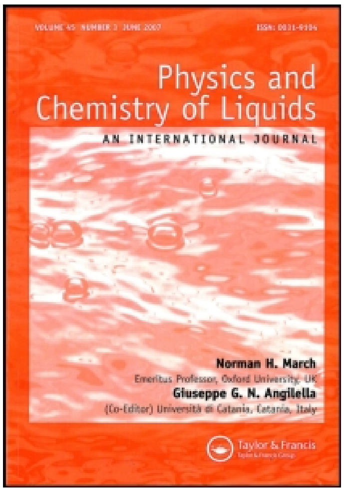

Physics and Chemistry of Liquids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713646857

Thermochemical behavior of dissolved carboxylic acid solutes: part 5 - mathematical correlation of 3,5-dinitrobenzoic acid solubilities with the abraham solvation parameter model

Kaci R. Hoover[a]; Rodrick Coaxum[a]; Eric Pustejovsky[a]; Jr. William E. Acree[a]; Michael H. Abraham[b]
[a] Department of Chemistry, P. O. Box 305070, University of North Texas, Denton, TX 76203-5070, USA
[b] Department of Chemistry, University College London, London, WC1H 0AJ, UK

To cite this Article Hoover, Kaci R. , Coaxum, Rodrick , Pustejovsky, Eric , Acree, William E. Jr. and Abraham, Michael H.(2004) 'Thermochemical behavior of dissolved carboxylic acid solutes: part 5 - mathematical correlation of 3,5-dinitrobenzoic acid solubilities with the abraham solvation parameter model', Physics and Chemistry of Liquids, 42: 5, 457 — 466

To link to this Article: DOI: 10.1080/00319100410001697891

URL: http://dx.doi.org/10.1080/00319100410001697891

Physics and Chemistry of Liquids
Vol. 42, No. 5, October 2004, pp. 457–466

THERMOCHEMICAL BEHAVIOR OF DISSOLVED CARBOXYLIC ACID SOLUTES: PART 5 – MATHEMATICAL CORRELATION OF 3,5-DINITROBENZOIC ACID SOLUBILITIES WITH THE ABRAHAM SOLVATION PARAMETER MODEL

KACI R. HOOVER[a], RODRICK COAXUM[a], ERIC PUSTEJOVSKY[a],
WILLIAM E. ACREE, JR.[a,]* and MICHAEL H. ABRAHAM[b]

[a]*Department of Chemistry, P. O. Box 305070, University of North Texas, Denton, TX 76203-5070, USA;* [b]*Department of Chemistry, University College London, 20 Gordon Street, London, WC1H 0AJ, UK*

(Received 12 January 2004)

In connection with the thermochemical behavior of dissolved carboxylic acid solutes, the Abraham general solvation model is used to calculate the numerical values of the solute descriptors for 3,5-dinitrobenzoic acid from experimental solubilities in organic solvents.

Keywords: 3,5-Dinitrobenzoic acid solubilities; Alcohol solvents; Partition coefficients; Molecular solute descriptors

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

---

*Corresponding author. E-mail: acree@unt.edu

ISSN 0031-9104 print: ISSN 1029-0451 online © 2004 Taylor & Francis Ltd
DOI: 10.1080/00319100410001697891

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 the 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 approach for the analysis and prediction of free energies of partition in chemical and biochemical systems. The method relies on the two linear free energy relationships, one for processes within condensed phases

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

and one for processes involving gas to condensed phase transfer

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

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/polarizability 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 the 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 not sufficient experimental data to even calculate the solute descriptor values. For this reason, solubilities of 3,5-dinitrobenzoic acid were measured in numerous organic solvents of varying polarity and hydrogen-bonding characteristics. 3,5-Dinitrobenzoic 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

3,5-Dinitrobenzoic acid was purchased from commercial source (Aldrich, 99+ %) and was used as received. The purity of the commercial sample was 99.8% (±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 that 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), 3-methyl-1-butanol (Aldrich, 99%, anhydrous), 1-decanol (Alfa Aesar, 99+%), 2-pentanol (Acros, 99+%), 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), and pentyl acetate (Aldrich, 99%) 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 ± 0.1°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 3,5-dinitrobenzoic 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 267 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 $\varepsilon \approx 6855\,\mathrm{L\,mol^{-1}\,cm^{-1}}$ to $\varepsilon \approx 5570\,\mathrm{L\,mol^{-1}\,cm^{-1}}$ for 3,5-dinitrobenzoic acid concentrations from 4.44×10^{-5} M to 2.00×10^{-4} M. Identical molar absorptivities were obtained for select 3,5-dinitrobenzoic 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 the molar mass of 3,5-dinitrobenzoic 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

TABLE I Experimental 3,5-dinitrobenzoic acid mole fraction solubilities, X_S, in select organic solvents at 25°C

Organic solvent	X_S
Ethanol	0.04620
1-Propanol	0.03637
1-Butanol	0.03169
1-Pentanol	0.03153
1-Hexanol	0.02997
1-Heptanol	0.03147
1-Octanol	0.03267
1-Decanol	0.03402
2-Propanol	0.03390
2-Butanol	0.02984
2-Methyl-1-propanol	0.02169
3-Methyl-1-butanol	0.02948
2-Pentanol	0.03308
Diethyl ether	0.02938
Diisopropyl ether	0.009087
Dibutyl ether	0.005787
Tetrahydrofuran	0.1431
1,4-Dioxane	0.08878
Ethyl acetate	0.04892
Butyl acetate	0.03787
Pentyl acetate	0.03088

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 3,5-dinitrobenzoic acid solubilities, X_S, in the 21 organic solvents studied are listed in Table I. Numerical values represent the average of between four and eight independent determinations. Reproducibility ranged from ±1.5% for solvents having the lower mole fraction solubilities to ±2.0% for solvents having the larger 3,5-dinitrobenzoic acid solubilities, where an extra dilution was necessary to keep the measured absorbances within the Beer–Lambert law region.

RESULTS AND DISCCUSION

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

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
Ethyl acetate (dry)	0.358	0.362	−0.449	−0.668	−5.016	4.155
Benzene	0.142	0.464	−0.588	−3.099	−4.625	4.491
(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
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
Ethyl acetate (dry)	0.203	−0.335	1.251	2.949	0.000	0.917
Benzene	0.107	−0.313	1.053	0.457	0.169	1.020
(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).

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

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

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 3,5-dinitrobenzoic acid in water, $\log C_W = -2.417$ [18,19] (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 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 was 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$^\circ$, is available. VP$^\circ$ 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

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

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

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 3,5-dinitrobenzoic acid, we first convert the experimental mole fraction solubilities of 3,5-dinitrobenzoic 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 $V = 131.0\,\text{cm}^3\,\text{mol}^{-1}$ was used for the molar volume of the hypothetical subcooled liquid 3,5-dinitrobenzoic acid. Dibutyl ether was excluded from the solubility analysis because we felt that dimerization of 3,5-dinitrobenzoic 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 3,5-dinitrobenzoic acid have been retrieved from the published literature [18,20–22]. The experimental aqueous solubility measurement is included in the regression analysis. The published literature extended correlation of Abraham and Le [23]

$$\begin{aligned}(\log C_W)/5 = 0.104 - 0.201 R_2 + 0.154\,\pi_2^H + 0.434\Sigma\alpha_2^H + 0.848\Sigma\beta_2^H \\ - 0.672\Sigma\alpha_2^H \cdot \Sigma\beta_2^H - 0.797 V_x\end{aligned} \tag{6}$$

and its updated version (unpublished)

$$\begin{aligned}(\log C_W)/5 = 0.079 - 0.191 R_2 + 0.064\,\pi_2^H + 0.231\Sigma\alpha_2^H + 0.651\Sigma\beta_2^H \\ - 0.157\Sigma\alpha_2^H \cdot \Sigma\beta_2^H - 0.666 V_x\end{aligned} \tag{7}$$

are used for the aqueous solubilities. The cross $\Sigma\alpha_2^{\mathrm{H}} \cdot \Sigma\beta_2^{\mathrm{H}}$ 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 38 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 3,5-dinitrobenzoic acid ($V_x = 1.2801$) is calculated from the individual atomic sizes and number of bonds in the molecule [24] and R_2 is estimated as 1.250. The set of 38 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: $\pi_2^H = 1.630$, $\Sigma\alpha_2^H = 0.700$, $\Sigma\beta_2^H = 0.590$, and $\log L^{(16)} = 6.9837$; and the vapor phase concentration was $\log C_G = -10.717$. The vapor phase concentration corresponds to a gas-to-water partition of $\log L_W = 8.30$, 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 $(\log C_W)/5 = -0.391$ and $(\log C_W)/5 = -0.427$, which are in good agreement with the published experimental value of $\log C_W = -2.417$ [18,19] (corrected for ionization), see above.

The final set of molecular descriptors reproduce the 38 experimental log P and log L values to within an overall standard deviation of 0.100 log units as shown in Table III. Individual standard deviations are 0.091 and 0.114 for the 20 calculated and observed log P values and 18 calculated and observed log L values, respectively. The aqueous solubility predictions are included in the log P statistical information. Statistically there is no difference between the set of 20 log P values and the total set of 38 log P and log L values, thus suggesting that the value of $\log C_G = -10.717$ is a feasible value for 3,5-dinitrobenzoic 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.

Although our descriptors account very well for the experimental data on solubilities and partition coefficients, we have to address the question as to whether the descriptors

TABLE III Comparison between observed and back-calculated partitions and molar solubilities of 3,5-dinitrobenzoic acid based upon Eqs. (1) and (2) and calculated molecular solute descriptors[a]

Solvent	$\log C_S$	*Equation* (1)			*Equation* (2)		
		$\log P^{\text{exp}}$	$\log P^{\text{calc}}$	$\log C_S^{\text{calc}}$	$\log L^{\text{exp}}$	$\log L^{\text{calc}}$	$\log C_S^{\text{calc}}$
1-Octanol (wet)		1.750	1.937		10.050	10.259	
Benzene		0.650	0.614		8.950	8.975	
Diethyl ether (wet)		1.530	1.665		9.830	9.959	
Diethyl ether (dry)	−0.555	1.862	1.775	−0.642	10.163	10.002	−0.715
Tetrahydrofuran (dry)	0.209	2.626	2.649	0.232	10.926	10.933	0.216
1,4-Dioxane (dry)	−0.005	2.412	2.504	−0.087	10.712	10.785	0.068
Ethanol (dry)	−0.128	2.289	2.164	−0.253	10.589	10.316	−0.401
1-Propanol (dry)	−0.326	2.091	2.045	−0.372	10.390	10.297	−0.420
2-Propanol (dry)	−0.366	2.051	2.055	−0.362	10.351	10.327	−0.390
1-Butanol (dry)	−0.469	1.948	1.813	−0.604	10.248	10.255	−0.462
1-Pentanol (dry)	−0.540	1.877	1.849	−0.568	10.177	10.203	−0.514
1-Hexanol (dry)	−0.621	1.796	1.856	−0.561	10.096	10.188	−0.529
1-Heptanol (dry)	−0.653	1.764	1.762	−0.655	10.064	10.077	−0.640
1-Octanol (dry)	−0.683	1.734	1.756	−0.661	10.034	10.014	−0.703
1-Decanol (dry)	−0.746	1.671	1.647	−0.770	9.971	9.984	−0.733
2-Butanol (dry)	−0.496	1.921	1.989	−0.428	10.221	10.270	−0.447
2-Methyl-1-propanol (dry)	−0.655	1.762	1.854	−0.563	10.062	10.154	−0.563
Ethyl acetate (dry)	−0.311	2.106	1.970	−0.447	10.406	10.292	−0.425
Gas-to-water		8.300	8.295		8.300	8.313	

[a] Numerical values of the descriptors used in these calculations are: $R_2 = 1.250$, $\pi_2^H = 1.630$, $\Sigma\alpha_2^H = 0.700$, $\Sigma\beta_2^H = 0.590$, $V_x = 1.2801$, and $\log L^{(16)} = 6.9837$.

TABLE IV Descriptors of select substituted benzoic acids

Substitutent	R_2	π_2^H	$\Sigma\alpha_2^H$	$\Sigma\beta_2^H$	V_x	$\log L^{(16)}$
Hydrogen	0.730	0.900	0.590	0.400	0.9317	4.5100
3-Methyl	0.730	0.890	0.600	0.400	1.0726	4.8187
4-Chloro	0.840	1.020	0.630	0.270	1.0541	4.9474
3-Nitro	0.990	1.180	0.730	0.520	1.1059	5.6011
4-Nitro	0.990	1.520	0.680	0.400	1.1059	5.7699
3,5-Dinitro	1.250	1.630	0.700	0.590	1.2801	6.9837

are simply "fitting parameters" or whether they do indeed reflect the chemical properties of the solute concerned, that is, in the present case 3,5-dinitrobenzoic acid. One way to do this evaluation, is to compare the descriptors for compounds that have been obtained from independent data sets. Then, if our descriptors for a series of substituted benzoic acids, for example, are in accord with general principles, we have confidence that they are not "fitting parameters." In Table IV the Abraham descriptors for a series of benzoic acids are collected, a number of which we have obtained by the methods outlined in this article.

For benzoic acid, 3-nitrobenzoic acid, and 3,5-dinitrobenzoic acid, there are steady increases in the descriptors R_2, π_2^H, $\Sigma\beta_2^H$, V_x, and $\log L^{(16)}$ exactly as expected. The hydrogen-bond acidity of 3,5-dinitrobenzoic acid is a little smaller than expected, however. Introduction of a chloro group decreases the overall basicity because electrons are withdrawn from the aromatic ring. However, each additional nitro group increases the total overall basicity because the extra basicity of the nitro group itself overcomes the ring deactivating effect of the nitro group. In general, our assigned descriptors follow standard chemical principles and are therefore not just fitting parameters to a set of experimental data.

Acknowledgments

This research was supported in part by the University of North Texas Research Council. Kaci Hoover thanks the University of North Texas and the US Department of Education for support provided under the Ronald E. McNair Postbaccalaureate Achievement Program.

References

[1] M.H. Abraham (1993). *Chem. Soc. Rev.*, **23**, 73–83.

[2] M.H. Abraham, G.S. Whiting, W.J. Shuely and R.M. Doherty (1998). *Can. J. Chem.*, **76**, 703–709.

[3] M.H. Abraham, G.S. Whiting, P.W. Carr and H. Ouyang (1998). *J. Chem. Soc., Perkin Trans.*, **2**, 1385–1390.

[4] M.H. Abraham, J.A. Platts, A. Hersey, A.J. Leo and R.W. Taft (1999). *J. Pharm. Sci.*, **88**, 670–679.

[5] M.H. Abraham, J. Andonian-Haftvan, J.P. Osei-Owusu, P. Sakellariou, J.S. Urieta, M.C. Lopez and R. Fuchs (1993). *J. Chem. Soc., Perkin Trans. 2*, 299–304.

[6] M.H. Abraham, F. Martins, R.C. Mitchell and C.J. Salter (1999). *J. Pharm. Sci.*, **88**, 241–247.

[7] M.H. Abraham, J. Le and W.E. Acree, Jr. (1999). *Collect. Czech. Chem. Commun.*, **64**, 1748–1760.

[8] M.H. Abraham, J. Le, W.E. Acree, Jr. and P.W. Carr (1999). *J. Phys. Org. Chem.*, **12**, 675–680.

[9] M.H. Abraham, A.M. Zissimos and W.E. Acree, Jr. (2003). *New J. Chem.*, **27**, 1041–1044.

[10] M.H. Abraham, A.M. Zissimos and W.E. Acree, Jr. (2001). *Phys. Chem. Chem. Phys.*, **3**, 3732–3736.

[11] M.H. Abraham, C.E. Green and W.E. Acree, Jr. (2000). *J. Chem. Soc., Perkin Trans. 2*, **2000**, 281–286.

[12] M.H. Abraham, C.E. Green, W.E. Acree, Jr., C.E. Hernández and L.E. Roy (1998). *J. Chem. Soc., Perkin Trans. 2*, 2677–2681.

[13] C.E. Green, M.H. Abraham, W.E. Acree, Jr., K.M. De Fina and T.L. Sharp (2000). *Pest Manag. Sci.*, **56**, 1043–1053.

[14] M.H. Abraham, N. Benjelloun-Dakhama, J.M.R. Gola, W.E. Acree, Jr., W.S. Cain and J.E. Cometto-Muniz (2000). *New J. Chem.*, **24**, 825–829.

[15] W.E. Acree, Jr. and M.H. Abraham (2002). *J. Solution Chem.*, **31**, 293–303.

[16] A.K. Charlton, C.R. Daniels, W.E. Acree, Jr. and M.H. Abraham (2003). *J. Solution Chem.*, **32**, 1087–1102.

[17] J.S. Fritz and N.M. Lisicki (1951). *Anal. Chem.*, **23**, 589–591.

[18] A. Seidell (1941). *Solubilities of Organic Compounds*, 3rd Edn. Van Nostrand, New York.

[19] J.C. Philip and F.B. Garner (1910). *J. Chem. Soc., Abstracts*, **95**, 1466–1473; *Chemical Abstracts*, **4**, 814.

[20] A.J. Leo (2002). *The Medicinal Chemistry Project*. Pomona College, Claremont, CA 91711, USA.

[21] N. Gulyaeva, A. Zaslavsky, P. Lechner, A. Chait and B. Zaslavsky (2003). *J. Peptide Res.*, **61**, 71–79.

[22] M.T. Bernabei, F. Forni, S. Bellei and R. Cameroni (1980). *Atti della Soc. Natural. Matemat. Modena*, **111**, 63–72.

[23] M.H. Abraham and J. Le (1999). *J. Pharm. Sci.*, **88**, 868–880.

[24] M.H. Abraham and J.C. McGowan (1987). *Chromatographia*, **23**, 243–246.