Solubility of Crystalline Nonelectrolyte Solutes in Organic Solvents: Mathematical Correlation of Benzil Solubilities with the Abraham General Solvation Model

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

$$\log(C_S/C_W) = c + r \cdot R_2 + s \cdot \sum \frac{H}{2} + a \cdot \sum \frac{H}{2} + b \cdot \sum \frac{H}{2} + v \cdot V_x$$
$$\log(C_S/C_G) = c + r \cdot R_2 + s \cdot \sum \frac{H}{2} + a \cdot \sum \frac{H}{2} + b \cdot \sum \frac{H}{2} + l \cdot \log L^{[16]}$$

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 the McGowan volume of the solute, $\sum \frac{H}{2}$ and $\sum \frac{H}{2}$ are measures of the solute hydrogen-bond acidity and basicity, $\sum \frac{H}{2}$ denotes the solute dipolarity/polarizability descriptor, and $L^{[16]}$ is the solute gas-phase dimensionless Ostwald partition coefficient into hexadecane at 25°C. 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 14.45 cm³·mol⁻¹ and calculate V_x as 163.74 cm³·mol⁻¹, and then solve a total of 51 equations to yield $\sum \frac{H}{2} = 1.59$, $\sum \frac{H}{2} = 0.620$ and $\log L^{[16]} = 7.6112$. These descriptors reproduce the 51 observed $\log(C_S/C_W)$ and $\log(C_S/C_G)$ values with a standard deviation of only 0.115 log units.

KEY WORDS: Benzil solubilities; organic solvents; partition coefficients.

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1. INTRODUCTION

The Gibbs free energy of solvation is an important thermodynamic variable that quantifies the Gibbs energy difference between a molecule in the gas phase and the molecule dissolved in a solvent. Free energies of solvation 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 distribution of a solute between two immiscible liquid phases. For example, the octanol/water partition coefficient is obtained from free energy of solvation of the solute molecule in wet 1-octanol minus its free energy of solvation in water. Solvation-free energies and partition coefficients are of critical importance in many pharmaceutical, environmental, and chemical engineering applications. Solute partitioning between two immiscible phases is the basis for all chromatographic separations.

Historically, many of the very early studies focused exclusively on developing correlational equations based upon octanol/water partition coefficients. As additional experimental data became available, researchers expanded their studies to include more organic solvents, as well as aqueous micellar solvent media. In this regard, Abraham and co-workers⁽¹⁻⁸⁾ developed expressions for describing the partition of solutes between water and an organic solvent and between the gas phase and a given solvent. To date, mathematical expressions have been deduced for approximately 40 dry solvents. The derived mathematical expressions allow one to predict the partitioning and solubility behavior of organic and organometallic solutes, provided that one knows the numerical values of the various solute descriptors.

Earlier papers⁽⁹⁻¹²⁾ developed the computational methodology for determining solute descriptors from measured solubility data for crystalline nonelectrolyte solutes dissolved in organic solvents for which the equation coefficients were known. In the present communication, we extend our earlier studies to include benzil. Experimental solubilities have been measured for benzil dissolved in 19 different organic solvents of varying polarity and hydrogen-bonding characteristics. Results of these measurements, combined with published solubility literature data⁽¹³⁻¹⁵⁾ and unpublished chromatographic data, are used to calculate numerical values of the solute descriptors for benzil. Once the solute descriptors are determined, the remaining benzil solubility data can be used to develop even more gas/liquid and water/organic solvent partition correlations based upon the Abraham general solvation model. For example, measured benzil solubilities in diethyl ether, dimethyl sulfoxide, 2,2,2-trifluoroethanol, and 2-methyl-2-propanol are currently being used to develop correlation equations for these four solvents. The derived correlation equations will be published in a subsequent paper.

Development of a single correlation equation requires experimental data for at least 50 or so different solutes. It is important that the data set contain solutes

that span as wide a range of solute descriptors as possible. In the case of volatile solutes, partition coefficients can be measured directly as the solute gas–liquid chromatographic retention volumes on the given organic solvent stationary phase, or can be calculated from infinite-dilution activity coefficients. This latter information is available in the published literature in the form of binary liquid–vapor equilibrium data. Solubility measurements provide a very convenient means for including nonvolatile solutes in the regression analysis. Here, the partition coefficient is calculated as the ratio of the solute molar solubility in the organic solvent under consideration and water (or saturated vapor concentration in the case of the gas/liquid partition).

2. MATERIALS AND METHODS

Benzil (Aldrich, 97%) was recrystallized three times from anhydrous methanol before use. *n*-Decane (TCI, 99+%), *n*-hexadecane (Aldrich, 99%), 2-methyl-1-pentanol (Aldrich, 99%), 1-decanol (Alfa Aesar, 99+%), 2-methyl-2-propanol (Arco Chemical Company, 99+%), 3,7-dimethyl-1-octanol (Aldrich, 99%), methyl acetate (Aldrich, 99.5%, anhydrous), chlorobenzene (Aldrich, 99.8%, anhydrous), 1-butanenitrile (Aldrich, 99+%), 1-propanenitrile (Aldrich, 99%), 2-propanone (Aldrich, 99.9+%, HPLC), 2-butanone (Aldrich, 99.5+%, HPLC), propylene carbonate (Aldrich, 99.7%, anhydrous), 2,2,2-trifluoroethanol (Aldrich, 99+%), diethyl ether (Aldrich, 99+%, anhydrous), diisopropyl ether (Aldrich, 99%, anhydrous), cyclohexanone (Aldrich, 99.8%), dimethyl sulfoxide (Aldrich, 99.8%, anhydrous) and acetonitrile (Aldrich, 99.8%, anhydrous) were stored over molecular sieves and distilled shortly before use. Gas chromatographic analysis showed solvent purities to be 99.7 mole % 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 3 days (often longer) with periodic agitation. After equilibration, the samples stood unagitated for 1 day in the constant-temperature bath to allow any finely dispersed solid particles to settle. Attainment of equilibrium was verified both by repetitive measurements after several additional days and by approaching equilibrium from supersaturation by pre-equilibrating the solutions at a higher temperature. Aliquots of saturated benzil solutions were transferred through a coarse filter into a tared volumetric flask to determine the amount of sample and then diluted quantitatively with 2-propanol for spectrophotometric analysis at 390 nm on a Bausch and Lomb Spectronic 2000 instrument. Concentrations of the dilute solutions were determined from a Beer–Lambert law absorbance vs. concentration working curve for nine standard solutions. The concentration of benzil in the standard solutions varied from $4.30 \times 10^{-3} \text{ M}$ to $2.15 \times 10^{-2} \text{ M}$. The calculated molar absorptivity of $\varepsilon \approx 65.8 \text{ L}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$ was constant over the concentration range studied.

Table I. Experimental Benzil Mole Fraction Solubilities in Selected Organic Solvents at 25.0°C

Organic solvent	X_s^{sat}
Decane	0.00855
Hexadecane	0.0118
Chlorobenzene	0.201
Diethyl ether	0.0674
Diisopropyl ether	0.0309
Methyl acetate	0.152
2-Propanone	0.160
2-Butanone	0.184
Cyclohexanone	0.241
2-Methyl-2-propanol	0.0106
2-Methyl-1-pentanol	0.0139
1-Decanol	0.0212
3,7-Dimethyl-1-octanol	0.0173
Acetonitrile	0.0635
1-Propanenitrile	0.129
1-Butanenitrile	0.151
Propylene carbonate	0.0940
Dimethyl sulfoxide	0.0228
2,2,2-Trifluoroethanol	0.0352

Experimental molar concentrations were converted to solubility mass fractions by multiplying by the molar mass of benzil, volume(s) of volumetric flask(s) used and any dilutions required to place the measured absorbances on the Beer–Lambert law absorbance vs. 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 benzil mole-fraction solubilities X_s^{sat} in the 19 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 with lower solute solubilities to $\pm 2.5\%$ for solvents having the larger solute solubilities, where an extra dilution was necessary to keep the measured absorbances within the Beer–Lambert law region.

3. RESULTS AND DISCUSSION

The Abraham general solvation model is based upon two particular linear free-energy relationships for describing the partition of solutes between water and a given solvent^(1–8)

$$\log P = c + r \cdot R_2 + s \cdot \frac{H}{2} + a \cdot \sum \frac{H}{2} + b \cdot \sum \frac{H}{2} + v \cdot V_x \quad (1)$$

and between the gas phase and a given solvent⁽¹⁶⁾

$$\log L = c + r \cdot R_2 + s \cdot \sum \frac{H}{2} + a \cdot \sum \frac{H}{2} + b \cdot \sum \frac{H}{2} + l \cdot \log L \quad (2)$$

The dependent variables in Eqs. (1, 2) are $\log P$ (the logarithm of the partition coefficient of solute between water and a given solvent) and $\log L$ (logarithm of the Ostwald solubility coefficient). The independent variables are the solute descriptors as follows: R_2 and V_x denote the excess molar refraction and McGowan volume of the solute, respectively, $\sum \frac{H}{2}$ and $\sum \frac{H}{2}$ are measures of the solute hydrogen-bond acidity and basicity, $\sum \frac{H}{2}$ denotes the solute dipolarity/polarizability descriptor, and $L^{[16]}$ is the solute gas-phase dimensionless Ostwald partition coefficient into hexadecane at 25°C. The Ostwald partition coefficient L is the inverse of the Henry's law constant ($\text{Pa} \cdot \text{m}^3 \cdot \text{mole}^{-1}$). It should be noted that the various coefficients c , r , s , a , b , v , and l depend on the solvent phase under consideration. The coefficient r gives the tendency of the phase to interact with solutes through polarizability-type interactions, mostly *via* electron pairs. The coefficient s is a measure of the solvent phase dipolarity/polarity, while the a and b coefficients represent the solvent phase hydrogen-bond basicity and acidity, respectively. Coefficients l and v are combination of the work needed to create a solvent cavity in which the solute will reside, and the general dispersion interaction energy between the solute and solvent phase. In the case of partition coefficients, where two solvent phases are involved, coefficients the c , r , s , a , b , v , and l represent differences in the solvent phase properties.

Equation (1) actually predicts partition coefficients, and for selected 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. 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 determination of solute descriptors 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 become available. Note that many of

Table II. Coefficients in Eqs. (1, 2) for Various Processes^a

Process/solvent	<i>c</i>	<i>r</i> ^b	<i>s</i>	<i>a</i>	<i>b</i>	<i>v</i> / <i>I</i> ^c
Water to solvent: Eq. (1)						
1-Octanol (Wet)	0.088	0.562	-1.054	0.034	-3.460	3.814
Hexane	0.361	0.579	-1.723	-3.599	-4.764	4.344
Heptane	0.325	0.670	-2.061	-3.317	-4.733	4.543
Octane	0.223	0.642	-1.647	-3.480	-5.067	4.526
Nonane	0.240	0.619	-1.713	-3.532	-4.921	4.482
Decane	0.160	0.585	-1.734	-3.435	-5.078	4.582
Hexadecane	0.087	0.667	-1.617	-3.587	-4.869	4.433
2,2,4-Trimethylpentane	0.288	0.382	-1.668	-3.639	-5.000	4.561
Cyclohexane	0.159	0.784	-1.678	-3.740	-4.929	4.577
Chlorobenzene	0.040	0.246	-0.462	-3.038	-4.769	4.640
Tetrachloromethane	0.260	0.573	-1.254	-3.558	-4.588	4.589
Dibutyl ether (dry)	0.203	0.369	-0.954	-1.488	-5.426	4.508
Acetonitrile (dry)	0.413	0.077	0.326	-1.566	-4.391	3.364
Benzene	0.142	0.464	-0.588	-3.099	-4.625	4.491
Toluene	0.143	0.527	-0.720	-3.010	-4.824	4.545
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
(Gas to water)	-0.994	0.577	2.549	3.813	4.841	-0.869
Gas to solvent: Eq. (2)						
1-Octanol (Wet)	-0.198	0.002	0.709	3.519	1.429	0.858
Hexane	0.292	-0.169	0.000	0.000	0.000	0.979
Heptane	0.275	-0.162	0.000	0.000	0.000	0.983
Octane	0.215	-0.049	0.000	0.000	0.000	0.967
Nonane	0.200	-0.145	0.000	0.000	0.000	0.980
Decane	0.156	-0.143	0.000	0.000	0.000	0.989
Hexadecane	0.000	0.000	0.000	0.000	0.000	1.000
2,2,4-Trimethylpentane	0.275	-0.244	0.000	0.000	0.000	0.972
Cyclohexane	0.163	-0.110	0.000	0.000	0.000	1.013
Chlorobenzene	0.053	-0.553	1.254	0.364	0.000	1.041
Tetrachloromethane	0.282	-0.303	0.460	0.000	0.000	1.047
Acetonitrile	-0.007	-0.595	2.461	2.085	0.418	0.738
Benzene	0.107	-0.313	1.053	0.457	0.169	1.020
Toluene	0.121	-0.222	0.938	0.467	0.099	1.012
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

Table II. (Continued)

Process/solvent	<i>c</i>	<i>r</i> ^b	<i>s</i>	<i>a</i>	<i>b</i>	<i>v</i> / <i>t</i> ^c
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
SPB-5 (120°C)	-2.620	0.000	0.293	0.212	0.000	0.504
SPB-5 (140°C)	-2.620	0.000	0.278	0.177	0.000	0.453
(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).

^bConsistent with R_2 in units of 10^{-1} -cm³-mol⁻¹.

^cCoefficient of V_x in processes A and coefficient of $\log L$ ^[16] in processes B; units consistent with V_x in units of 10^{-2} cm³-mol⁻¹.

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 can be obtained from

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

the molar solubility of the solid in water, C_W , and in the solvent, C_S , provided that three specific conditions are met. First, the same solid phase must be in equilibrium with the saturated 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 must refer to the solubility of the neutral form. We use the solubility of benzil in water, $\log C_W = -4.05$ ⁽¹⁶⁾, together with the available solubilities in a variety of nonaqueous organic solvents⁽¹³⁻¹⁵⁾ to deduce $\log P$ values for the partition of benzil from water to the solvents (see Table III). There is also one direct experimental octanol/water value, $\log P = 3.38$, in the MedChem data base.⁽¹⁸⁾

For partition of solutes between the gas phase and solvents, Eq. (2) is used. Solubilities can also be used to calculate $\log L$ values, provided that the solid saturated vapor pressure P_{vap}^o at 25°C is available. P_{vap}^o can be transformed into the gas-phase concentration, C_G , and the gas-water and gas-solvent partitions, L_W

Table III. Comparison Between Observed and Back-Calculated Partitions and Molar Solubilities of Benzil Based Upon Eqs. (1, 2)

Solvent	Log C_S	Log P^{exp}	Eq. (1)		Log L^{exp}	Eq. (2)	
			Log P^{calc}	Log C_S^{calc}		Log L^{calc}	Log C_S^{calc}
1-Octanol (wet)		3.38	3.32		8.25	8.35	
Hexane	-1.36	2.69	2.62	-1.43	7.56	7.50	-1.42
Heptane	-1.35	2.70	2.52	-1.53	7.57	7.52	-1.40
Octane	-1.35	2.70	2.80	-1.25	7.57	7.50	-1.42
Nonane	-1.35	2.70	2.70	-1.35	7.57	7.45	-1.47
Decane	-1.36	2.69	2.60	-1.45	7.56	7.48	-1.44
Hexadecane	-1.39	2.66	2.72	-1.33	7.53	7.61	-1.31
Isooctane	-1.45	2.60	2.60	-1.45	7.47	7.32	-1.60
Cyclohexane	-1.01	3.04	3.04	-1.01	7.91	7.71	-1.21
Chlorobenzene	0.23	4.28	4.28	0.23	9.12	9.17	0.25
Tetrachloromethane	-0.11	3.94	3.94	-0.11	8.81	8.55	-0.37
Dibutyl ether (dry)	-0.71	3.34	3.24	-0.81			
Acetonitrile (dry)	0.02	4.07	3.83	-0.22	8.94	8.92	0.00
Benzene	0.23	4.28	4.36	0.31	9.15	9.20	0.20
Toluene	0.10	4.15	4.21	0.16	8.97	9.06	0.14
Methanol (dry)	-0.73	3.32	3.34	-0.71	8.19	8.29	-0.63
Ethanol (dry)	-0.76	3.29	3.45	-0.60	8.16	8.27	-0.65
1-Propanol (dry)	-0.81	3.24	3.23	-0.82	8.11	8.00	-0.92
2-Propanol (dry)	-0.97	3.08	3.19	-0.86	7.95	8.01	-0.91
1-Butanol (dry)	-0.85	3.20	3.23	-0.82	8.07	8.15	-0.77
1-Pentanol (dry)	-0.86	3.19	3.24	-0.81	8.06	8.10	-0.82
1-Hexanol (dry)	-0.91	3.14	3.33	-0.72	8.01	8.11	-0.81
1-Heptanol (dry)	-0.94	3.11	3.34	-0.81	7.98	8.17	-0.75
1-Octanol (dry)	-0.97	3.08	3.29	-0.76	7.95	8.06	-0.86
1-Decanol (dry)	-0.96	3.09	3.22	-0.83	7.96	8.01	-0.91
SPB-5 (120°C)					1.672	1.682	
SPB-5 (140°C)					1.272	1.260	

and L_S , can be obtained through Eqs. (4, 5), respectively

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

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

As before, the computational method will be valid if conditions discussed above are met. Aihara⁽¹⁷⁾ reported the vapor pressure of benzil as a function of temperature. From his correlation equation

$$\log P_{\text{vap}}^{\circ} = 12.708 - 5140.8/T \quad (6)$$

a value of $P_{\text{vap}}^{\circ} = 2.92 \times 10^{-5}$ mm Hg is calculated, which corresponds to a vapor phase concentration of $\log C_G = -8.80$.

Combining the two sets of linear free-energy relations, we have a total of 49 equations for which the partition data and equation coefficients are available. Gas-liquid chromatographic (GLC) retention data exist for benzil on an SPB-5 stationary phase at both 120°C ($\log L = 1.672$) and 140°C ($\log L = 1.272$).⁽¹⁹⁾ The chromatographic data provide two additional equations. The characteristic McGowan volume of benzil is 163.74 cm³·mol⁻¹ and R_2 is estimated as 14.45 cm³·mol⁻¹. $\sum \frac{H}{2}$ is set equal to zero, as would be the case for a solute that has no hydrogen-bond acidity. The set of 51 equations can be solved to yield the values of the three unknown solute descriptors, $\frac{H}{2}$, $\sum \frac{H}{2}$, and $\log L^{[16]}$ that best reproduce the dependent variables. A preliminary analysis showed that it was possible to reproduce the 49 dependent variables based upon the solubilities with an overall standard deviation of 0.14 log units. By making a very small adjustment to the $\log C_G$ value, $\log C_G = -8.92$, gives exact agreement with the GLC data. We prefer to include the GLC data because this gives a direct connection to the gas-phase $\log L$ values. The Abraham general solvation model provides a quantitative connection between solubility in nonaqueous solvents and GLC retention data. There is no other model, to our knowledge, that includes such diverse systems. All $\log L$ partitions were recalculated using $\log C_G = -8.92$, and the resulting 51 equations were solved to yield the three solute descriptors $\frac{H}{2} = 1.59$, $\sum \frac{H}{2} = 0.620$, and $\log L^{[16]} = 7.6112$. These numerical results enabled the experimental $\log P$ and $\log L$ partitions to be back-calculated to within an overall standard deviation of 0.115 log units. The calculated values of $\log P$, $\log L$ and $\log C_S$ are given in Table III. The individual standard deviations are 0.124 and 0.109 for the 25 calculated and observed $\log P$ values and 26 calculated and observed $\log L$ values, respectively. Statistically there is no difference between the set of 25 $\log P$ values and the total set of 51 $\log P$ and $\log L$ values, thus suggesting that the $\log C_G = -8.92$ is a feasible value for benzil. Whether or not the assumed value is in accord with present or 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).

Readers will note that while we have applied the Abraham general solvation model to a mathematical description of the solubility of benzil in organic solvents, the computational methodology can be applied to drug molecules and other molecules of pharmaceutical interest. The methodology requires experimental solubility data for the drug molecule in water and in about a dozen or so solvents for which equation coefficients are known. The solute descriptors, after they have been calculated, can be used to predict the solute solubility in any of the organic solvents for which equation coefficients are known. The computational process can be reversed. The Abraham general solvation model can also be used to screen experimental data sets for possible outlier data points in need of remeasurement and to estimate a number of physicochemical and biological

properties of pharmaceutical importance. For example, outlier data points would be identified by large differences between experimental and calculated values. In the case of benzil we can now estimate the blood–brain distribution,^(20,21) permeation from water through human skin,⁽²²⁾ nasal pungency threshold,^(23,24) eye irritation threshold,⁽²⁵⁾ aqueous narcosis,⁽²⁶⁾ and plant cuticle uptake⁽²⁷⁾ through previously derived correlations. Each estimation requires as input parameters the numerical values of the benzil solute descriptors.

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