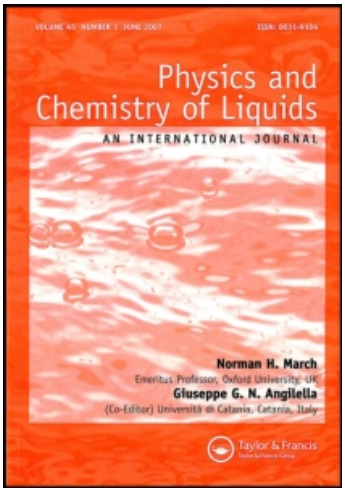

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Mathematical correlation of 4-aminobenzoic acid solubilities in organic solvents with the abraham solvation parameter model

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MATHEMATICAL CORRELATION OF 4-AMINOBENZOIC ACID SOLUBILITIES IN ORGANIC SOLVENTS WITH THE ABRAHAM SOLVATION PARAMETER MODEL

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

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

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

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 1.0750 and calculate V_x as 1.0315, and then solve a total of 26 equations to yield $\pi_2^H = 1.6500$, $\Sigma\alpha_2^H = 0.9400$ and $\Sigma\beta_2^H = 0.6000$. These descriptors reproduce the observed $\log(C_S/C_W)$ values with a standard deviation of only 0.120 log units. The $\log(C_S/C_G)$ correlation could not be used in the present study because of lack of experimental vapor pressure data for 4-aminobenzoic acid at 298.15 K.

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

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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 on the substance's known organic solvent/air partition coefficients. Expressions can also be found in the environmental literature relating to 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 [1–16] is one of the most useful approaches for the analysis and prediction of free energies of partition. The basic model has been applied to numerous chemical and biological systems. For example, predictive equations exist for estimating the nonspecific aquatic toxicity of organic compounds to the fathead minnow (*Pimephales promelas*) [17]

$$-\log \mathrm{LC}_{50} = 0.99 + 0.24 \cdot R_2 + 0.40 \cdot \Sigma\alpha_2^{\mathrm{H}} - 3.65 \cdot \Sigma\beta_2^{\mathrm{H}} + 3.39 \cdot V_x \qquad (1)$$

to the golden orfe (*Leuciscus idus melanotus*) [17]

$$-\log \mathrm{LC}_{50} = 0.15 + 1.40 \cdot R_2 + 1.02 \cdot \Sigma\alpha_2^{\mathrm{H}} - 2.17 \cdot \Sigma\beta_2^{\mathrm{H}} + 2.80 \cdot V_x \qquad (2)$$

and to the guppy (*Poecilia reticulata*) [17]

$$-\log \mathrm{LC}_{50} = 0.71 + 0.60 \cdot R_2 + 0.36 \cdot \Sigma\alpha_2^{\mathrm{H}} - 3.15 \cdot \Sigma\beta_2^{\mathrm{H}} + 3.33 \cdot V_x \qquad (3)$$

where the subscript 2 denotes the solute. The dependent variable in Eqs. (1)–(3), $-\log \mathrm{LC}_{50}$, is the negative logarithm of the lethal molar concentration for killing one-half of that aquatic species after a 96-h exposure to that organic chemical. The independent variables, or descriptors, are solute properties as follows: R_2 and V_x refer to the excess molar refraction and McGowan volume of the solute, respectively, and $\Sigma\alpha_2^{\mathrm{H}}$ and $\Sigma\beta_2^{\mathrm{H}}$ are measures of the solute hydrogen-bond acidity and hydrogen-bond basicity. The Abraham solute dipolarity/polarizability descriptor (denoted as π_2^{H}) and gas phase dimensionless Ostwald partition coefficient into hexadecane at 298 K (denoted as $L^{(16)}$) were not used in the above correlations. Similar equations have been developed for immobilization of the water flea (*Daphnia magna*) [17] and for the inhibition of bioluminescence in prokaryote (*Vibrio fischeri*; the acute Microtox test) [17]. The Abraham solvation parameter model has also been used to estimate

solubilities [11–16,18–20] and partition coefficients [4,7–10] of nonelectrolyte solutes dissolved in organic solvents, chromatographic retention times [1,21], rat blood-brain distribution [22–24], permeation from water through human skin [24,25], nasal pungency threshold [26–28], eye irritation threshold [29,30], plant cuticle uptake [31] and human intestinal absorption [32,33]. Each estimate requires, as input parameters, the numerical values of the solute descriptors for the molecule under consideration.

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 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 acetylsalicyclic 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 4-aminobenzoic acid were measured in numerous organic solvents of varying polarity and hydrogen-bonding characteristics. 4-Aminobenzoic acid is expected to exist almost exclusively in monomeric form in each of the solvents studied. The results of these measurements are interpreted using the Abraham solvation parameter model.

MATERIALS AND METHODS

4-Aminobenzoic acid was purchased from commercial source (Aldrich, 99%) and was used as received. 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+%) and 1,4-dioxane (Aldrich, 99.8%, anhydrous) were stored over molecular sieves and distilled shortly before use. Gas chromatographic analysis showed solvent purities to be 99.7 mol% 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 4-aminobenzoic 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 289 nm on a Bausch and Lomb Spectronic 2000. Concentrations of the dilute solutions were

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

Organic solvent	X_S
Ethanol	0.05062
1-Propanol	0.03316
1-Butanol	0.03139
1-Pentanol	0.02630
1-Hexanol	0.02664
1-Heptanol	0.02277
1-Octanol	0.02088
1-Decanol	0.01736
2-Propanol	0.03218
2-Butanol	0.02808
2-Methyl-1-propanol	0.01751
3-Methyl-1-butanol	0.01989
2-Pentanol	0.02325
1,4-Dioxane	0.06998

determined from a Beer–Lambert law absorbance *versus* concentration working curve for nine standard solutions. The standard solutions ranged in concentration from 2.87×10^{-5} M to 9.57×10^{-5} M. Identical absorbances were obtained for select 4-aminobenzoic acid standard solutions that also contained up to 2 vol% of the neat alcohol solvents.

Experimental molar concentrations were converted to (mass/mass) solubility fractions by multiplying by the molar mass of 4-aminobenzoic 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 the solvent. Experimental 4-aminobenzoic acid solubilities, X_S, in the 14 organic solvents studied are listed in Table I. Numerical values represent the average of between four and eight independent determinations, and were reproducible to within ±1.5%.

RESULTS AND DISCUSSION

The Abraham solvation parameter method relies on two linear free energy relationships, one for processes within condensed phases

$$\log \mathrm{SP} = c + r \cdot R_2 + s \cdot \pi_2^{\mathrm{H}} + a \cdot \Sigma\alpha_2^{\mathrm{H}} + b \cdot \Sigma\beta_2^{\mathrm{H}} + v \cdot V_x \tag{4}$$

and one for processes involving gas to condensed phase transfer

$$\log \mathrm{SP} = c + r \cdot R_2 + s \cdot \pi_2^{\mathrm{H}} + a \cdot \Sigma\alpha_2^{\mathrm{H}} + b \cdot \Sigma\beta_2^{\mathrm{H}} + 1 \cdot \log L^{(16)} \tag{5}$$

where log SP denotes some property of a series of solutes in a fixed phase. 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.

Equation (4) can predict 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. (6)) 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

TABLE II Coefficients in Eq. (4) for various processes[a]

Process/solvent	*c*	*r*	*s*	*a*	*b*	*v*
Water to solvent: Eq. (4)						
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
Isobutanol (wet)	0.249	0.480	−0.639	−0.050	−2.284	2.758
1-Pentanol (wet)	0.175	0.575	−0.787	0.020	−2.837	3.249
Dibutyl ether (wet)	0.252	0.677	−1.506	−0.807	−5.249	4.815
Butyl acetate (wet)	−0.468	0.712	−0.397	0.010	−3.743	3.865
Cyclohexane	0.159	0.784	−1.678	−3.740	−4.929	4.577
Heptane	0.325	0.670	−2.061	−3.317	−4.733	4.543
Benzene	0.142	0.464	−0.588	−3.099	−4.625	4.491
Dichloromethane	0.314	0.001	0.022	−3.238	−4.137	4.259
Chloroform	0.327	0.157	−0.391	−3.191	−3.437	4.191
Carbon tetrachloride	0.260	0.573	−1.254	−3.558	−4.588	4.589
Diethyl ether (dry)	0.330	0.401	−0.814	−0.457	−4.949	4.320
1,4-Dioxane (dry)	0.098	0.350	−0.083	−0.556	−4.826	4.172
Ethanol (dry)	0.208	0.409	−0.959	0.186	−3.645	3.928
1-Propanol (dry)	0.148	0.436	−1.098	0.389	−3.893	4.036
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	0.335	−1.099	0.069	−3.570	3.990
Acetone (dry)	0.335	0.349	−0.231	−0.411	−4.793	3.963
(Gas to water)	−0.994	0.577	2.549	3.813	4.841	−0.869

[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).

in Eq. (4) 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

$$\mathrm{SP} = P = C_S/C_\mathrm{W} \quad \text{or} \quad \log \mathrm{SP} = \log P = \log C_\mathrm{S} - \log C_\mathrm{W} \tag{6}$$

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. (4) will lead to predicted molar solubilities through Eq. (6). 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-aminobenzoic acid in water, $\log C_\mathrm{W} = -1.37$ [34], to convert the predicted partition coefficients to saturation solubilities, which can then be compared to the experimentally determined values.

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. (4) and (5) 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 acetylsalicyclic acid dissolved in 13 alcohols, 4 ethers and ethyl acetate were 0.123 and 0.138 log units. Benzil [15] and acetylsalicyclic acid [16] exhibited solubilities exceeding 1 M in several of the organic solvents studied. In the case of acetylsalicyclic 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 in turn were also in the 1–3 M range. Such arguments do not explain why Eqs. (4) and (5) 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. (5) is used (Equation coefficients are given elsewhere [18–20].). 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 Eqs. (7) and (8), respectively.

$$SP = L_W = C_W/C_G \quad \text{or} \quad \log SP = \log L_W = \log C_W - \log C_G \tag{7}$$

$$SP = L_S = C_S/C_G \quad \text{or} \quad \log SP = \log L_S = \log C_S - \log C_G \tag{8}$$

As before, the computational method will be valid if conditions discussed earlier are met. We are unable to find an experimental vapor pressure for 4-aminobenzoic acid at 298.15 K, or a gas–liquid partition coefficient for 4-aminobenzoic acid in hexadecane in the published literature. The latter value is needed to calculate the numerical value of $\log L^{(16)}$ needed in the Eq. (5) calculations. For the aforementioned reasons our determinations of the numerical values of the solute descriptors of 4-aminobenzoic acid will be based entirely upon Eq. (4) and available solubility and "practical" partition coefficient data.

To determine the solute descriptors for 4-aminobenzoic acid, we first convert the experimental mole fraction solubilities of 4-aminobenzoic acid into molar solubilities

TABLE III Comparison between observed and back-calculated partitions and molar solubilities of 4-aminobenzoic acid based upon Eq. (4) and calculated molecular solute descriptors[a]

Solvent	$\log C_S^{exp}$	$\log P^{exp}$	*Eq. (4)*	
			$\log P^{calc}$	$\log C_s^{calc}$
1-Octanol (wet)		0.830	0.843	
Isobutanol (wet)		0.890	1.138	
1-Pentanol (wet)		0.900	1.163	
Diethyl ether (wet)		0.540	0.434	
Dibutyl ether (wet)		−0.430	−0.446	
Butyl acetate (wet)		1.170	1.393	
Heptane		−3.740	−3.627	
Cyclohexane		−3.410	−3.519	
Benzene		−1.460	−1.385	
Dichloromethane		−0.800	−0.781	
Chloroform		−0.920	−0.888	
Carbon tetrachloride		−2.480	−2.557	
Diethyl ether (dry)	−0.888	0.482	0.442	−0.928
1,4-Dioxane (dry)	−0.096	1.274	1.222	−0.148
Ethanol (dry)	−0.082	1.288	1.105	−0.265
1-Propanol (dry)	−0.360	1.010	0.998	−0.372
2-Propanol (dry)	−0.384	0.986	1.036	−0.334
1-Butanol (dry)	−0.470	0.900	0.671	−0.699
1-Pentanol (dry)	−0.616	0.754	0.696	−0.674
1-Hexanol (dry)	−0.670	0.700	0.673	−0.697
1-Heptanol (dry)	−0.792	0.578	0.520	−0.850
1-Octanol (dry)	−0.877	0.493	0.552	−0.818
1-Decanol (dry)	−1.040	0.330	0.394	−0.976
2-Butanol (dry)	−0.520	0.850	0.909	−0.461
2-Methyl-1-propanol (dry)	−0.724	0.646	0.762	−0.608
Acetone	−0.158	1.212	1.155	−0.215

[a]Numerical values of the descriptors used in these calculations are: $R_2 = 1.075$, $\pi_2^H = 1.650$, $\Sigma\alpha_2^H = 0.940$, $\Sigma\beta_2^H = 0.600$ and $V_x = 1.0315$.

by dividing X_S, by the ideal molar volume of the saturated solution (i.e., $C_S \approx X_S/[X_S V_{Solute} + (1 - X_S)V_{Solvent}]$). A value of $V = 106.49\ cm^3\ mol^{-1}$ was used for the molar volume of the hypothetical subcooled liquid 4-aminobenzoic acid. Available practical partition coefficient data for 4-aminobenzoic acid is then retrieved from the published literature [35,36], along with experimental solubility data [37] for 4-aminobenzoic dissolved in acetone and diethyl ether. Combining the two sets of linear free energy relationships we have a total of 26 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-aminobenzoic acid ($V_x = 1.0315$) is calculated from the individual atomic sizes and number of bonds in the molecule [38] and R_2 is estimated as 1.075. The set of 26 equations were then solved using Microsoft "Solver" to yield the values of the three unknown solute descriptors that best described the combined log P experimental partitioning data. The final set of molecular descriptors were: $\pi_2^H = 1.650$, $\Sigma\alpha_2^H = 0.940$ and $\Sigma\beta_2^H = 0.600$. The final set of molecular descriptors reproduce the 26 experimental log P to within an overall standard deviation of 0.120 log units as shown in Table III. 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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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*, 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, *J. Solution Chem.*, **32**, 1087–1102.
[17] A.D. Gunatillkea and C.F. Poole (1999). *Anal. Commun.*, **36**, 235–242.

[18] C.R. Daniels, A.K. Charlton, R.M. Wold, W.E. Acree, Jr. and M.H. Abraham (2003). *Can. J. Chem.*, **81**, 1492–1501.
[19] R. Coaxum, K.R. Hoover, E. Pustejovsky, D.M. Stovall, W.E. Acree, Jr. and M.H. Abraham (2004). *Phys. Chem. Liq.*, **42**, 313–322.
[20] C.R. Daniels, A.K. Charlton, W.E. Acree, Jr. and M.H. Abraham (2004). *Phys. Chem. Liq.*, **42**, 305–312.
[21] M.H. Abraham, C.F. Poole and S.K. Poole (1999). *J. Chromatogr. A*, **842**, 79–114.
[22] J.A. Platts, M.H. Abraham, Y.H. Zhao, A. Hersey, L. Ijaz and D. Butina (2001). *Eur. J. Med. Chem.*, **36**, 719–730.
[23] M.H. Abraham, H.S. Chadha and R.C. Mitchell (1994). *J. Pharm. Sci.*, **83**, 1257–1268.
[24] M.H. Abraham, H.S. Chadha, F. Martins, R.C. Mitchell and M.W. Bradbury (1999). *Pestic. Sci.*, **55**, 78–88.
[25] M.H. Abraham, F. Martins and R.C. Mitchell (1997). *J. Pharm. Pharmacol.*, **49**, 858–865.
[26] M.H. Abraham, R. Kumarshing, J.E. Cometto-Muniz, W.S. Cain, M. Roses, E. Bosch and M.L. Diaz (1998). *J. Chem. Soc., Perkin Trans. 2*, 2405–2412.
[27] M.H. Abraham, R. Kumarsing, J.E. Cometto-Muniz and W.S. Cain (1998). *Arch. Toxicol.*, **72**, 227–232.
[28] M.H. Abraham, J. Andonian-Haftvan, J.E. Cometto-Muniz and W.S. Cain (1996). *Fundam. Appl. Toxicol.*, **31**, 71–76.
[29] M.H. Abraham, R. Kumarshing, J.E. Cometto-Muniz and W.S. Cain (1998). *Toxicol. in Vitro*, **12**, 403–408.
[30] M.H. Abraham, M. Hassanisandi, M. Jalali-Heravi, T. Ghafourian, W.S. Cain and J.E. Cometto-Muniz (2003). *Toxicol. Sci.*, **76**, 384–391.
[31] J.A. Platts and M.H. Abraham (2000). *Environ. Sci. Technol.*, **34**, 318–323.
[32] M.H. Abraham, Y.H. Zhao, J. Le, A. Hersey, C.N. Luscombe, D.P. Reynolds, G. Beck, B. Sherborne and I. Cooper (2002). *Eur. J. Med. Chem.*, **37**, 595–605.
[33] Y.H. Zhao, J. Le, M.H. Abraham, A. Hersey, P.J. Eddershaw, C.N. Luscombe, D. Boutina, G. Beck, B. Sherborne, I. Cooper and J. Platts (2001). *J. Pharm. Sci.*, **90**, 749–784.
[34] X.Q. Chen, S.J. Cho, Y. Li and S. Venkatesh (2002). *J. Pharm. Sci.*, **91**, 1838–1852.
[35] A.J. Leo (2002). *The Medicinal Chemistry Project*, Pomona College, Claremont, CA 91711, USA.
[36] S. Okada, H. Nakahara, C. Yomota and K. Mochida (1985). *Chem. Pharm. Bull.*, **33**, 4916–4922.
[37] J. Barra, M.-A. Pena and P. Bustamante (2000). *Eur. J. Pharm. Sci.*, **10**, 153–161.
[38] M.H. Abraham and J.C. McGowan (1987). *Chromatographia*, **23**, 243–246.