Thermochemical Investigations of Associated Solutions: 5. Calculation of Solute–Solvent Equilibrium Constants from Solubility in Mixtures Containing Two Complexing Solvents

WILLIAM E. ACREE, JR.^x AND JAMES W. MCCARGAR

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Abstract □ Solubilities are reported for carbazole in binary dibutyl ether plus 1-chlorohexane mixtures at 25 °C. Results of these measurements are compared with solution models developed for solubility in systems containing specific solute–solvent interactions. A simple stoichiometric complexation model based on a 1:1 carbazole:dibutyl ether complex could describe the measured solubility to within an average absolute deviation of 1.7%. The calculated equilibrium constant, though, was about one-half of values previously determined from carbazole solubilities in several binary dibutyl ether plus alkane mixtures. A more sophisticated solution model, derived by assuming both 1:1 carbazole:dibutyl ether and carbazole:chlorohexane complexes, could describe the solubilities to within 2.4%. This latter model enables the carbazole–chlorohexane association constant to be calculated from experimental carbazole solubilities and a priori knowledge of the carbazole–dibutyl ether equilibrium constant.

The use of binary solvents for influencing solubility and multiphase partitioning has many potential applications in the pharmaceutical industry. Maximum realization of these applications, however, 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 the solubility and partition coefficients of a molecule based solely on a consideration of molecular structure is desired; but for more practical applications, a less fundamental approach must often suffice.

In the first paper in this series, Acree et al.¹ extended the basic nearly ideal binary solvent (NIBS) model to systems containing association between the solute (component A) and a complexing cosolvent (component C):

$$K_{AC}^{\phi} = \phi_{AC}/\phi_{A_1} \phi_{C_1} \quad (2)$$

A relatively simple expression was developed for the determination of solute–solvent equilibrium constants from the measured solubility as a function of solvent composition and the excess Gibbs free energy of the binary solvent mixture:

$$RT \left[\ln (a_A^{\text{solid}}/\phi_{A_1}^{\text{sat}}) - 1 + \bar{V}_A \left(\frac{\phi_{A_1}^{\text{sat}}}{\bar{V}_A} + \frac{\phi_B}{\bar{V}_B} + \frac{\phi_C}{\bar{V}_C} \right) \right] = \\ (1 - \phi_A^{\text{sat}})^2 [\phi_B^o (\Delta \bar{G}_B^{\text{fh}})^* + \phi_C^o (\Delta \bar{G}_C^{\text{fh}})^* - \\ \bar{V}_A (X_B^o \bar{V}_B + X_C^o \bar{V}_C)^{-1} \Delta \bar{G}_{BC}^{\text{fh}}] \quad (3)$$

where a_A^{solid} is the activity of the solid solute (defined as the ratio of the fugacity of the solid to the fugacity of the pure subcooled liquid), ϕ_A^{sat} is the overall volume fraction solubility, $\bar{V}$ is the molar volume of the component (designated by

subscript), and X_B^o and X_C^o are the mole fraction compositions of the solvent mixture (calculated as if the solute were not present). The overall volume fraction solubility, ϕ_A^{sat} , is related to the solubility of the *uncomplexed* solute and the equilibrium constant by

$$\phi_A^{\text{sat}} = \phi_{A_1}^{\text{sat}} [1 + \bar{V}_A K_{AC}^{\phi} \phi_{C_1}/(\bar{V}_A + \bar{V}_C)] \quad (4)$$

The quantities $(\Delta \bar{G}_A^{\text{fh}})^*_B$ and $(\Delta \bar{G}_A^{\text{fh}})^*_C$ are calculated from the appropriate binary reduction of eq 3:

$$(\Delta \bar{G}_A^{\text{fh}})^*_B = (1 - \phi_A^{\text{sat}})^{-2} RT \left[\ln (a_A^{\text{solid}}/\phi_{A_1}^{\text{sat}}) - \right. \\ \left. (1 - \phi_A^{\text{sat}})(1 - \frac{\bar{V}_A}{\bar{V}_B}) \right] \quad (5)$$

$$(\Delta \bar{G}_A^{\text{fh}})^*_C = (1 - \phi_A^{\text{sat}})^{-2} RT \left[\ln (a_A^{\text{solid}}/\phi_{A_1}^{\text{sat}}) - \right. \\ \left. 1 + \bar{V}_A \left(\frac{\phi_{A_1}^{\text{sat}}}{\bar{V}_A} + \frac{\phi_C}{\bar{V}_C} \right) \right] \quad (6)$$

using the molar volumes of the pure components, $\bar{V}_i$, and the solubilities in the pure solvents. The superscript (o) denotes that the solvent compositions are calculated as if the solute were not present.

Postulating the formation of a 1:1 anthracene:benzene complex, the authors demonstrated that eq 3 could describe the solubility of anthracene in benzene plus *n*-heptane and benzene plus isooctane mixtures to within a maximum deviation of 4% using a single value of $K_{AC}^{\phi} = 1.91$. More importantly, it was noted that the determination of solute–solvent equilibrium constants from solubility measurements does depend on the manner in which nonspecific interactions are incorporated into the model. In the case of anthracene solubilities, failure to include nonspecific interactions led to a calculated value of $K_{AC}^{\phi} = 4.07$ for the anthracene:benzene complex in solvent mixtures containing *n*-heptane.

Subsequent studies by McCargar and Acree^{2,3} compared numerical values for the carbazole–dibutyl ether association constant calculated from measured carbazole solubilities in nine different binary dibutyl ether plus alkane solvent mixtures. A simple stoichiometric complexation model based entirely on specific solute–solvent interactions required two equilibrium constants to mathematically describe the experimental solubilities. Calculated equilibrium constants in cyclooctane cosolvent were significantly different from values for the isooctane cosolvent system. In comparison, eq 3 described the solubility data to within an average absolute

deviation of ~2% using a single carbazole–dibutyl ether association constant, which varied from $K_{AC}^\phi = 22$ for *n*-heptane to $K_{AC}^\phi = 30$ for isooctane. Calculation of nearly identical K_{AC}^ϕ values is impressive, particularly if one realizes that the nine cosolvents studied covered approximately a fivefold range in molar volumes.

The success of eq 3 in describing measured carbazole solubilities suggests the possibility that the NIBS model may provide a foundation from which to develop expressions for more complex systems. To pursue this idea further, the basic NIBS model is extended to systems in which both solvents are capable of forming specific solute–solvent complexes. An expression is derived for the determination of solute–solvent association parameters from solubility measurements. The calculational procedure is illustrated for a *presumed* carbazole:chlorohexane complex using measured carbazole solubilities in binary chlorohexane plus dibutyl ether mixtures and a previously reported K_{AC}^ϕ value for the carbazole:dibutyl ether complex.

Experimental Section

Carbazole (Aldrich; 99%) was recrystallized several times from absolute ethanol, giving a melting point of $246.5 \pm 0.5^\circ\text{C}$ (lit. value⁴ 247–248 °C). Dibutyl ether (Aldrich; Gold Label) and 1-chlorohexane (Aldrich; 99%) were stored over molecular sieves shortly before use to remove trace amounts of water. Binary solvent mixtures were prepared by weight so that compositions could be calculated to 0.0001 mol fraction.

Excess solute and solvent were placed in amber glass bottles and allowed to equilibrate in a constant temperature bath at $25.0 \pm 0.1^\circ\text{C}$ 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 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 spectrophotometrically at 292 nm on a Bausch and Lomb Spectronic 2000. Experimental solubilities are listed in Table I. Numerical values represent the average of four determinations, with the measurements being reproducible to within $\pm 2\%$.

Extension of the Nearly Ideal Binary Solvent Model (NIBS) Approach to Two Complexing Solvents—The NIBS treatment has been shown to be quite dependable for estimating heats of solution,⁵ gas–liquid partition coefficients,^{6,7} and solubilities^{8–13} in binary solvent systems that are free of association. The specific form of the NIBS equation which has been most successful for describing the excess chemical potential of solutes is based on a simple mixing model of a multicomponent system:

$$\Delta G_{1,2,\dots,N}^{\text{mix}} = RT \sum_{i=1}^N n_i \ln \phi_i + \left(\sum_{i=1}^N n_i \bar{V}_i \right) \left(\sum_{i=1}^N \sum_{j>i}^N \phi_i \phi_j A_{ij} \right) \quad (7)$$

in which n_i is the number of moles of component i , ϕ_i is the volume fraction, and A_{ij} is a binary interaction parameter that is independent of solvent composition. The application of eq 7 to a pentanary system

takes the form of

$$\begin{aligned} \Delta G^{\text{mix}} = & RT (n_{A_1} \ln \phi_{A_1} + n_{B_1} \ln \phi_{B_1} + n_{C_1} \ln \phi_{C_1} + \\ & n_{AB} \ln \phi_{AB} + n_{AC} \ln \phi_{AC}) + \\ & (n_{A_1} \bar{V}_A + n_{B_1} \bar{V}_B + n_{C_1} \bar{V}_C + n_{AB} \bar{V}_{AB} + n_{AC} \bar{V}_{AC}) \\ & (\phi_{A_1} \phi_{B_1} A_{A_1 B_1} + \phi_{A_1} \phi_{C_1} A_{A_1 C_1} + \\ & \phi_{A_1} \phi_{AB} A_{A_1 AB} + \phi_{A_1} \phi_{AC} A_{A_1 AC} + \phi_{B_1} \phi_{C_1} A_{B_1 C_1} + \\ & \phi_{B_1} \phi_{AB} A_{B_1 AB} + \phi_{B_1} \phi_{AC} A_{B_1 AC} + \phi_{C_1} \phi_{AB} A_{C_1 AB} + \\ & \phi_{C_1} \phi_{AC} A_{C_1 AC} + \phi_{AB} \phi_{AC} A_{AB AC}) \end{aligned} \quad (10)$$

The only assumptions are that the molar volumes of the AB and AC complexes equal the sum of the molar volumes of their constituents (i.e., $\bar{V}_{AB} = \bar{V}_A + \bar{V}_B$ and $\bar{V}_{AC} = \bar{V}_A + \bar{V}_C$). The chemical potentials of the individual components relative to the pure liquids ($\mu_i^\bullet$) are obtained through the appropriate differentiation:

$$\mu_{A_1} - \mu_{A_1}^\bullet = RT \left[\ln \phi_{A_1} + 1 - \frac{\bar{V}_{A_1}}{\bar{V}_{\text{solution}}} \right] +$$

$$\begin{aligned} & \bar{V}_A [\phi_{B_1} (1 - \phi_{A_1}) A_{A_1 B_1} + \phi_{C_1} (1 - \phi_{A_1}) A_{A_1 C_1} + \\ & \phi_{AB} (1 - \phi_{A_1}) A_{A_1 AB} + \phi_{AC} (1 - \phi_{A_1}) A_{A_1 AC} - \\ & \phi_{B_1} \phi_{C_1} A_{B_1 C_1} - \phi_{B_1} \phi_{AB} A_{B_1 AB} - \phi_{B_1} \phi_{AC} A_{B_1 AC} - \\ & \phi_{C_1} \phi_{AB} A_{C_1 AB} - \phi_{C_1} \phi_{AC} A_{C_1 AC} - \phi_{AB} \phi_{AC} A_{AB AC}] \end{aligned} \quad (11)$$

or

$$\mu_{B_1} - \mu_{B_1}^\bullet = RT \left[\ln \phi_{B_1} + 1 - \frac{\bar{V}_{B_1}}{\bar{V}_{\text{solution}}} \right] +$$

$$\bar{V}_B [\phi_{A_1} (1 - \phi_{B_1}) A_{A_1 B_1} + \phi_{C_1} (1 - \phi_{B_1}) A_{B_1 C_1} +$$

Table I—Comparison Between the Experimental and Predicted Solubilities for Carbazole in Binary 1-Chlorohexane (B) Plus Dibutyl Ether (C) Mixtures

X_C°	X_A^{sat}	Calculated Values of $X_A^{\text{sat}^a}$		
		$(K_{AB}^\phi = 0; K_{AC}^\phi = 10)$	$(K_{AB}^\phi = 0; K_{AC}^\phi = 24)$	$(K_{AB}^\phi = 2; K_{AC}^\phi = 24)$
0.000 0	0.002 55	—	—	—
0.085 3	0.003 35	0.003 43	0.004 61	0.003 48
0.172 7	0.003 96	0.004 10	0.005 90	0.004 19
0.272 2	0.004 61	0.004 63	0.006 67	0.004 74
0.347 5	0.005 09	0.004 91	0.006 92	0.005 02
0.448 1	0.005 10	0.005 15	0.006 96	0.005 25
0.549 1	0.005 26	0.005 28	0.006 77	0.005 36
0.653 1	0.005 33	0.005 31	0.006 44	0.005 38
0.759 4	0.005 32	0.005 27	0.006 02	0.005 32
0.872 5	0.005 30	0.005 17	0.005 55	0.005 20
1.000 0	0.005 01	—	—	—

^a Based on eq 29; properties used for the calculations are the molar volumes and solubility parameters of dibutyl ether ($\bar{V}_C = 170.41 \text{ cm}^3/\text{mol}$, $\delta_C = 7.76 \text{ cal}^{1/2} \cdot \text{cm}^{-3/2}$), 1-chlorohexane ($\bar{V}_B = 138.11 \text{ cm}^3/\text{mol}$, $\delta_B = 8.36 \text{ cal}^{1/2} \cdot \text{cm}^{-3/2}$), and carbazole ($\bar{V}_A = 150 \text{ cm}^3/\text{mol}$); these values are based on data in refs. 16–19; determined at 25°C .

$$\begin{aligned} & \phi_{AB} (1 - \phi_{B_1}) A_{B_1AB} + \phi_{AC} (1 - \phi_{B_1}) A_{B_1AC} - \\ & \phi_{A_1} \phi_{C_1} A_{A_1C_1} - \phi_{A_1} \phi_{AB} A_{A_1AB} - \\ & \phi_{A_1} \phi_{AC} A_{A_1AC} - \phi_{C_1} \phi_{AB} A_{C_1AB} - \\ & \phi_{C_1} \phi_{AC} A_{C_1AC} - \phi_{AB} \phi_{AC} A_{ABAC} \end{aligned} \quad (12)$$

or

$$\begin{aligned} \mu_{C_1} - \mu_C^\bullet &= RT \left[\ln \phi_{C_1} + 1 - \frac{\bar{V}_C}{\bar{V}_{\text{solution}}} \right] + \\ & \bar{V}_C [\phi_{A_1} (1 - \phi_{C_1}) A_{A_1C_1} + \phi_{B_1} (1 - \phi_{C_1}) A_{B_1C_1} + \\ & \phi_{AB} (1 - \phi_{C_1}) A_{C_1AB} + \phi_{AC} (1 - \phi_{C_1}) A_{C_1AC} - \\ & \phi_{A_1} \phi_{B_1} A_{A_1B_1} - \phi_{A_1} \phi_{AB} A_{A_1AB} - \phi_{A_1} \phi_{AC} A_{A_1AC} - \\ & \phi_{B_1} \phi_{AB} A_{B_1AB} - \phi_{B_1} \phi_{AC} A_{B_1AC} - \phi_{AB} \phi_{AC} A_{ABAC}] \end{aligned} \quad (13)$$

where $\bar{V}_{\text{solution}}$ is

$$\frac{1}{\bar{V}_{\text{solution}}} = \frac{\phi_{A_1}}{\bar{V}_A} + \frac{\phi_{B_1}}{\bar{V}_B} + \frac{\phi_{C_1}}{\bar{V}_C} + \frac{\phi_{AB}}{\bar{V}_A + \bar{V}_B} + \frac{\phi_{AC}}{\bar{V}_A + \bar{V}_C} \quad (14)$$

the molar volume of the *true* solution.

Equations 11–14 obviously contain far too many parameters for useful applications, but reasonable assumptions enable the number to be greatly reduced. Treatment of the A_{A_1AB} , A_{B_1AB} , A_{A_1AC} , and A_{C_1AC} interaction parameters in a manner similar to that employed by Bertrand¹⁴ for the chloroform:triethylamine complex leads to

$$A_{A_1AB} = \bar{V}_B^2 (\bar{V}_A + \bar{V}_B)^{-2} A_{A_1B_1} \quad (15)$$

$$A_{B_1AB} = \bar{V}_A^2 (\bar{V}_A + \bar{V}_B)^{-2} A_{A_1B_1} \quad (16)$$

$$A_{A_1AC} = \bar{V}_C^2 (\bar{V}_A + \bar{V}_C)^{-2} A_{A_1C_1} \quad (17)$$

$$A_{C_1AC} = \bar{V}_A^2 (\bar{V}_A + \bar{V}_C)^{-2} A_{A_1C_1} \quad (18)$$

The remaining three interaction parameters are approximated as follows:

$$A_{B_1AC} = \frac{\bar{V}_C A_{B_1C_1}}{\bar{V}_A + \bar{V}_C} + \frac{\bar{V}_A A_{A_1B_1}}{\bar{V}_A + \bar{V}_C} - \frac{\bar{V}_A \bar{V}_C A_{A_1C_1}}{(\bar{V}_A + \bar{V}_C)^2} \quad (19)$$

$$A_{C_1AB} = \frac{\bar{V}_B A_{B_1C_1}}{\bar{V}_A + \bar{V}_B} + \frac{\bar{V}_A A_{A_1C_1}}{\bar{V}_A + \bar{V}_B} - \frac{\bar{V}_A \bar{V}_B A_{A_1B_1}}{(\bar{V}_A + \bar{V}_B)^2} \quad (20)$$

$$\begin{aligned} A_{ABAC} &= \frac{\bar{V}_B \bar{V}_C A_{B_1C_1}}{(\bar{V}_A + \bar{V}_C)(\bar{V}_A + \bar{V}_B)} + \\ & \frac{\bar{V}_A \bar{V}_B A_{A_1B_1}}{(\bar{V}_A + \bar{V}_B)(\bar{V}_A + \bar{V}_C)} - \frac{\bar{V}_A \bar{V}_B A_{A_1B_1}}{(\bar{V}_A + \bar{V}_B)^2} + \\ & \frac{\bar{V}_A \bar{V}_C A_{A_1C_1}}{(\bar{V}_A + \bar{V}_B)(\bar{V}_A + \bar{V}_C)} - \frac{\bar{V}_A \bar{V}_C A_{A_1C_1}}{(\bar{V}_A + \bar{V}_C)^2} \end{aligned} \quad (21)$$

Substitution of these approximations into eq 11, after suitable mathematical manipulations, yields the following expression for the chemical potential of *uncomplexed* component A:

$$\mu_{A_1} - \mu_A^\bullet = RT \left[\ln \phi_{A_1} + 1 - \frac{\bar{V}_A}{\bar{V}_{\text{solution}}} \right] +$$

$$\begin{aligned} & \bar{V}_A [\phi_B (1 - \phi_A) A_{A_1B_1} + \\ & \phi_C (1 - \phi_A) A_{A_1C_1} - \phi_B \phi_C A_{B_1C_1}] \end{aligned} \quad (22)$$

Similar expressions can be derived for $\mu_{B_1} - \mu_B^\bullet$ and $\mu_{C_1} - \mu_C^\bullet$.

As shown in many thermodynamic textbooks (e.g., Acree¹⁵), the chemical potential of stoichiometric component A is equal to the chemical potential of the monomeric (uncomplexed) species in solution

$$\mu_{A_1} = \mu_A \quad (23)$$

Using this condition, the chemical potential of the solid solute (at saturation) is expressed as

$$\begin{aligned} \mu_A - \mu_A^\bullet &= RT \ln a_A^{\text{solid}} = RT \left[\ln \phi_{A_1}^{\text{sat}} + 1 - \frac{\bar{V}_A}{\bar{V}_{\text{solution}}} \right] + \\ & \bar{V}_A (1 - \phi_A^{\text{sat}})^2 [\phi_B^0 A_{A_1B_1} + \phi_C^0 A_{A_1C_1} - \phi_B^0 \phi_C^0 A_{B_1C_1}] \end{aligned} \quad (24)$$

where $\phi_B^0 = 1 - \phi_C^0 = \phi_B/(\phi_B + \phi_C)$ and a_A^{solid} is the activity of the solid solute. This activity, defined as the ratio of the fugacity of the solid to the fugacity of the pure subcooled liquid, is calculated from the molar enthalpy of fusion (ΔH_A^{fus}) at the normal melting point temperature.

$$\ln a_A^{\text{solid}} = \int_{T_m}^T (\Delta H_A^{\text{fus}}/RT^2) dT \quad (25)$$

Inspection of eq 24 reveals that, for model systems obeying this expression, the $A_{A_1B_1}$ and $A_{A_1C_1}$ interaction parameters can be eliminated from the basic model via the saturation solubilities in the pure solvents. The $A_{B_1C_1}$ parameter can be eliminated via the excess Gibbs free energy of the binary solvent mixture calculated according to eq 7. Performing these substitutions,

$$\begin{aligned} RT \left[\ln (a_A^{\text{solid}}/\phi_{A_1}^{\text{sat}}) - 1 + \frac{\bar{V}_A}{\bar{V}_{\text{solution}}} \right] &= \\ (1 - \phi_A^{\text{sat}})^2 [\phi_B^0 (\Delta \bar{G}_A^{\text{fh}})^* + \phi_C^0 (\Delta \bar{G}_A^{\text{fh}})^* - \\ & \bar{V}_A (X_B^0 \bar{V}_B + X_C^0 \bar{V}_C)^{-1} \Delta \bar{G}_{BC}^{\text{fh}}] \end{aligned} \quad (26)$$

where

$$\begin{aligned} \Delta \bar{G}_A^{\text{fh}})^* &= (1 - \phi_A^{\text{sat}})^{-2} RT \left[\ln (a_A^{\text{solid}}/\phi_{A_1}^{\text{sat}}) - \right. \\ & \left. 1 + \bar{V}_A \left(\frac{\phi_{A_1}^{\text{sat}}}{\bar{V}_A} + \frac{\phi_B}{\bar{V}_B} \right) \right] \end{aligned} \quad (27)$$

and

$$\begin{aligned} (\Delta \bar{G}_A^{\text{fh}})^* &= (1 - \phi_A^{\text{sat}})^{-2} RT \left[\ln (a_A^{\text{solid}}/\phi_{A_1}^{\text{sat}}) - \right. \\ & \left. 1 + \bar{V}_A \left(\frac{\phi_{A_1}^{\text{sat}}}{\bar{V}_A} + \frac{\phi_C}{\bar{V}_C} \right) \right] \end{aligned} \quad (28)$$

The volume fraction solubility of the uncomplexed solute is calculated from the overall volume fraction solubility, ϕ_A^{sat} , and the equilibrium constants $\phi_A^{\text{sat}} = \phi_{A_1}^{\text{sat}} [1 + \bar{V}_A K_{AB}^0 \phi_B/(\bar{V}_A + \bar{V}_B) + \bar{V}_A K_{AC}^0 \phi_C/(\bar{V}_A + \bar{V}_C)]$. Liquid phase compositions for eqs 27 and 28 refer to the saturated pure solvents.

Results and Discussion

Despite the complex appearance of eq 26, its application to solubilities in mixed solvents is relatively straightforward.

Table II—Calculated Carbazole Solubilities in Binary *n*-Hexane (B) Plus 1-Chlorohexane (C) Mixtures Based on the Infinite Dilution Form of Equation 3

X_C^o	Calculated Values of X_A^{sat}			
	$K_{AC}^\phi = 0$	$K_{AC}^\phi = 1$	$K_{AC}^\phi = 2$	$K_{AC}^\phi = 3$
0.000 0	0.000 139 ^a	—	—	—
0.100 0	0.000 195	0.000 197	0.000 200	0.000 205
0.200 0	0.000 270	0.000 274	0.000 282	0.000 293
0.300 0	0.000 369	0.000 376	0.000 391	0.000 409
0.400 0	0.000 500	0.000 511	0.000 532	0.000 557
0.500 0	0.000 672	0.000 686	0.000 714	0.000 746
0.600 0	0.000 893	0.000 911	0.000 944	0.000 982
0.700 0	0.001 177	0.001 197	0.001 233	0.001 272
0.800 0	0.001 536	0.001 556	0.001 590	0.001 625
0.900 0	0.001 989	0.002 002	0.002 026	0.002 050
1.000 0	0.002 550	—	—	—

^a Experimental value taken from ref 2.

When the solute solubility is sufficiently small, $\phi_A^{sat} \approx 0$ and $1 - \phi_A^{sat} \approx 1$, eq 26 can be written

$$\begin{aligned} \ln \phi_A^{sat} = & \phi_B^o \ln (\phi_A^{sat})_B + \phi_C^o \ln (\phi_A^{sat})_C - \\ & \phi_B^o \ln [1 + \bar{V}_A K_{AB}^\phi / (\bar{V}_A + \bar{V}_B)] - \\ & \phi_C^o \ln [1 + \bar{V}_A K_{AC}^\phi / (\bar{V}_A + \bar{V}_C)] + \ln [1 + \\ & \bar{V}_A K_{AB}^\phi \phi_B^o / (\bar{V}_A + \bar{V}_B) + \bar{V}_A K_{AC}^\phi \phi_C^o / (\bar{V}_A + \bar{V}_C)] + \\ & \frac{\bar{V}_A \Delta \bar{G}_{BC}^{fh}}{RT (X_B^o \bar{V}_B + X_C^o \bar{V}_C)} \end{aligned} \quad (29)$$

in terms of overall solubility in the two pure solvents $(\phi_A^{sat})_B$ and $(\phi_A^{sat})_C$. In the absence of solute-solvent complexation (i.e., $K_{AB}^\phi = K_{AC}^\phi = 0$), and in the special case when $K_{AB}^\phi / (\bar{V}_A + \bar{V}_B) = K_{AC}^\phi / (\bar{V}_A + \bar{V}_C)$, eq 29 reduces to an expression derived earlier (eq VV of Acree and Bertrand⁸) for systems containing only nonspecific interactions.

Determination of equilibrium constants depends, to a large extent, on what information is available. Optimized values for both K_{AB}^ϕ and K_{AC}^ϕ can be obtained via nonlinear least squares analysis of eq 29, provided one has a sufficient number of experimental data points for a meaningful computation. A single equilibrium constant can be obtained from solute solubility at a particular solvent composition (i.e., $\phi_B \approx 0.5$), but this requires a priori knowledge of the second association constant.

Table I compares experimental carbazole solubilities in binary dibutyl ether plus chlorohexane mixtures to values calculated from eq 29 with various K_{AB}^ϕ and K_{AC}^ϕ values. Solute and solvent properties needed in the calculations were taken from the literature, except for binary solvent excess Gibbs free energies, which were estimated from the solubility parameter approach:

$$\Delta \bar{G}_{BC}^{ex} = \phi_B^o \phi_C^o (X_B^o \bar{V}_B + X_C^o \bar{V}_C) (\delta_B - \delta_C)^2 \quad (30)$$

$$\Delta \bar{G}_{BC}^{fh} = \Delta \bar{G}_{BC}^{ex} + RT [\ln (X_B^o \bar{V}_B + X_C^o \bar{V}_C) - X_B^o \ln \bar{V}_B - X_C^o \ln \bar{V}_C] \quad (31)$$

where δ_i is the solubility parameter of component *i*. Inspection of Table I reveals that the solubility data can be rationalized in terms of a single carbazole-dibutyl ether association complex, though the numerical value of $K_{AC}^\phi = 10.0$ is less than one-half of values reported previously for inert hydrocarbon cosolvents such as *n*-hexane, *n*-octane, cyclohexane, and isooctane. This dramatic change in K_{AC}^ϕ may result from a weak carbazole:chlorohexane complex

between the hydrogen on carbazole and one of the three lone electron pairs on chlorine. Assuming both carbazole:dibutyl ether and carbazole:chlorohexane complexes, the solubility data can be described to within an average absolute deviation of 2.4% using $K_{AB}^\phi = 2.0$ and $K_{AC}^\phi = 24.0$. Readers are reminded that the calculation of equilibrium constants for a presumed carbazole:chlorohexane complex does not imply that the authors believe such a complex actually exists in solution. As in all cases, the presence of molecular complexes should be supported by independent measurements involving calorimetry, spectroscopy, etc.

Equation 29 is interesting from a mathematical standpoint in that fairly small changes in the value of K_{AB}^ϕ may have a rather pronounced effect on the calculated solubility near $K_{AB}^\phi = 0$. This is particularly true in systems having both a very weak and very strong solute:solvent complex. The term $\bar{V}_A K_{AB}^\phi \phi_B^o / (\bar{V}_A + \bar{V}_B)$ becomes negligible compared with $\bar{V}_A K_{AC}^\phi \phi_C^o / (\bar{V}_A + \bar{V}_C)$ inside the logarithm. As shown in Table I, the calculated carbazole solubility is $X_A^{sat} = 0.00692$ at $X_C^o = 0.3475$ in the absence of specific carbazole:chlorohexane complexation, and differs significantly from $X_A^{sat} = 0.00502$ for $K_{AB}^\phi = 2.0$. Sensitivity of eq 29 to K_{AB}^ϕ values may prove to be useful in the development of an experimental method for identifying weak association complexes in solution. It is doubtful that previous methods based on measured carbazole solubilities in binary inert alkane plus chlorohexane mixtures would suggest the possible existence of such weak complexes. Carbazole solubilities calculated from eq 3 with association constants varying from $K_{AC}^\phi = 0$ to $K_{AC}^\phi = 3.0$ (Table II), with chlorohexane denoted as the complexing solvent and *n*-hexane the inert cosolvent, differ by only a few percent.

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