

Solubility in Binary Solvent Systems III: Predictive Expressions Based on Molecular Surface Areas

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Abstract □ The nearly ideal binary solvent model, which has led to successful predictive equations for the partial molar Gibbs free energy of the solute in binary solvent mixtures, was extended to include molecular surface areas as weighting factors. Two additional expressions were derived and compared to previously developed equations (based on molar volumes as weighting factors) for their ability to predict anthracene and naphthalene solubilities in mixed solvents from measurements in the pure solvents. The most successful equation in terms of goodness of fit involved a surface fraction average of the excess Gibbs free energy relative to Raoult's law and predicted experimental solubilities in 25 systems with an average deviation of 1.7% and a maximum deviation of 7.5%. Two expressions approximating weighting factors with molar volumes provided accurate predictions in many of the systems studied but failed in their ability to predict anthracene solubilities in solvent mixtures containing benzene.

Keyphrases □ Binary solvents—solubility, predictive expressions based on molecular surface areas □ Solubility—binary solvent systems, predictive expressions based on molecular surface areas □ Molecular surface area—solubility in binary solvent systems □ Anthracene—prediction of solubility in binary solvent systems based on molecular surface areas □ Naphthalene—prediction of solubility in binary solvent systems based on molecular surface areas

The use of binary solvents for influencing solubility and multiphase partitioning has many potential applications in the pharmaceutical industry. However, maximum realization of these applications depends on the development of equations that enable *a priori* prediction of solution behavior in mixed solvents from a minimum number of additional observations. Ideally, the ability to predict a drug molecule's solubility and partition coefficients based solely on a consideration of molecular structure is desired,

but for more practical applications, a less fundamental approach must often suffice.

The nearly ideal binary solvent (NIBS) approach developed previously (1–6) provides a relatively simple method for estimating the excess partial molar properties of a solute, \bar{Z}_3^{ex} , at infinite dilution in a binary solvent (components 1 and 2):

$$\bar{Z}_3^{\text{ex}} = f_1^0(\bar{Z}_3^{\text{ex}})_1 + f_2^0(\bar{Z}_3^{\text{ex}})_2 - \Gamma_3(X_1^0\Gamma_1 + X_2^0\Gamma_2)^{-1}\bar{Z}_{12}^{\text{ex}} \quad (\text{Eq. 1})$$

$$f_1^0 = 1 - f_2^0 = X_1^0\Gamma_1/(X_1^0\Gamma_1 + X_2^0\Gamma_2) \quad (\text{Eq. 2})$$

in terms of a weighted mole fraction average of the properties of the solute in the two pure solvents [$(\bar{Z}_3^{\text{ex}})_1$ and $(\bar{Z}_3^{\text{ex}})_2$] and a contribution due to the unmixing of the solvent pair by the presence of the solute. This equation leads to accurate predictions of solubilities (3, 5–8), gas–liquid partition coefficients (4, 9), and enthalpies of solution (1, 2) in systems of nonspecific interactions when the weighting factors (Γ_i) are approximated with molar volumes.

A simpler approximation of equating all three weighting factors provides considerably poorer predictions for systems in which the molar volumes of the components differ appreciably. The superiority of expressions based on molar volumes suggests that the relative sizes of the molecules are an important consideration. The use of surface areas as weighting factors may be revealing, since surface area often represents a different measure of molecular size.

Experimental solubilities of naphthalene (10–12) and *p*-dibromobenzene (13) are available in the literature for several binary solvent mixtures and can be used to compare the various approximations for weighting factors. However, these systems encompass a narrow two-fold range of mole fraction solubilities. The applicability of Eq. 1 is not very sensitive to errors in the relative magnitude of the weighting factors whenever the solubility of the solute is identical (or nearly identical) in both the pure solvents, but these errors become much more significant as the range of solubilities increases. For this reason, anthracene solubilities were determined in several mixtures containing benzene, which cover up to a sixfold range.

During the course of this investigation, it was noted that the NIBS model predicted a slight maximum solubility in binary solutions of cyclohexane and *n*-heptane. Such synergistic effects in simple systems are usually explained by solubility parameter theory in terms of the solubility parameter of the solute being bracketed by the solubility parameters of the two pure solvents (14, 15). However, the solubility parameter of anthracene ($\delta = 9.9$) is far greater than either the solubility parameters of cyclohexane ($\delta = 8.2$) or *n*-heptane ($\delta = 7.4$). Solubility determinations of anthracene in this binary solvent mixture will provide an additional test of the basic NIBS model.

EXPERIMENTAL

Anthracene¹ was used as received. Cyclohexane², *n*-heptane³, isooctane³, *n*-octane⁴, cyclooctane⁴, *n*-hexane⁴, and benzene⁵ were stored over molecular sieves⁶. Binary solvent mixtures were prepared by weight so that compositions could be calculated to a mole fraction of 0.0001.

Excess solute and solvent were placed in amber glass bottles and allowed to equilibrate in a constant-temperature bath at 25.0° for several days. The attainment of equilibrium was verified by repetitive measurements after several additional days and in some cases by approaching equilibrium from supersaturation by pre-equilibrating the solution at a higher temperature. Aliquots of saturated anthracene solutions were transferred through a coarse filter into a tared volumetric flask to determine the amount of sample and diluted quantitatively with methanol. Concentrations were determined spectrophotometrically⁷ at 356 nm. Experimental solubilities of anthracene in several binary solvent mixtures are given in Table I, with the measurements being reproducible to within $\pm 1\%$.

RESULTS AND DISCUSSION

The following three equations have been derived previously for solubility in binary solvent systems containing only nonspecific interactions:

$$RT \ln(a_3^{\text{solid}}/X_3^{\text{sat}}) = (1 - X_3^{\text{sat}})^2 [X_1^0(\bar{G}_3^{\text{ex}})_1 + X_2^0(\bar{G}_3^{\text{ex}})_2 - \bar{G}_{12}^{\text{ex}}] \quad (\text{Eq. 3})$$

$$RT \ln(a_3^{\text{solid}}/X_3^{\text{sat}}) = (1 - \phi_3^{\text{sat}})^2 [\phi_1^0(\bar{G}_3^{\text{ex}})_1 + \phi_2^0(\bar{G}_3^{\text{ex}})_2 - V_3(X_1^0V_1 + X_2^0V_2)^{-1} \bar{G}_{12}^{\text{ex}}] \quad (\text{Eq. 4})$$

and:

$$RT \left[\ln(a_3^{\text{solid}}/\phi_3^{\text{sat}}) - (1 - \phi_3^{\text{sat}}) \left(1 - \frac{V_3}{(X_1^0V_1 + X_2^0V_2)} \right) \right] = (1 - \phi_3^{\text{sat}})^2 [\phi_1^0(\bar{G}_3^{\text{ex}})_1 + \phi_2^0(\bar{G}_3^{\text{ex}})_2 - V_3(X_1^0V_1 + X_2^0V_2)^{-1} \bar{G}_{12}^{\text{ex}}] \quad (\text{Eq. 5})$$

in which V_i is the molar volume of a pure liquid, X_i is mole fraction, ϕ_i is volume fraction, \bar{G}_{12}^{ex} is the molar excess Gibbs free energy of the binary solvent relative to Raoult's law, and:

$$\bar{G}_{12}^{\text{ex}} = \bar{G}_{12}^{\text{ex}} + RT[\ln(X_1^0V_1 + X_2^0V_2) - X_1^0 \ln V_1 - X_2^0 \ln V_2] \quad (\text{Eq. 6})$$

Table I—Solubility of Anthracene in Several Binary Solvents at 25.0°

Solvent (1)	+	Solvent (2)	X_1^0	X_3^{Sat}
<i>n</i> -Hexane	+	Cyclohexane	0.0000	0.001574
			0.1735	0.001572
			0.3565	0.001544
			0.4498	0.001515
			0.5571	0.001478
			0.7646	0.001398
<i>n</i> -Octane	+	Cyclohexane	1.0000	0.001290
			0.0000	0.001574
			0.1463	0.001648
			0.3114	0.001717
			0.3954	0.001749
			0.5519	0.001774
Cyclooctane	+	Cyclohexane	0.7930	0.001832
			1.0000	0.001850
			0.0000	0.001574
			0.1746	0.001704
			0.3412	0.001824
			0.4475	0.001882
<i>n</i> -Heptane	+	Cyclohexane	0.5533	0.001989
			0.7580	0.002096
			1.0000	0.002258
			0.0000	0.001574
			0.1542	0.001608
			0.3283	0.001642
Isooctane	+	Cyclohexane	0.4230	0.001640
			0.5250	0.001621
			0.7236	0.001605
			1.0000	0.001571
			0.0000	0.001574
			0.1385	0.001488
<i>n</i> -Hexane	+	Benzene	0.2988	0.001407
			0.3895	0.001362
			0.5391	0.001283
			0.7725	0.001182
			1.0000	0.001087
			0.0000	0.007418
Benzene	+	<i>n</i> -Heptane	0.1442	0.006274
			0.3093	0.004908
			0.3842	0.004317
			0.4963	0.003549
			0.7365	0.002242
			1.0000	0.001290
Benzene	+	Cyclohexane	0.0000	0.001571
			0.2323	0.002283
			0.4637	0.003375
			0.5546	0.003922
			0.7103	0.005022
			0.8280	0.005987
Benzene	+	Cyclohexane	1.0000	0.007418
			0.0000	0.001574
			0.2320	0.002592
			0.4380	0.003802
			0.5427	0.004506
			0.6357	0.005154
Cyclooctane	+	Benzene	0.8317	0.006482
			1.0000	0.007418
			0.0000	0.007418
			0.1416	0.006814
			0.3045	0.005708
			0.3984	0.005282
Benzene	+	Isooctane	0.4935	0.004745
			0.6685	0.003740
			1.0000	0.002258
			0.0000	0.001087
			0.3127	0.001983
			0.5398	0.003144
Benzene	+	Cyclohexane	0.6354	0.003830
			0.7209	0.004571
			0.8591	0.005840
			1.0000	0.007418
			0.0000	0.001574
			0.1746	0.001704

Numerical values of \bar{G}_{12}^{ex} can be found in the chemical literature for many common binary systems. For example, the thermodynamic excess properties of several hundred binary systems have been listed (16). The superscript (0) indicates that the solvent composition is calculated as if the solute were not present. The activity of the solid solute (a_3^{solid}), relative to the supercooled liquid, can be calculated by:

$$\ln a_3^{\text{solid}} = -\frac{\Delta H_3^{\text{fus}}(T_m - T)}{R T_m T} + \frac{\Delta C_p(T_m - T)}{RT} - \frac{\Delta C_p}{R} \ln(T_m/T) \quad (\text{Eq. 7})$$

¹ Aldrich 99.9%.

² Phillips 99.5 weight percent.

³ Phillips 99 mole percent.

⁴ Aldrich Chemical Co.

⁵ Fischer Scientific Co.

⁶ Linde Type 4A.

⁷ Cary 118 Spectrophotometer.

Table II—Comparison of Predictive Equations for the Solubilities of Naphthalene, *p*-Dibromobenzene, and Anthracene in Various Binary Solvent Mixtures at 25°

Solute	Solvent System	Data Ref.	RMS Deviations ^a (%) for the Predictive Equations					\bar{G}_{12}^{ex} Ref.
			3	4	5	8	9	
Naphthalene	Benzene + Cyclohexane	10	-1.4	-1.2	-1.1	+0.4	+0.6	41
Naphthalene	Benzene + <i>n</i> -Hexane	10	+2.3	1.4	1.4	+1.9	+2.2	42
Naphthalene	Cyclohexane + Hexadecane	11	-4.0	+2.9	+1.4	+2.8	+1.5	43
Naphthalene	<i>n</i> -Hexane + Hexadecane	11	-6.8	+1.8	+0.8	+1.7	+0.6	44
Naphthalene	Benzene + Hexadecane	10	+9.2	+2.4	+0.7	+3.3	+2.5	45
Naphthalene	Cyclohexane + <i>n</i> -Hexane	11	0.8	0.6	0.6	0.8	0.8	28
Naphthalene	Benzene + Toluene	10	+0.5	+0.5	+0.6	+0.5	+0.7	29
Naphthalene	Cyclohexane + Toluene	12	-1.8	-0.9	-0.8	+1.0	+1.0	30
Naphthalene	Cyclohexane + Ethylbenzene	12	-1.7	0.3	0.3	+1.4	+1.5	31
<i>p</i> -Dibromobenzene	Hexadecane + Carbon tetrachloride	13	+5.4	+1.8	-0.8	NA	NA	45
<i>p</i> -Dibromobenzene	Cyclohexane + Carbon tetrachloride	13	-0.6	-1.5	-1.5	NA	NA	41
<i>p</i> -Dibromobenzene	<i>n</i> -Hexane + Hexadecane	13	-8.5	+1.6	0.6	+1.7	0.5	44
Anthracene	Cyclohexane + <i>n</i> -Heptane	—	1.0	0.6	0.6	0.6	+1.0	32
Anthracene	Cyclohexane + Cyclooctane	—	-1.4	0.9	0.9	+1.0	+1.2	33
Anthracene	Cyclohexane + Octane	—	-1.3	+0.6	+0.7	+0.9	+1.5	34
Anthracene	Cyclohexane + Isooctane	—	+1.9	-1.2	-1.0	+0.5	+1.1	35
Anthracene	Cyclohexane + <i>n</i> -Hexane	—	-1.2	-1.2	-1.1	0.3	0.3	28
Anthracene	Benzene + <i>n</i> -Heptane	—	+10.6	2.1	1.6	+5.9	+6.9	36
Anthracene	Benzene + <i>n</i> -Heptane	—	+7.9	-4.6	-3.8	+2.1	+3.1	37
Anthracene	Benzene + Cyclohexane	—	-6.9	-7.7	-7.5	-1.8	-1.7	41
Anthracene	Benzene + Cyclohexane	38	-6.2	-6.8	-6.6	1.1	1.1	41
Anthracene	Benzene + Carbon tetrachloride	38	-3.1	-2.1	-2.0	NA	NA	41
Anthracene	Benzene + <i>n</i> -Hexane	—	+2.7	-6.0	-5.4	+2.6	+3.1	42
Anthracene	Benzene + Cyclooctane	—	1.8	-8.3	-7.7	-3.6	3.0	39
Anthracene	Benzene + Isooctane	—	+10.5	-11.6	-10.7	+1.8	+3.0	40

^a RMS deviations (%) = $(100/N^{1/2}) \left\{ \sum_{j=1}^N [\ln(X_{\text{calc}}^{\text{sat}}/X_{\text{exp}}^{\text{sat}})]^2 \right\}^{1/2}$; the algebraic sign indicates that all deviations were of the same sign.

from the molar heat of fusion (ΔH_f^{fus}) at the normal melting point (T_m) and the differences between the molar heat capacities of the liquid and solid.

Introduction of molecular surface areas (A_i) into Eq. 1 results in the development of two more predictive expressions:

$$RT \ln(a_3^{\text{solid}}/X_3^{\text{sat}}) = (1 - \theta_3^{\text{sat}})^2 [\theta_1^0(\bar{G}_3^{\text{ex}})_1 + \theta_2^0(\bar{G}_3^{\text{ex}})_2 - A_3(X_1^0 A_1 + X_2^0 A_2)^{-1} \bar{G}_{12}^{\text{ex}}] \quad (\text{Eq. 8})$$

and:

$$RT \left[\ln(a_3^{\text{solid}}/\phi_3^{\text{sat}}) - (1 - \phi_3^{\text{sat}}) \left(1 - \frac{V_3}{(X_1^0 V_1 + X_2^0 V_2)} \right) \right] = (1 - \theta_3^{\text{sat}})^2 [\theta_1^0(\bar{G}_3^{\text{h}})_1 + \theta_2^0(\bar{G}_3^{\text{h}})_2 - A_3(X_1^0 A_1 + X_2^0 A_2)^{-1} \bar{G}_{12}^{\text{h}}] \quad (\text{Eq. 9})$$

depending on whether a regular solution model (Eq. 8) or a Flory-Huggins model (Eq. 9) is used to describe solution ideality. The use of these five predictive equations for solubility predictions in binary solvents is as follows: the quantities $(\bar{G}_3^{\text{ex}})_i$ or $(\bar{G}_3^{\text{h}})_i$ are calculated from the experimental solubility of the solute in the pure solvents, then these properties are used in the appropriate equation to calculate the solubility as X_3^{sat} or ϕ_3^{sat} in the solvent mixture using a reiterative process. The quantity $(1 - f_3^{\text{sat}})$ is taken as unity in the first approximation, and convergence is rapid unless the solubility is large. A numerical example is presented in the Appendix illustrating the prediction of naphthalene solubility in a binary mixture containing *n*-hexane and carbon tetrachloride using Eq. 4.

The predictive abilities of these equations are compared in Table II for 25 systems for which solubility data and the excess free energy of the binary solvent are available at or near the same temperature. Surface areas of the individual molecules were taken from tabulated values presented in previous reports (17–20), with the exception that the surface area of carbon tetrachloride was provided⁸. In all cases, the surface areas exclude solvent molecules which may be located within the atomic radii. Table III lists numerical values of the surface areas and molar volumes used in these predictions.

Based on surface areas as weighting factors for the excess free energy relative to Raoult's law, Eq. 8 is seen to be the most generally applicable with an overall average (RMS) deviation⁹ of 1.7% and a maximum error

⁸ The authors thank Robert S. Pearlman, University of Texas, for providing the surface area of carbon tetrachloride.

⁹ RMS Deviations (%)

$$= (100/N^{1/2}) \left\{ \sum_{j=1}^N [\ln(X_{\text{calc}}/X_{\text{exp}})]^2 \right\}^{1/2}$$

and these values are then averaged for all of the systems listed in Table II.

for a single data point of 7.5%. This maximum deviation occurs in a system (benzene-*n*-heptane) in which conflicting values of \bar{G}_{12}^{ex} have been reported. As shown in Table II, deviations between predicted and observed solubilities depend to a large extent on which literature source is used for the solvent properties. This leads to two sets of predicted anthracene solubilities that differ from each other by as much as 6%. Discrepancies in the reported values of \bar{G}_{12}^{ex} were not noted for the remaining 15 binary solvent systems. The primary advantage of Eq. 8 over expressions based on molar volumes, Eqs. 4 and 5, is its applicability to anthracene solubilities in solvent mixtures containing benzene. If these systems are excluded from the calculations, Eqs. 4 and 5 are slightly better than equations based on surface areas. All five equations correctly predict a maximum mole fraction solubility for anthracene in cyclohexane-*n*-heptane mixtures.

Solubility in simple binary solvents, C_3^{sat} , was described (21) as:

$$C_3^{\text{sat}} = K_1 C_1 + K_2 C_2 \quad (\text{Eq. 10})$$

and:

$$K_i = (C_3^{\text{sat}})_i / C_i^* \quad i = 1, 2$$

where C is molar concentration, and C_i^* is the concentration in a pure solvent. For solutes of limited solubility, it was demonstrated (4) that Eq. 3 is equivalent to:

$$X_3^{\text{sat}} = X_1^0 (X_3^{\text{sat}})_1 + X_2^0 (X_3^{\text{sat}})_2 \quad (\text{Eq. 11})$$

While Eq. 11 gives reasonable predictions for several of the anthracene systems studied, these predictions are off by as much as 50% for *p*-benzoquinone in the *n*-heptane-carbon tetrachloride system (8) and off by a factor of two for benzil in the isooctane-carbon tetrachloride system (7)¹⁰. Inspection of Eq. 4 reveals that the mathematical form is incapable of completely describing systems having either a maximum or minimum mole fraction solubility. Anthracene exhibits a maximum solubility in binary mixtures of cyclohexane and *n*-heptane, and a slight minimum solubility has been observed for iodine in binary mixtures containing cyclohexane and octamethylcyclotetrasiloxane (6). It has been suggested

¹⁰ For solutes having greater solubility $C_i = X_i/(X_1 V_1 + X_2 V_2 + X_3 V_3)$ and Eq. 10 can be shown to be equivalent to:

$$\frac{X_3^{\text{sat}}}{1 - X_3^{\text{sat}}} = X_1^0 \left(\frac{X_3^{\text{sat}}}{1 - X_3^{\text{sat}}} \right)_{X_2^0=1} + X_2^0 \left(\frac{X_3^{\text{sat}}}{1 - X_3^{\text{sat}}} \right)_{X_1^0=1}$$

This consideration does not significantly alter the large deviations for the solubilities of *p*-benzoquinone and benzil. This extended form cannot predict either a maximum or minimum solubility.

Table III—Properties Used in Calculations

Component	\bar{V} , ml/mole	\bar{A} , Å ² /mole	
Benzene	89.41	109.5	
Carbon tetrachloride	97.08	118.7	
Cyclohexane	108.76	120.8	
Hexadecane	294.12	323.2	
<i>n</i> -Heptane	147.48	160.3	
<i>n</i> -Hexane	131.51	142.1	
Cyclooctane	134.88	148.8	
Octane	163.46	178.4	
Isooctane	166.09	163.1	
Toluene	106.84	126.5	
Ethylbenzene	123.06	144.9	
Naphthalene	123.00	155.8	($a_3^{\text{solid}} = 0.312$)
<i>p</i> -Dibromobenzene	118.00	156.6	($a_3^{\text{solid}} = 0.248$)
Anthracene	150.00	202.2	($a_3^{\text{solid}} = 0.01049$)

(22) that the incorporation of mixed solvates into Eq. 11 is a way to explain maximum solubilities:

$$1 \cdot 3 + 2 = 1 \cdot 2 \cdot 3$$

$$K^{\#} = \frac{C_{1 \cdot 2 \cdot 3}}{C_{1 \cdot 3} C_2}$$

$$C_3^{\text{sat}} = K_1 C_1 + K_2 C_2 + K^{\#} K_1 C_1 C_2 \quad (\text{Eq. 12})$$

Postulation of mixed solvates is not needed in the nearly ideal binary solvent model, as its predictive equations correctly predict the existence of the maximum anthracene solubility as well as the minimum iodine solubility.

The Scatchard–Hildebrand (23) equation:

$$RT \ln(a_3^{\text{solid}}/X_3^{\text{sat}}) = V_3(1 - \phi_3^{\text{sat}})^2 (\delta_{12} - \delta_3)^2 \quad (\text{Eq. 13})$$

$$\delta_{12} = \frac{\phi_1 \delta_1 + \phi_2 \delta_2}{\phi_1 + \phi_2} \quad (\text{Eq. 14})$$

describes solubility in simple binary solvent mixtures in terms of the solubility parameters (δ_i) of the individual pure components. For liquids, the solubility parameters are available in the literature or can be determined experimentally from the temperature dependence of vapor pressures. The solubility parameters of crystalline compounds are obtained indirectly from solubility measurements, and several calculated methods (24–26) have been suggested recently for determining the best value of δ_3 . Examination of Eqs. 13 and 14 reveals that the solute should exhibit a maximum mole fraction solubility only when its solubility parameter is between the solubility parameters of the two pure solvents. Since the solubility parameter of anthracene ($\delta = 9.9$) is greater than either the solubility parameter of cyclohexane ($\delta = 8.2$) or *n*-heptane ($\delta = 7.4$), a maximum anthracene solubility would not be predicted by Eq. 13. Similar failures of Eq. 6 have been observed for benzoic acid in cyclohexane–*n*-heptane and cyclohexane–*n*-hexane mixtures (5) and for anthracene in benzene–iodobenzene, benzene–iodoethane, cyclohexane–iodoethane, and cyclohexane–iodoethane mixtures (27). It was noted (5) that Eqs. 3–5 predicted the existence of maximum benzoic acid solubilities for both the monomeric and dimeric treatment of monofunctional carboxylic acids. Because of the unavailability of binary \bar{G}_{12}^{ex} values, it was not possible to apply the NIBS model to the anthracene solubilities listed above. The fact that the nearly ideal binary solvent model correctly predicts maximum solubilities in three of these binary solvent mixtures suggests its greater application.

CONCLUSIONS

An important consequence of this research involves earlier contentions that the failure of Eq. 1 may be taken as an indication of specific solute–solvent or solvent–solvent interactions. While this concept is relatively straightforward in principle, its practical applications are complicated by the various weighting factor approximations. For example, does the failure of Eqs. 4 and 5 to predict anthracene solubilities in binary solvent mixtures containing benzene indicate specific solute–solvent (π – π) interactions, or does the success of Eq. 8 indicate that surface areas provide better approximations of weighting factors in systems containing both a planar solute and solvent molecule.

Unfortunately, this research does not indicate clearly whether weighting factors are better approximated with molar volumes or surface areas. From the standpoint of calculational simplicity and the ready availability of molar volumes, Eq. 4 is preferred, and some support for

this form can be found in its adaptability to the Scatchard–Hildebrand solubility parameter theory. Similar support for Eq. 8 (and Eq. 9) can be found in correlations of partition coefficients with surface areas and in several semi-empirical expressions developed for predicting liquid–vapor equilibria. However, Eq. 5 is also applicable to polymer solutions, and this form often is preferred, because it is more directly related to gas–liquid chromatographic partition coefficients and to molarity-based equilibrium constants.

APPENDIX

The following example illustrates the prediction of naphthalene solubility in a binary solvent mixture containing *n*-hexane and carbon tetrachloride. For calculational purposes, the initial mole fraction composition of the solvent mixture is taken to be $X_1^0 = X_{\text{hexane}}^0 = 0.5000$. This corresponds to a volume fraction of *n*-hexane of $\phi_1^0 = 0.5753$. The naphthalene solubilities in the pure solvents, $(X_3^{\text{sat}})_1 = 0.1168$ and $(X_3^{\text{sat}})_2 = 0.2591$ are taken from a previous report (10), and the excess free energy of mixing of the solvent mixture at $X_1^0 = 0.5000$, $\bar{G}_{12}^{\text{ex}} = 35.5$ cal/mole, is taken from other reported data (46).

The NIBS prediction begins by calculating the excess partial molar Gibbs free energy of the solute (\bar{G}_3^{ex})_{*i*} in the two pure solvents: For *n*-hexane:

$$(\bar{G}_3^{\text{ex}})_1 = (1 - 0.1101)^{-2} (1.987)(298.15) \ln(0.312/0.1168) = 735.02 \text{ cal/mole}$$

and for carbon tetrachloride:

$$(\bar{G}_3^{\text{ex}})_2 = (1 - 0.3070)^{-2} (1.987)(298.15) \ln(0.312/0.2591) = 229.2 \text{ cal/mole}$$

The properties in the two pure solvents are then combined with \bar{G}_{12}^{ex} to give:

$$(1.987)(298.15) \ln(0.312/X_3^{\text{sat}}) = (1 - \phi_3^{\text{sat}})^2 [(0.5753)(735.02) + (0.4247)(229.2) - (123.00)(114.30)^{-1} (35.5)]$$

In the first approximation ($1 - \phi_3^{\text{sat}} \approx 1$), and solving for the mole fraction solubility gives:

$$X_3^{\text{sat}} = 0.1383$$

The first approximation is then used to calculate $(1 - \phi_3^{\text{sat}})$, and this quantity is then used to obtain a second approximation:

$$(1.987)(298.15) \ln(0.312/X_3^{\text{sat}}) = (1 - 0.1483)^2 [(0.5753)(735.02) + (0.4247)(229.2) - (123.00)(114.30)^{-1} (35.5)]$$

The second approximation of X_3^{sat} ($= 0.1729$) is used to calculate a new value of $(1 - \phi_3^{\text{sat}})$, and the calculations are repeated until a constant mole fraction solubility is obtained. As mentioned previously, this convergence is quite rapid unless the solubility is large.

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