420$, $\Sigma\beta_2^H = 0.440$ and $\log L^{(16)} = 4.6770$; and the vapor phase concentration was $\log C = -6.36$. The vapor phase concentration corre-sponds to a gas-to-water partition of $\log L_W = 4.30$, which is in good agreement with the calculated values based upon Eqs. (1) and (2) (the last numerical entry in Table III). Equations (6) and (7) gave aqueous molar solubilities of $(\log C_W)/5 = -0.338$ and $(\log C_W)/5 = -0.367$, which are in good agreement with published experimental value.

The final set of molecular descriptors reproduce the 47 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 0.080 and 0.067 for the 26 calculated and observed $\log P$ values and 21 calculated and observed $\log L$ values, respectively. Calculated values based upon Eqs. (6) and (7) are included in the $\log P$ statistics. Statistically there is no difference between the set of 26 $\log P$ values and the total set of 47 $\log P$

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

			Eq. (1)			Eq. (2)	
Solvent	$\log C_S$	$\log P^{exp}$	$\log P^{calc}$	$\log C_S^{calc}$	$\log L^{exp}$	$\log L^{calc}$	$\log C_S^{calc}$
1-Octanol (wet)		2.270	2.196		6.570	6.519	
Chloroform		1.760	1.756		6.060	6.123	
Toluene		1.230	1.411		5.530	5.720	
Cyclohexane		0.650	0.492		4.950	4.820	
Diethyl ether (wet)		2.050	2.077		6.350	6.370	
Diethyl ether (dry)	0.203	2.263	2.195	0.135	6.563	6.490	0.130
Tetrahydrofuran (dry)	0.456	2.516	2.649	0.589	6.816	6.950	0.590
1,4-Dioxane (dry)	0.427	2.487	2.402	0.342	6.787	6.681	0.321
Ethanol (dry)	0.325	2.385	2.389	0.329	6.685	6.617	0.257
1-Propanol (dry)	0.248	2.308	2.323	0.263	6.608	6.594	0.234
2-Propanol (dry)	0.282	2.342	2.303	0.243	6.642	6.606	0.246
1-Butanol (dry)	0.205	2.265	2.220	0.160	6.565	6.609	0.249
1-Pentanol (dry)	0.172	2.232	2.255	0.195	6.532	6.576	0.216
1-Hexanol (dry)	0.137	2.197	2.226	0.166	6.497	6.537	0.177
1-Heptanol (dry)	0.103	2.163	2.198	0.138	6.460	6.518	0.158
1-Octanol (dry)	0.063	2.123	2.096	0.036	6.423	6.405	0.045
1-Decanol (dry)	0.016	2.076	2.109	0.049	6.376	6.419	0.059
2-Butanol (dry)	0.242	2.302	2.291	0.231	6.602	6.591	0.231
2-Methyl-1-propanol (dry)	0.106	2.166	2.236	0.176	6.466	6.559	0.199
2-Methyl-2-propanol (dry)	0.329	2.389	2.297	0.237	6.689	6.620	0.260
Ethyl acetate (dry)	0.170	2.230	2.214	0.154	6.530	6.537	0.177
HPLC BK-20/10 ($t'_R/10$)		1.658	1.654				
HPLC BK-40/10 ($t'_R/10$)		2.352	2.378				
Thin layer (RM_w)		1.967	2.139				
Gas-to-Water		4.368	4.300		4.395	4.300	

[a]Numerical values of the descriptors used in these calculations are: $R_2 = 0.730$, $\pi_2^H = 0.840$, $\Sigma\alpha_2^H = 0.420$, $\Sigma\beta_2^H = 0.440$, $V_x = 1.0726$ and $\log L^{(16)} = 4.6770$.

and $\log L$ values, thus suggesting that the value of $\log C_G = -6.36$ is a feasible value for 2-methylbenzoic 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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