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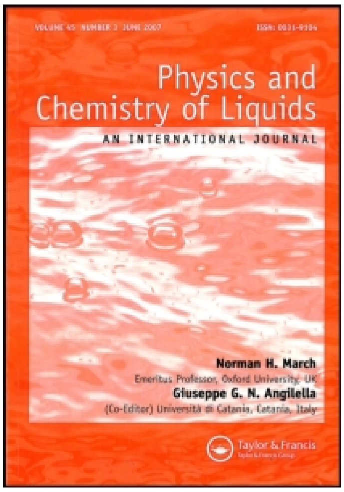

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Thermochemical Investigations of Associated Solutions. 3. Effect of the Inert Cosolvent on Solute-Solvent Association Constants Calculated from Solubility Measurements

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Thermochemical Investigations of Associated Solutions. 3. Effect of the Inert Cosolvent on Solute–Solvent Association Constants Calculated from Solubility Measurements

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Solubilities are reported for carbazole in binary solvent mixtures containing dibutyl ether with *n*-hexane, *n*-heptane, *n*-octane, cyclohexane, cyclooctane, methylcyclohexane and isooctane at 25°C. The results of these measurements are compared to solution models previously developed for solubility in systems containing specific solute–solvent interactions. A simple stoichiometric complexation model based primarily on specific solute–solvent interactions required two equilibrium constants to mathematically describe the experimental solubilities in binary dibutyl ether mixtures. Calculated equilibrium constants in cyclooctane cosolvent were significantly different from values for the isooctane cosolvent system. In comparison, an expression derived by including nonspecific interaction contributions described the solubility data to within an average absolute deviation of 2% using a single carbazole–dibutyl ether association constant, which varied from $K^{\phi}_{AC} = 22$ for *n*-heptane to $K^{\phi}_{AC} = 30$ for isooctane.

Key Words: Nonspecific interactions, equilibrium constants.

INTRODUCTION

The use of binary solvents for influencing solubility and multiphase partitioning has many potential applications in both the chemical and

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pharmaceutical industry. Maximum realization of these applications depends, to a large extent, on the development of equations that enable researchers to predict solution behavior in mixed solvents from a minimum number of observed values. Ideally, the ability to predict quantitatively a molecule's solubility and partition coefficients based solely on a consideration of molecular structure is desired. Several group contribution models[1–6] have been developed in recent years to address this need.

Study of the solubility process also provides, at a more fundamental level, an understanding of molecular interaction in solution. The interpretation of solution nonideality generally has followed two dissimilar lines; the "physical" approach originated by van Laar[7] and the "chemical" approach proposed by Dolezalek[8]. The physical approach may be described in terms of a random distribution of molecules throughout the entire solution while the chemical approach may be characterized in terms of a specific geometric orientation of one molecule with respect to an adjacent molecule. Even in systems known to contain specific interactions, the need to properly account for nonspecific interactions has been recognized. Arnett *et al.*[9] with their "pure base" calorimetric method for determining enthalpies of hydrogen bond formation attempted to separate specific and nonspecific interactions. The sensitivity of the numerical results to the selection of "model" compound and inert solvent raised important doubts regarding the overall effectiveness of this particular method[10]. Saluja *et al.*[11] used a somewhat similar rationale in their comparison of enthalpies of transfer of alkanes and the corresponding alkenes from the vapor state to methanol, dimethylformamide, benzene and cyclohexane, with the more exothermic values for the alkenes in methanol and dimethylformamide attributed to dipole-induced dipole interactions between the solvent and the polarizable π-bond. Subsequent studies by Stephenson and Fuchs reported enthalpies of interaction of ketones[12], aromatic[13], nitrogen base[14] and hydroxylic[15] solutes with solvents of varying polarity. Bertrand[16] demonstrated that neglect of nonspecific interactions in the chloroform and triethylamine system can lead to an appreciable error in the enthalpy of complex formation determined with the ideal associated solution model. Fenby *et al.*[17] presented a similar analysis of the diethyl ether + chloroform system. Thermodynamic consequences of the ideal associated solution model have been presented in three recent monographs[18–20] and a review[21], along with discussions of applications to select nonelectrolyte systems.

Many of the remaining methods for estimating complex formation constants can be classified as solubility methods. That is, the increase in solubility of a solute at constant fugacity in a complexing-inert solvent mixture, relative to the solubility in pure inert solvent, is generally attributed to the formation of molecular complexes. This primary assumption is common to several thermodynamic methods, such as the partition of solutes between two immiscible liquid phases, the measurement of infinite dilution gas-liquid chromatographic partition coefficients and the increase in solubility of solids. The techniques for calculating formation constants are essentially identical for all solubility methods, as are the difficulties in properly assessing what portion of solubility enhancement is due to nonspecific interactions.

In two earlier papers Acree and Rytting reported solubilities for benzil[22] and *p*-benzoquinone[23] in binary solvent mixtures containing carbon tetrachloride in which the mole fraction solubility of benzil and *p*-benzoquinone cover a 14-fold and 6-fold range, respectively. The experimental data were interpreted with solution models developed previously for solubility in systems containing specific solute-solvent interactions and with models of purely nonspecific interactions. A stoichiometric complexation model based entirely on specific interactions (nonspecific interactions ignored) required several equilibrium constants to mathematically describe the experimental results, while the Nearly Ideal Binary Solvent (NIBS) model, based on nonspecific interactions, described adequately the observed solubilities without introducing a single equilibrium constant.

The success of the NIBS approach in predicting the binary solvent effect on both benzil and *p*-benzoquinone solubilities suggested the possibility that this solution may provide a foundation for approximations of the physical interactions even in a system known to contain chemical interactions. To pursue this idea further, Acree *et al.*[24] extended the basic NIBS model to systems containing association between the solute (component A) and a complexing cosolvent (component C)

$$\mathrm{A} + \mathrm{C} \rightleftharpoons \mathrm{AC}$$

$$K^{\phi}_{\mathrm{AC}} = \phi_{\mathrm{AC}}/(\phi_{\mathrm{A}_1}\,\phi_{\mathrm{C}_1})$$

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

$$\begin{aligned}\mathrm{RT}\left[\ln(a_{\mathrm{A}}^{\mathrm{solid}}/\phi_{\mathrm{A}_1}^{\mathrm{sat}}) - 1 + \bar{V}_{\mathrm{A}}\left(\frac{\phi_{\mathrm{A}_1}}{\bar{V}_{\mathrm{A}}} + \frac{\phi_{\mathrm{B}}}{\bar{V}_{\mathrm{B}}} + \frac{\phi_{\mathrm{C}}}{\bar{V}_{\mathrm{C}}}\right)\right] \\ = (1 - \phi_{\mathrm{A}}^{\mathrm{sat}})^2[\phi_{\mathrm{B}}^0(\Delta\bar{G}_{\mathrm{A}}^{fh})_{\mathrm{B}}^{*} + \phi_{\mathrm{C}}^0(\Delta\bar{G}_{\mathrm{A}}^{fh})_{\mathrm{C}}^{*} \\ - \bar{V}_{\mathrm{A}}(X_{\mathrm{B}}^0\bar{V}_{\mathrm{B}} + X_{\mathrm{C}}^0\bar{V}_{\mathrm{C}})^{-1}\Delta\bar{G}_{\mathrm{BC}}^{fh}] \qquad (1)\end{aligned}$$

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with the overall volume fraction solubility, ϕ_A^{sat}, being related to the solubility of the *uncomplexed* solute and the equilibrium constant by

$$\phi_{\mathrm{A}}^{\mathrm{sat}} = \phi_{\mathrm{A}_1}^{\mathrm{sat}}[1 + \bar{V}_A \mathrm{K}_{\mathrm{AC}}^{\phi} \phi_{\mathrm{C}_1}/(\bar{V}_{\mathrm{A}} + \bar{V}_{\mathrm{C}})] \tag{2}$$

and the quantities $(\Delta\bar{G}_{\mathrm{A}}^{fh})_{\mathrm{B}}^{*}$ and $(\Delta\bar{G}_{\mathrm{A}}^{fh})_{\mathrm{C}}^{*}$ being calculated from the appropriate binary reduction of Eq. (1)

$$(\Delta\bar{G}_{\mathrm{A}}^{fh})_{\mathrm{B}}^{*} = (1 - \phi_{\mathrm{A}}^{\mathrm{sat}})^{-2}\mathrm{RT}\left[\ln(a_{\mathrm{A}}^{\mathrm{solid}}/\phi_{\mathrm{A}}^{\mathrm{sat}}) - (1 - \phi_{\mathrm{A}}^{\mathrm{sat}})\left(1 - \frac{\bar{V}_{\mathrm{A}}}{\bar{V}_{\mathrm{B}}}\right)\right]$$

$$(\Delta\bar{G}_{\mathrm{A}}^{fh})_{\mathrm{C}}^{*} = (1 - \phi_{\mathrm{A}}^{\mathrm{sat}})^{-2}\mathrm{RT}\left[\ln(a_{\mathrm{A}}^{\mathrm{solid}}/\phi_{\mathrm{A}_1}^{\mathrm{sat}}) - 1 + \bar{V}_{\mathrm{A}}\left(\frac{\phi_{\mathrm{A}_1}}{\bar{V}_{\mathrm{A}}} + \frac{\phi_{\mathrm{C}}}{\bar{V}_{\mathrm{C}}}\right)\right]$$

using the molar volumes of the pure components, $\bar{V}_i$, and the solubilities in the two pure solvents. The superscript (0) denotes that the solvent compositions are calculated as if the solute were not present.

Postulating the formation of a 1:1 anthracene-benzene complex, Acree *et al.* demonstrated that equation 1 could describe the solubility of anthracene in benzene + *n*-heptane and benzene + isooctane mixtures to within a maximum deviation of 4% using a single value of $\mathrm{K}_{\mathrm{AC}}^{\phi}$ of 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 $\mathrm{K}_{\mathrm{AC}}^{\phi} = 4.07$ for the anthracene-benzene complex in solvent mixtures containing *n*-heptane.

In a follow-up study comparing iodine solubilities in binary solvent mixtures, Acree[25] compared the solubility-based association constant for the iodine-benzene complex, $\mathrm{K}_{\mathrm{AC}}^{c} = 0.393\ \mathrm{M}^{-1}$, to the spectroscopic values of Bhowmik[26] determined in cyclohexane ($\mathrm{K}_{\mathrm{AC}}^{c} = 0.260\ \mathrm{M}^{-1}$), methylcyclohexane ($\mathrm{K}_{\mathrm{AC}}^{c} = 0.252\ \mathrm{M}^{-1}$) and *n*-heptane ($\mathrm{K}_{\mathrm{AC}}^{c} = 0.246\ \mathrm{M}^{-1}$) solvents. Deviations of this magnitude are to be expected in comparing independently determined equilibrium constants, particularly in the case of weak association complexes as both specific and nonspecific interactions play an important role in determining the total nonideality of the solution.

To gain additional insight into the limitations and applications of Eq. (1), we have measured carbazole solubilities in solvent mixtures containing dibutyl ether with *n*-hexane, *n*-heptane, *n*-octane, cyclohexane, methylcyclohexane, cyclooctane and isooctane. These systems were selected primarily because the mole fraction solubility of carbazole in dibutyl ether, $X_a^{sat} = 0.00501$, is more than 25 times greater than in the alkane solvents. The large solubility enhancement observed in these seven binary solvent systems will provide a more demanding test of the descriptive ability of Eq. (1) than did previous iodine and anthracene solubilities which covered a relatively narrow 8-fold range of mole fractions. Results of these measurements also will be used to evaluate both the effect that the inert cosolvent has on the calculated association constant and the relative importance of nonspecific interactions in systems believed to contain a strong association complex.

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MATERIALS AND METHODS

Carbazole (Aldrich 99%) was recrystallized several times from absolute ethanol, giving a melting point of 246.5 ±0.5°C (literature value 247-248°C[27]). Cyclohexane (Aldrich HPLC grade), *n*-hexane (Aldrich 99%), *n*-heptane (Aldrich HPLC grade), *n*-octane (Aldrich Gold Label), methylcyclohexane (Aldrich Gold Label), cyclooctane (Aldrich Gold Label) and isooctane (Aldrich HPLC grade) were stored over molecular sieves (Type 4A) to remove trace amounts of water. Binary solvent mixtures were prepared by weight so that solvent compositions could be calculated to 0.0001 mole fraction.

Excess carbazole and solvent were placed in amber glass bottles and allowed to equilibrate in a constant temperature shaker bath at 25.0 ±0.1°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 carbazole 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 of carbazole in the seven binary solvent systems studied are listed in Table 1. Numerical values represent the average of between 4 and 6 independent determinations, with the measurements being reproducible to within ±2%. In pure dibutyl ether and isooctane our experimental carbazole solubilities are in excellent agreement with previously reported values of $X_A^{sat} = 0.00494$ and $X_A^{sat} = 0.000128$, respectively[28].

Table 1 Mole fraction solubilities of carbazole in several binary solvent mixtures at 25°C.

Solvent (B) + Solvent (C)	X_C^0	X_A^{sat}
n-Hexane + Dibutyl ether	0.0000	0.000139
	0.0789	0.000333
	0.1602	0.000590
	0.2498	0.000838
	0.3404	0.001166
	0.4368	0.001615
	0.5382	0.002049
	0.6435	0.002662
	0.7581	0.003392
	0.8748	0.003963
	1.0000	0.005011
n-Heptane + Dibutyl ether	0.0000	0.000173
	0.0906	0.000392
	0.1816	0.000642
	0.2738	0.000943
	0.3632	0.001301
	0.4672	0.001771
	0.5620	0.002275
	0.6640	0.002761
	0.7654	0.003263
	0.8739	0.004012
	1.0000	0.005011
n-Octane + Dibutyl ether	0.0000	0.000198
	0.1028	0.000474
	0.2030	0.000804
	0.2963	0.001120
	0.3835	0.001492
	0.4902	0.001864
	0.5949	0.002463
	0.6907	0.002966
	0.7885	0.003605
	0.8873	0.004339
	1.0000	0.005011
Cyclohexane + Dibutyl ether	0.0000	0.000183
	0.0665	0.000442
	0.1372	0.000687
	0.2143	0.001013
	0.2975	0.001434
	0.3876	0.001772
	0.4895	0.002296
	0.5996	0.002888
	0.7135	0.003406
	0.8510	0.004103
	1.0000	0.005011

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Table 1 (*Continued*)

Solvent (B) + Solvent (C)	X_C^0	X_A^{sat}
Methylcyclohexane + Dibutyl ether	0.0000	0.000196
	0.0877	0.000500
	0.1650	0.000797
	0.2453	0.001123
	0.3347	0.001545
	0.4294	0.001959
	0.5339	0.002450
	0.6885	0.003278
	0.7417	0.003656
	0.8568	0.004356
	1.0000	0.005011
Cyclooctane + Dibutyl ether	0.0000	0.000309
	0.0859	0.000747
	0.1689	0.001098
	0.2523	0.001511
	0.3438	0.002028
	0.4423	0.002520
	0.5445	0.002997
	0.6486	0.003431
	0.7699	0.004120
	0.8629	0.004578
	1.0000	0.005011
Isooctane + Dibutyl ether	0.0000	0.000126
	0.1026	0.000350
	0.1971	0.000596
	0.2948	0.000901
	0.3911	0.001246
	0.4933	0.001761
	0.5933	0.002303
	0.6925	0.002751
	0.7878	0.003356
	0.8888	0.004081
	1.0000	0.005011

SOLUBILITY PARAMETER MODEL

The Scatchard-Hildebrand solubility parameter approach is frequently used to estimate the solubility of nonpolar solutes in systems containing only nonspecific interactions[29]

$$RT \ln(a_A^{solid}/X_A^{sat}) = \bar{V}_A(1 - \phi_A^{sat})^2(\delta_A - \delta_{Solvent})^2 \tag{3}$$

where δ_A and $\delta_{Solvent}$ refer to the solubility parameters of the solute and solvent, respectively. Theoretical derivation of Eq. 3 required the assumption that the interaction energy between unlike molecules is

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Table 2 Molar volumes and solubility parameters of carbazole, dibutyl ether and alkane solvents

Component (i)	$\bar{V}_i$(cm^3/mol)	δ_i(cal/cm^3)$^{1/2}$ [a]
n-Hexane	131.51	7.27
n-Heptane	147.48	7.50
n-Octane	163.46	7.54
Cyclohexane	108.76	8.19
Cyclooctane	134.88	8.51[b]
Dibutyl ether	170.41	7.76
Isooctane	166.09	6.86
Methylcyclohexane	128.32	7.83[c]
Carbazole	150.00[d]	10.00[d]

[a] Unless otherwise noted, solubility parameters are taken from Hoy[46].

[b] Calculated from the calorimetric data of Cox and Pilcher[47].

[c] Calculated from data in Majer *et al.*[48]

[d] Value from Anderson *et al.*[28]

given by the geometric mean of the like pairs, $\varepsilon_{12} = (\varepsilon_{11}\varepsilon_{22})^{1/2}$, which is true only for nonpolar molecules interacting *via* London forces[30].

Failure of Eq. (3) to describe the thermodynamic behavior of complexing systems is fairly well-documented in the chemical literature. In fact, researchers often go so far as to imply that failure of Eq. (3) to qualitatively describe a particular system suggests that complexation occurs. Comparison of solubility parameters listed in Table 2 reveals that the mole fraction solubility of carbazole in cyclohexane ($\delta = 8.19$), cyclooctane ($\delta = 8.51$) and methylcyclohexane ($\delta = 7.83$) should be greater than its solubility in dibutyl ether ($\delta = 7.76$). However, the observed solubility is 16–28 times higher in dibutyl ether than in the three cycloalkanes, a result that cannot be accounted for by solubility parameter theory but is readily explainable by assuming the formation of carbazole-dibutyl ether association complexes. Spectroscopic studies of carbazole with similar ethers, such as tetrahydrofuran[31,32] and dipropyl ether[33], also suggest complexation between carbazole and dibutyl ether.

SIMPLE STOICHIOMETRIC COMPLEXATION MODELS

Stoichiometric complexation models have been used frequently to quantitatively explain enhanced solubilities of a polar organic solute in binary mixtures containing an inert hydrocarbon and a polar cosolvent.

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The basic model assumes complexation between the solute, A, and an interacting cosolvent, C[28, 34–37]:

$$A_1 + C_1 \rightleftharpoons AC \xrightleftharpoons{+C_1} AC_2 \xrightleftharpoons{+C_1} AC_3 \cdots AC_n$$

Each reaction is described by an appropriate equilibrium constant with concentrations expressed in molarities:

$$K^c_{AC} = \frac{C_{AC}}{C^{sat}_{A_1} C_{C_1}} \tag{4}$$

$$K^c_{AC_n} = \frac{C_{AC_n}}{C_{AC_{n-1}} C_{C_1}} \tag{5}$$

where $C^{sat}_{A_1}$ is the saturation solubility of solute in pure inert hydrocarbon (assumed to represent the free solute concentration in binary mixtures as well) and C_{C_1} is the free (uncomplexed) ligand concentration. This particular model assumes only a single solute molecule is present in each complex, but the mathematical form of the resulting equations is not significantly altered by additional solute molecules per complex. Furthermore, the model requires that all equilibrium constants be independent of binary solvent compositions upto and including the pure dibutyl ether complexing solvent.

The total solubility of solute in any system, C^{sat}_A, can be expressed as:

$$C^{sat}_A = C^{sat}_{A_1} + K^c_{AC} C^{sat}_{A_1} C_{C_1} + K^c_{AC} K^c_{AC_2} C^{sat}_{A_1} C^2_{C_1} + \cdots \tag{6}$$

and the total concentration of complexing agent, C_C, as:

$$C_C = C_{C_1} + K^c_{AC} C^{sat}_{A_1} C_{C_1} + 2K^c_{AC} K^c_{AC_2} C^{sat}_{A_1} C^2_{C_1} + \cdots \tag{7}$$

If only 1:1 solute-solvent complexes are present, Eqs (6) and (7) can be combined to give:

$$\begin{array}{c}\text{Fractional change}\\ \text{in solubility}\end{array} = \frac{C^{sat}_A - C^{sat}_{A_1}}{C^{sat}_{A_1}} = \frac{K^c_{AC} C_C}{1 + K^c_{AC} C^{sat}_{A_1}} \tag{8}$$

and a plot of the fractional change in solubility versus added ligand gives a straight line, with the equilibrium constant calculated from the slope.

Direct graphical evaluation of equilibrium constants is also possible for systems having both 1:1 and 1:2 solute-solvent complexes. Suitable mathematical manipulations of Eqs (6) and (7) result in:

$$\frac{C^{sat}_A - C^{sat}_{A_1}}{C_C - 2(C^{sat}_A - C^{sat}_{A_1})} = \alpha + \beta[C_C - 2(C^{sat}_A - C^{sat}_{A_1})] \tag{9}$$

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where $\alpha = K^c_{AC}C^{sat}_{A_1}/(1 - K^c_{AC}C^{sat}_{A_1})$ and $\beta = K^c_{AC}K^c_{AC_2}C^{sat}_{A_1}/(1 - K^c_{AC}C^{sat}_{A_1})^2$. Plots of the left-hand side of Eq. (9) versus $C_C - 2(C^{sat}_A - C^{sat}_{A_1})$ gives a straight line. The two equilibrium constants, K^c_{AC} and $K^c_{AC_2}$, are easily calculated from the slope and intercept.

Figures 1 and 2 depict the graphical determination of potential equilibrium constants calculated from Eqs (8) and (9) for carbazole solubilities in binary mixtures containing dibutyl ether. Numerical values of the association constants, along with the specific model used and statistical information, are listed in Table 3. Association constants calculated from a 1:1 stoichiometric complexation model vary appreciably with cosolvent, irrespective of whether the least-squared line was forced to pass through the origin as required by Eq. (8). Assumption of

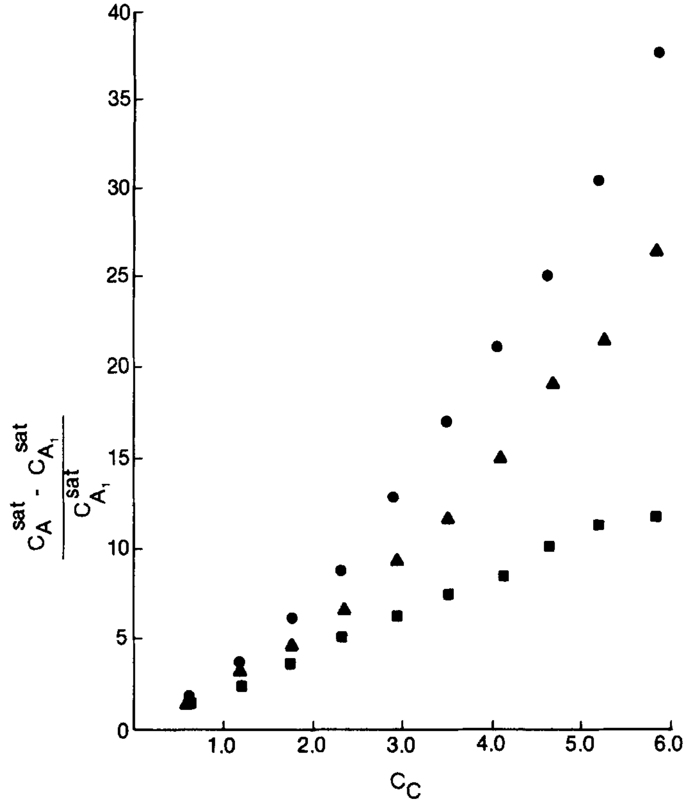

Figure 1 Graphical determination of K^c_{AC} association constant for presumed AC carbazole-dibutyl ether molecular complex in isooctane (●), cyclooctane (■) and *n*-hexane (▲) cosolvents. Deviations from linearity, noted in both isooctane and *n*-hexane, are explained by higher-order AC_n complexes (see Eqs (8) and (9)).

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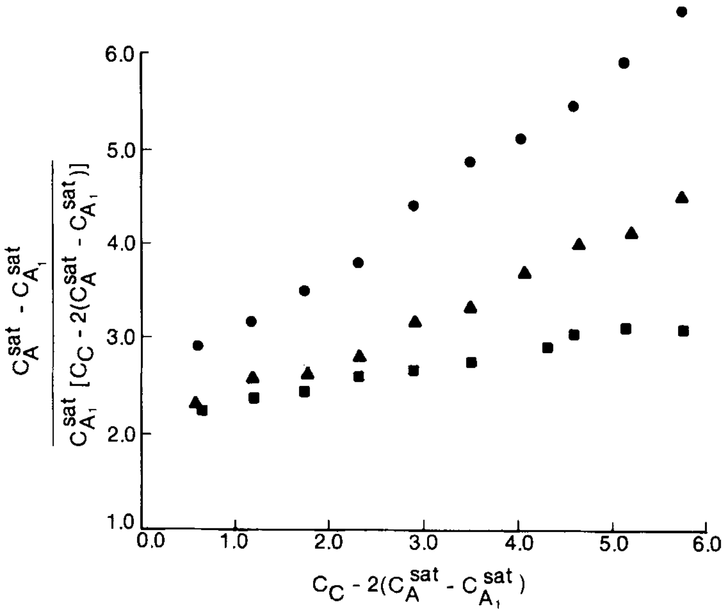

Figure 2 Graphical determination of both K_{AC}^c and $K_{AC_2}^c$ constants for presumed carbazole-dibutyl ether molecular complexes in isooctane (●), *n*-hexane (▲) and methylcyclohexane (■) *via* Eq. (9).

Table 3 Association constants for presumed carbazole-dibutyl ether complexes calculated from solubility data

	Equation (8)			Equation (9)		
Inert cosolvent	K_{AC}^c (M^{-1})	K_{AC}^c $(M^{-1})^b$	r^a	K_{AC}^c (M^{-1})	$K_{AC_2}^c$ (M^{-1})	r^a
n-Hexane	4.74	3.90	0.987	1.93	0.225	0.991
n-Heptane	4.24	3.50	0.988	1.72	0.232	0.995
n-Octane	4.19	3.44	0.990	1.96	0.180	0.992
Cyclohexane	2.87	2.64	0.997	2.10	0.0589	0.958
Methylcyclohexane	3.29	2.96	0.997	2.13	0.0879	0.992
Cyclooctane	2.08	2.10	0.998	2.13	0.00142	—
Isooctane	6.77	5.47	0.986	2.33[c]	0.301[c]	0.996

[a] Correlation coefficient.

[b] Least squares through origin.

[c] Literature values of $K_{AC}^c = 2.5\ M^{-1}$ and $K_{AC_2}^c = 0.25\ M^{-1}$ from Anderson *et al.*[28]. These values were obtained using the simplex method of least squares.

a second carbazole-dibutyl ether complex did reduce the variation in the first step-wise association constant, but at the expense of variation in $K^c_{AC_2}$. Least-squares analysis of solubility data indicated that the AC_2 complex is negligible in the case of cyclooctane where $K^c_{AC_2} = 0.00142\ M^{-1}$, while for the isooctane cosolvent the value of $K^c_{AC_2} = 0.301\ M^{-1}$ corresponds to the AC_2 complex contributing to approximately 57% of the total solubility enhancement at a dibutyl ether concentration of 4.08 M. Inspection of Figure 1 further reveals that a plot of the fractional change in solubility versus dibutyl ether concentration is concave upwards for both isooctane and the three *n*-alkanes as would be expected in systems having more than a single AC solute-solvent complex. In comparison, the plots are nearly linear for the cycloalkane cosolvents and introduction of a second complex does not significantly improve the correlation.

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The stoichiometric complexation model considered here requires that each equilibrium constant be independent of solvent composition. Different numerical values of K^c_{AC} (and $K^c_{AC_2}$) for each cosolvent studied give a nonunique description for the behavior of carbazole in pure dibutyl ether, thus violating basic assumptions used in deriving Eqs. (8) and (9). Failure to include all carbazole-dibutyl ether complexes in solution may cause the observed variation in the equilibrium constants. From structural considerations it does not seem reasonable to postulate the formation of higher-order AC_n complexes, and the very limited molar solubility of carbazole makes it improbable that an appreciable concentration of A_2C complex would be present. Rather, it is more likely that variation in association constants results from ignored nonspecific interactions which may play an important role in determining the total nonideality of the solution.

EXTENDED NIBS MODEL

Nonspecific interactions can be incorporated into the equilibrium constant calculation using Eq. (1) derived from the NIBS model. Despite the complex appearance of Eq. (1), its predictive application to solubilities in mixed solvents is relatively straightforward, and is similar in concept to the numerical example presented in an earlier paper[38] for systems containing only nonspecific interactions. The quantities $(\Delta\bar{G}_A^{fh})_B^*$ and $(\Delta\bar{G}_A^{fh})_C^*$ are calculated from the volume fraction solubility of the solid in the pure solvents using an *assumed* value for the equilibrium constant. These quantities, along with the excess Gibbs free energy of the binary solvent mixture (usually obtained from the

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literature), are then used in Eq. (1) to calculate $\phi_{A_1}^{sat}$ *via* a reiterative approach. The entire procedure can be repeated until one obtains the numerical value of K_{AC}^{ϕ} which best describes the experimental solubility in a particular binary solvent mixture.

When the solubility is sufficiently small, $\phi_A^{sat} \approx 0$ and $1 - \phi_A^{sat} \approx 1$, very reasonable estimates of K_{AC}^{ϕ} are often obtainable from a simplified form of Eq. (1) relating the overall solute solubility in the binary solvent mixture to the solubility in the two pure solvents, $(\phi_A^{sat})_B$ and $(\phi_A^{sat})_C$:

$$\ln \phi_A^{sat} = \phi_B^0 \ln(\phi_A^{sat})_B + \phi_C^0 \ln(\phi_A^{sat})_C + \ln[1 + \bar{V}_A K_{AC}^{\phi} \phi_C^0/(\bar{V}_A + \bar{V}_C)]$$
$$- \phi_C^0 \ln[1 + \bar{V}_A K_{AC}^{\phi}/(\bar{V}_A + \bar{V}_C)] + \frac{\bar{V}_A \Delta\bar{G}_{BC}^{fh}}{RT(X_B^0 \bar{V}_B + X_C^0 \bar{V}_C)} \qquad (10)$$

To calculate the equilibrium constant, one substitutes the solute solubility at a particular solvent composition (e.g. $\phi_C = 0.5$) into Eq. (10) and solves the resulting mathematical expression for K_{AC}^{ϕ}. For example, if one wished to evaluate the carbazole-dibutyl ether association constant from the solubility in the dibutyl ether + *n*-octane system at $X_C^0 = 0.4902$ ($\phi_C^0 = 0.5006$), one solves Eq. (10) using values of $(\phi_A^{sat})_C = 0.004414$, $(\phi_A^{sat})_B = 0.000182$ and $\phi_A^{sat} = 0.001676$ based on the ideal molar volume approximation, and $\Delta\bar{G}_{BC}^{fh} = 2.16$ cal/mole estimated from the solubility parameter approach

$$\Delta\bar{G}_{BC}^{ex} = \phi_B^0 \phi_C^0 (X_B^0 \bar{V}_B + X_C^0 \bar{V}_C)(\delta_B - \delta_C)^2 \qquad (11)$$

$$\Delta\bar{G}_{BC}^{fh} = \Delta\bar{G}_{BC}^{ex} + RT[\ln(X_B^0 \bar{V}_B + X_C^0 \bar{V}_C) - X_B^0 \ln \bar{V}_B - X_C^0 \ln \bar{V}_C] \qquad (12)$$

The calculated value of the association constant is $K_{AC}^{\phi} = 23.0$, which differs slightly from an "optimized" $K_{AC}^{\phi} = 25.0$ for the *n*-octane cosolvent. The optimized equilibrium constant enabled back-calculation of the solubility data to within an average absolute deviation of 1.7%, compared to a value of 3.5% for $K_{AC}^{\phi} = 23.0$. Deviations of this magnitude are comparable to those noted in earlier papers[22,23,38–44] documenting the ability of the basic NIBS model to predict iodine, naphthalene, benzil, *p*-dibromobenzene, stannic iodide, *p*-benzoquinone, anthracene, biphenyl, pyrene and benzoic acid in systems containing only nonspecific interactions.

Table 4 lists numerical values of the carbazole-dibutyl ether association constant calculated *via* Eq. (10). Inspection of Table 4 reveals that the optimized constants do vary slightly from a value of $K_{AC}^{\phi} = 22$ in *n*-heptane to $K_{AC}^{\phi} = 30$ in isooctane. Part of the observed variation in K_{AC}^{ϕ} may arise from the manner in which experimental uncertainties are propagated in the extended NIBS model. It must be remembered that four measured quantities are needed to calculate the equilibrium

Table 4 Association constant for presumed carbazole-dibutyl ether complex calculated from the extended NIBS model.

Inert Cosolvent	K^{ϕ}_{AC}	K^{c}_{AC}	Deviation (%)[a]
n-Hexane	24.0	1.91	2.0
n-Heptane	22.0	1.76	1.8
n-Octane	25.0	1.99	1.7
Cyclohexane	24.0	1.91	2.2
Methylcyclohexane	26.0	2.07	1.8
Cyclooctane	25.0	1.99	2.1
Isooctane	30.0	2.39	1.7

[a] Deviation (%) = $(100/N) \sum |\ln (X_A^{calc}/X_A^{exp})|$

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constant. Carbazole solubility in each pure solvent and binary solvent mixture was reproducible to within ±2%, and the estimated $\Delta\bar{G}^{fh}_{BC}$ values are believed to be accurate to ±20 cal/mol. Lack of experimental Gibbs free energies of mixing for the binary dibutyl ether + alkane solvent mixtures necessitated that all $\Delta\bar{G}^{fh}_{BC}$ values be estimated by the solubility parameter model. Furthermore, Eq. (10) is derived from the basic NIBS model[39,45] and any errors in predicting the nonspecific interaction contributions, which are perhaps as large as 4–5%, would carry over into the equilibrium constant calculation. A calculated carbazole-dibutyl ether association constant of $K^{\phi}_{AC} = 22$ in the *n*-heptane cosolvent may be identical, at least within the limitations of the extended NIBS model, to a value of $K^{\phi}_{AC} = 26$ in the cyclooctane cosolvent. Based on these observations, we believe that the extended NIBS model does provide a more realistic description of the thermochemical properties of carbazole in binary dibutyl ether + alkane solvent mixtures than did the very simple stoichiometric complexation model discussed previously. As noted in Table 3 K^{c}_{AC} association constants calculated *via* Eq. (8) differed by as much as 325% in the seven alkane cosolvents studied.

It is possible to show the importance of including nonspecific interactions by comparing association constants calculated from Eq. (8) (nonspecific interactions ignored) and Eq. (10) (nonspecific interactions included). Although the numerical value of $K^{\phi}_{AC} = 30$ for isooctane is much larger than the equilibrium constant $K^{c}_{AC} = 6.77$ used in Eq. (8), direct comparison requires both constants to be based on an identical concentration scale. Doing this conversion:

$$K^{c}_{AC} = K^{\phi}_{AC} \bar{V}_A \bar{V}_C / (\bar{V}_A + \bar{V}_C)$$

one finds that the molarity-based equilibrium constant of Eq. (8) ($K^c_{AC} = 6.77\ M^{-1}$) is actually over 2 times greater than the molarity-based equilibrium constant of Eq. (10) ($K^c_{AC} = 2.39\ M^{-1}$). These calculations further support earlier contentions[22,24] that equilibrium constants determined from solution models based entirely on specific interactions may not truly represent specific solute-solvent interactions, but rather, in some cases, the failure of the particular solution model to properly describe nonspecific interactions. This comparison, combined with an earlier solubility study involving the weaker iodine-benzene complex[25], also shows that nonspecific interactions can be important irrespective of the strength of the solute-solvent complexation.

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