Thermochemical Investigations of Hydrogen-Bonded Solutions: Part 12. Development of Expression for Predicting Solute Solubility in Binary Alcohol Water Solvent Mixtures Based Upon Mobile Order Theory

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THERMOCHEMICAL INVESTIGATIONS OF HYDROGEN-BONDED SOLUTIONS: PART 12. DEVELOPMENT OF EXPRESSION FOR PREDICTING SOLUTE SOLUBILITY IN BINARY ALCOHOL + WATER SOLVENT MIXTURES BASED UPON MOBILE ORDER THEORY

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The unconventional solution model of Mobile Order, which has previously been shown to provide a very accurate thermodynamic description of anthracene and pyrene solubilities in binary hydrocarbon + alcohol and alcohol + alcohol solvent mixtures, is extended to aqueous-alcohol solvent systems. An expression is derived for predicting the solubility of an inert crystalline solute in binary alcohol + water mixtures from measured solubilities in both neat liquid solvents plus hydrogen-bonding stability constants. Applications and limitations of the newly-derived equation are assessed using published solubility for 4-chlorobiphenyl dissolved in binary methanol + water, ethanol + water and 1-propanol + water solvent mixtures.

Keywords: Solubility predictions; hydrogen-bonding; binary solvent mixtures; Mobile Order theory.

INTRODUCTION

This work continues a systematic search for mixing models which will provide reasonable mathematical descriptions of the thermochemical

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properties of ternary nonelectrolyte solutions which contain compo-
nents capable of self-association. To date, we have examined both the
application and limitations of Mobile Order theory to describe the
solubilities of anthracene dissolved in 24 different binary alcohol + al-
kane, [1] 35 binary alcohol + alcohol, [2–4] and 32 binary alco-
hol + 2-alkoxyethanol solvent mixtures, [5] and of pyrene dissolved in
24 binary alcohol + alcohol solvent mixtures. [6] The basic model
[7–16] assumes all molecular groups perpetually move in the liquid,
and that neighbors of a given external atom in a molecule constantly
change identity. All molecules of a given kind dispose of the same
volume, equal to the total volume V of the liquid divided by the
number N_A molecules of the same kind, ie., Dom $A = V/N_A$. The
center of this domain perpetually moves. Highest mobile disorder is
achieved whenever groups visit all parts of their domain without pref-
erence. Preferential contacts lead to deviations with respect to this
"random" visiting. This is especially true in the case of hydrogen-
bonding which requires that a hydroxylic hydrogen atom follow most
of the time the proton acceptor group of a neighboring molecule in its
walk through the liquid, thus originating a kind of "mobile order".

The thermodynamics of Mobile Order expresses the equilibrium
condition in terms of time fractions for the time schedule of a given
molecule, and not in terms of concentrations of various entities in the
ensemble. Thus, in the case of alcohols and alkoxyalcohols one con-
siders the time fraction $\gamma_{Ch.}$ and not the concentrations of the various
i-mers in the ensemble (this does not mean that these *i*-mers do not
exist, but their concentrations do not govern the thermodynamic
probability). $\gamma_{Ch.}$ is the fraction of the time during which a given
molecule of the ensemble is free from H-bonding, this means; does not
possess the energy of the H-bond. But it is by no means the fraction of
the time during which the molecule is free at both sides. A molecule
bonded at one side is free from H-bonding only half of the time.

For an inert crystalline solute dissolved in a binary alcohol
(B) + alcohol (C) or alcohol (B) + 2-alkoxyethanol (C) solvent mixture
the volume fraction saturation solubility (ϕ_A^{sat}) is given by: [2, 5]

$$RT \left\{ \ln(a_A^{solid}/\phi_A^{sat}) - 0.5[1 - V_A/(x_B^0 V_B + x_C^0 V_C)] \right.$$

$$+ 0.5 \ln [V_A/(x_B^0 V_B + x_C^0 V_C)] - (V_A/V_B) \phi_B^0 [\phi_B^0 (K_B/V_B)$$

$$+ \phi_C^0(K_{BC}/V_C)]/[1 + \phi_B^0(K_B/V_B) + \phi_C^0(K_{BC}/V_C)]$$

$$- (V_A/V_C)\phi_C^0[\phi_B^0(K_{CB}/V_B) + \phi_C^0(K_C/V_C)]/[1 + \phi_B^0(K_{CB}/V_B)$$

$$+ \phi_C^0(K_C/V_C)]\}$$

$$= V_A[\phi_B^0(\delta_A' - \delta_B')^2 + \phi_C^0(\delta_A' - \delta_C')^2 - \phi_B^0\phi_C^0(\delta_B' - \delta_C')^2] \quad \text{(Eqn.1)}$$

whenever the saturation solubility is sufficiently low that $1 - \phi_A^{\text{sat}} = 1.0$. The symbols δ_A', δ_B' and δ_C' denote the modified solubility parameters of the solute and self-associating alcohols, respectively. The remaining symbols are defined in detail in the Appendix. Contributions from nonspecific inter-actions are incorporated into Mobile Order theory through the $V_A[\phi_B^0(\delta_A' - \delta_B')^2 + \phi_C^0(\delta_A' - \delta_C')^2 - \phi_B^0\phi_C^0(\delta_B' - \delta_C')^2]$ term. Through suitable mathematical manipulations, the $V_A\phi_B^0(\delta_A' - \delta_B')^2$ and $V_A\phi_C^0(\delta_A' - \delta_C')^2$ terms were eliminated from the basic model in favor of measured solubility data in both pure solvents, $(\phi_A^{\text{sat}})_B$ and $(\phi_A^{\text{sat}})_C$. The final derived expression

$$\ln \phi_A^{\text{sat}} = \phi_B^0 \ln(\phi_A^{\text{sat}})_B + \phi_C^0 \ln(\phi_A^{\text{sat}})_C$$

$$- 0.5 [\ln(x_B^0 V_B + x_C^0 V_C) - \phi_B^0 \ln V_B - \phi_C^0 \ln V_C]$$

$$- (V_A/V_B)\phi_B^0[\phi_B^0(K_B/V_B) + \phi_C^0(K_{BC}/V_C)]/[1 + \phi_B^0(K_B/V_B)$$

$$+ \phi_C^0(K_{BC}/V_C)] + (V_A K_B \phi_B^0/V_B^2)(1 + K_B/V_B)^{-1}$$

$$- (V_A/V_C)\phi_C^0[\phi_B^0(K_{CB}/V_B) + \phi_C^0(K_C/V_C)]/[1 + \phi_B^0(K_{CB}/V_B)$$

$$+ \phi_C^0(K_C/V_C)] + (V_A K_C \phi_C^0/V_C^2)(1 + K_C/V_C)^{-1}$$

$$+ V_A \phi_B^0 \phi_C^0 (\delta_B' - \delta_C')^2 (RT)^{-1} \quad \text{(Eqn. 2)}$$

does not require a prior knowledge of the solute's enthalpy of fusion and melting point temperature, which would be needed to calculate the numerical value of a_A^{solid} at the temperature corresponding to the solubility measurements.

Four previous papers [2–4, 6] have shown that Eqn. (2) provides very reasonable predications of the saturated mole fraction solubilities

of both anthracene and pyrene dissolved in binary alcohol + alcohol solvent mixtures using a single equilibrium constant of $K_B = K_C = 5,000$ cm^3 mol^{-1} for self-association and of $K_{BC} = K_{CB} = 5,000$ cm^3 mol^{-1} for heterogeneous H-bond chain formation. The overall average absolute deviations between predicted and observed solubilities were 1.6% and 2.2%, respectively, for anthracene and pyrene. More recently, McHale et al. [5] showed that Mobile Order theory provided reasonably accurate predications for anthracene solubility in 32 different binary alcohol + 2-alkoxyethanol solvent mixtures. Here, the 2-alkoxyethanol cosolvent was treated as a pseudo-monofunctional alcohol, with hydrogen-bond formation occurring largely through the hydroxylic OH group, rather than the oxygen ether linkage. All homogeneous self-association and heterogeneous cross-association stability constants were again set equal to $K_i = 5,000$ cm^3 mol^{-1}. Acree [17] and Pandey et al. [18] successfully extended Mobile Order theory to excess enthalpies of ternary hydrocarbon + hydrocarbon + alcohol and hydrocarbon + alcohol + alcohol systems. Several published papers [2–4, 6, 19–23] have further documented that the predictive accuracy of Mobile Order theory equations are often comparable to (and sometimes even superior than) the corresponding expressions derived from the more conventional thermodynamic treatments such as the Nearly Ideal Binary Solvent (NIBS), Extended NIBS, Wilson, Mecke-Kempter and Kretschmer-Wiebe models.

Although most of the afore-mentioned studies have involved either neat alcohols or binary alkane + alcohol and alcohol + alcohol mixtures, a few recent applications [13,24] considered the more complex aqueous solutions. Unlike alcohols, the water molecule possesses two protons capable of hydrogen-bond participation. When all of oxygen's first electron pairs have found hydroxylic protons for their hydrogen-bonding, the second set of electron pairs still have numerous hydroxylic protons at their disposal. Thus, in water a second insertion must be considered, though admittedly with a considerably smaller stability constant. Electron donor power of the water molecule is weakened by the first hydrogen-bond. [25]

In the present study we explore the applicability of using Mobile Order theory to describe the thermochemical behavior of an inert solute dissolved in aqueous-alcohol solvent mixtures. A relatively

simple expression is derived for predicting saturation solubility from measured solute solubilities in both pure solvents plus assumed numerical values for all stability constants. Applicability of the newly-derived equation is evaluated using published solubility data for 4-chlorobiphenyl dissolved in binary methanol + water, ethanol + water and 1-propanol + water solvent mixtures. [26] The three systems considered should provide a very demanding test of the application and limitations of Mobile Order theory as the experimental mole fraction solubilities cover up to a 3×10^5-fold range. The present investigation differs from that of Nelis and coworkers [13] in that nonspecific interactions are incorporated into the basic thermodynamic model. Moreover, data interpretation is not complicated by the presence of a second immiscible liquid phase as was the case in the liquid-liquid equilibrium study of Nelis et al.

DEVELOPMENT OF PREDICTIVE EXPRESSION

Essential features of Mobile Order theory, pertaining to a ternary mixture containing an inert solute (component A), an alcohol cosolvent (component B) and water (component W), will be briefly reviewed to facilitate development of the final derived equation. The Gibbs free energy of mixing for the ternary solution is separated into three contributions:

$$\Delta G_{ABW}^{mix} = (\Delta G_{ABW})_{conf} + (\Delta G_{ABW})_{chem} + (\Delta G_{ABW})_{phys} \quad \text{(Eqn. 3)}$$

The first term describes the configurational entropy based upon the Huyskens and Haulait-Pirson [27] definition of solution ideality

$$(\Delta G_{ABW})_{conf} = (0.5) RT [n_A \ln \phi_A + n_B \ln \phi_B$$

$$+ n_W \ln \phi_W + n_A \ln x_A + n_B \ln x_B + n_W \ln x_W] \quad \text{(Eqn. 4)}$$

whereas the latter two terms in Eqn. (3) result from formation of hydrogen-bonded complexes and weak nonspecific physical interactions in the ternary solution, respectively.

The chemical contribution depends upon

$$(\Delta G_{ABW})_{chem} = n_B\,RT \ln{(\gamma_{Bh:}/\gamma^{\circ}_{Bh:})} + n_w\,RT \ln{(\gamma_{Wh:}/\gamma^{\circ}_{Wh:})} \quad \text{(Eqn. 5)}$$

the time fractions that the hydroxylic protons are free in the ternary mixture ($\gamma_{Bh:}$ and $\gamma_{Wh:}$) and in the neat alcohol ($\gamma^{\circ}_{Bh:}$) and water ($\gamma^{\circ}_{Wh:}$). Readers will note that $(\Delta G_{ABW})_{chem}$ is determined relative to the pure liquid solvents in accordance with standard thermodynamic practice. The maximum possible number of hydrogen bonds is governed by the functional groups present and the characteristics of the self-associating components. Alcohols have one hydrogen "donor" site and the lone pairs on the oxygen atom provide two "acceptor" sites. In principal the second electron pair could be used for hydrogen-bonding. Electron donor power of the alcohol molecule is weakened by the first hydrogen-bond. The hydroxylic proton of an alcohol molecule will in general give the preference to the first pair of the oxygen atom, and under such circumstances the second pair of electrons of an alcohol molecule in the liquid will have difficulty finding a partner unless the second cosolvent has unsatisfied donor sites.

Water, on the other hand, has two hydrogen "donor" sites and the lone pairs on the oxygen atom provide two "acceptor" sites. Unlike alcohols, hydrogen-bonding is not complete when all of the first electron pairs have found hydroxylic protons for their hydrogen-bonding. The second electron pairs on water (and for that matter on the alcohol) still have numerous hydroxylic protons at their disposal. Thus, in water a second insertion must be considered, though with a considerably smaller stability constant. It can be readily shown that this set of conditions leads to the following expression for the Gibbs free energy for the hydrogen-bonding contribution: [13]

$$(\Delta G_{ABW})_{chem} = n_B\,RT \ln{\{(1 + K^*_B/V_B)/[1 + K_B((\phi_B/V_B) + (\phi_W/V_W))]\}}$$

$$+ n_W\,RT \ln{\{[1 + (K^*_{W1}/V_W) + (K^*_{W1}K^*_{W2}/V_W^2)]/}$$

$$[1 + K_{W1}((\phi_B/V_B) + (\phi_W/V_W))$$

$$+ K_{W1}K_{W2}((\phi_B/V_B) + (\phi_W/V_W))^2]\} \qquad \text{(Eqn. 6)}$$

where the time fractions in the ternary solution

$$\gamma_{Bh} = 1/\{1 + K_B[(\phi_B/V_B) + (\phi_W/V_W)]\} \qquad \text{(Eqn. 7)}$$

$$\gamma_{Wh} = 1/\{1 + K_{W1}[(\phi_B/V_B) + (\phi_W/V_W)]$$

$$+ K_{W1}K_{W2}[(\phi_B/V_B) + (\phi_W/V_W)]^2\} \qquad \text{(Eqn. 8)}$$

and in the pure liquids

$$\gamma^*_{Bh} = 1/[1 + (K^*_B/V_B)] \qquad \text{(Eqn. 9)}$$

$$\gamma^*_{Wh} = 1/[1 + (K^*_{W1}/V_W) + (K^*_{W1}K^*_{W2}/V_W^2)] \qquad \text{(Eqn. 10)}$$

are given by Eqns. (7)–(10). Both cosolvents are allowed to form self-associated species and to participate in the formation of hetero-geneous cross-associated H-bonded linear chains. As a simplifying approximation, only the first electron pair on the alcoholic oxygen atom is counted when determining the number of available "acceptor" sites for hydrogen-bond formation. This particular assumption may need to be revisited at a later data. Inherent in the above treatment is the additional provision that the stability/equilibrium constants in the ternary mixture (K_B, K_{W1} and K_{W2}) are not necessarily equal to the values in the neat solvents, which are denoted by the superscript (*). The earlier study of Nelis *et al.* [13] suggested that water's much smaller second equilibrium constant, K_{W2}, was slightly larger in aqueous-alcohol mixtures that in neat water. The authors noted a slight compositional dependence in K_{W2} in the case of the secondary and tertiary alcohols studied. At this time no special significance is given to the authors' observations as their thermodynamic model complete-ly neglected nonspecific interactions. Incorporation of nonspecific interactions may significantly alter this earlier conclusion.

Physical nonspecific interactions are expressed in terms of the Scatchard-Hildebrand solubility parameter type model

$$(\Delta G_{ABW})_{phys} = (n_A V_A + n_B V_B + n_W V_W)[\phi_A\phi_B(\delta'_A - \delta'_B)^2$$

$$+ \phi_A\phi_W(\delta'_A - \delta'_W)^2 + \phi_B\phi_W(\delta'_B - \delta'_W)^2] \qquad \text{(Eqn. 11)}$$

Modified solubility parameters, δ_i', account for only nonspecific inter-actions, and in the case of both water and alcohol solvents, the hydro-gen-bonding contributions were removed. Numerical values of δ_i' are available in several published compilations, [9-11] and were either estimated using known values for similar solvents or deduced by re-gressing experimental solubility data of solid n-alkanes in organic solvents and in water in accordance with the configurational entropic model of Huyskens and Haulait-Pirson. [27] Any errors or uncertain-ties in the measured alkane data would naturally affect the calculated numerical values of δ_i', as would any shortcomings of the Huyskens and Haulait-Pirson model to back-calculate the observed mole frac-tion solubilities.

Combining Eqns. (3), (4), (6) and (11), the Gibbs free energy of mixing (per stoichiometric mole of mixing) is written as

$$\Delta G_{ABW}^{mix} = (0.5)\,RT\,[n_A \ln \phi_A + n_B \ln \phi_B + n_W \ln \phi_W + n_A \ln x_A$$

$$+ n_B \ln x_B + n_W \ln x_W] + n_B\,RT \ln \{(1 + K_B^*/V_B)/[1 + K_B((\phi_B/V_B)$$

$$+ (\phi_W/V_W))]\} + n_W\,RT \ln \{[1 + (K_{W1}^*/V_W)$$

$$+ (K_{W1}^* K_{W2}^*/V_W^2)]/[1 + K_{W1}((\phi_B/V_B) + (\phi_W/V_W))$$

$$+ K_{W1} K_{W2}((\phi_B/V_B) + (\phi_W/V_W))^2]\}$$

$$+ (n_A V_A + n_B V_B + n_W V_W)\,[\phi_A \phi_B(\delta_A' - \delta_B')^2$$

$$+ \phi_A \phi_W(\delta_A' - \delta_W')^2 + \phi_B \phi_W(\delta_B' - \delta_W')^2] \qquad \text{(Eqn. 12)}$$

Thermodynamic principles relate solubility to chemical potential. For a system obeying Eqn. (12) the solubility of a sparingly soluble crystal-line solute ($\phi_A^{sat} = 0$) is

$$RT \ln a_A^{solid} = RT \{\ln \phi_A^{sat} + 0.5\,[1 - V_A/(x_B^0 V_B + x_W^0 V_W)]$$

$$+ 0.5 \ln [V_A/(x_B^0 V_B + x_W^0 V_W)]\} + RT\,\phi_B^0\,(V_A/V_B)\,K_B[(\phi_B^0/V_B)$$

$$+ (\phi_W^0/V_W)]/\{1 + K_B(\phi_B^0/V_B) + (\phi_W^0/V_W)]\}$$

$$+ RT \phi_W^0 (V_A/V_W)/\{1 + K_{W1}[(\phi_B^0/V_B) + (\phi_W^0/V_W)]$$

$$+ 2 K_{W1} K_{W2}[(\phi_B^0/V_B) + (\phi_W^0/V_W)]^2\}/\{1 + K_{W1}[(\phi_B^0/V_B)$$

$$+ (\phi_W^0/V_W)] + K_{W1} K_{W2}[(\phi_B^0/V_B) + (\phi_W^0/V_W)]^2\}$$

$$+ V_A[\phi_B^0 (\delta_A' - \delta_B')^2 + \phi_W^0 (\delta_A' - \delta_W')^2$$

$$- \phi_B^0 \phi_W^0 (\delta_B' - \delta_W')^2] \qquad \text{(Eqn. 13)}$$

obtained by differentiating ΔG_{ABW}^{mix} with respect to n_A. In the above expression the superscript ($^\circ$) denotes the initial binary solvent compositions calculated as if the solute were not present, and a_A^{solid} is the activity of the solid solute. This latter quantity is defined as the ratio of the fugacity of the solid to the fugacity of the pure hypothetical sub-cooled liquid. The numerical value of a_A^{solid} can be computed from

$$\ln a_A^{solid} = - \Delta H_A^{fus}(T_{mp} - T)/(RTT_{mp})$$

$$+ \Delta C_p (T_{mp} - T)/RT - (\Delta C_p/R) \ln (T_{mp}/T) \qquad \text{(Eqn. 14)}$$

the molar enthalpy of fusion, ΔH_A^{fus}, at the normal melting point temperature, T_{mp}, and the difference between molar heat capacities of the solid and hypothetical sub-cooled liquid, ΔC_p.

Careful examination of Eqn. (13) reveals that the $(\delta_A' - \delta_B')^2$ and $(\delta_A' - \delta_W')^2$ terms can be eliminated from the basic model via

$$RT \ln a_A^{solid} = RT \{\ln (\phi_A^{sat})_B + 0.5(1 - V_A/V_B) - 0.5 \ln (V_A/V_B)$$

$$+ (V_A/V_B)(K_B^*/V_B)/[1 + (K_B^*/V_B)]\} + V_A(\delta_A' - \delta_B')^2$$
$$\text{(Eqn. 15)}$$

and

$$RT \ln a_A^{solid} = RT \{\ln (\phi_A^{sat})_W + 0.5(1 - V_A/V_W) - 0.5 \ln (V_A/V_W)$$

$$+ (V_A/V_W) [(K_{W1}^*/V_W) + 2 (K_{W1}^*/V_W)(K_{W2}^*/V_W)]/$$

$$[1 + (K_{W1}^*/V_W) + (K_{W1}^*/V_W)(K_{W2}^*/V_W)]\}$$

$$+ V_A(\delta'_A - \delta'_W)^2 \qquad\qquad (Eqn.\ 16)$$

where $(\phi_A^{sat})_B$ and $(\phi_A^{sat})_W$ denote the solubilities in the two pure solvents. Readers should note that in order for Eqn. (13) to reduce to the correct thermodynamic description of solute solubility in both neat solvents that all three mixture equilibrium/stability constants (K_B, K_{W1} and K_{W2}) must equal the pure solvent stability constants (K_B^*, K_{W1}^* and K_{W2}^*) as the mole/volume fraction of the second cosolvent approaches zero. This particular constraint can be realized in one of two ways. Either the mixture and pure solvent stability constants are equal (ie., $K_i = K_i^*$) or the mixture stability constants must be solvent dependent such that $\lim K_i = K_i^*$ as $x_i^0 \rightarrow 1$. Nelis et al. [13] suggested that water's second stability constant, K_{W2}, might be slightly larger in aqueous-alcohol mixtures than in neat water, perhaps even solvent dependent in the case of secondary and tertiary alcohols. The authors, however, failed to ensure that this limiting constraint was realized.

After removal of the $(\delta'_A - \delta'_B)^2$ and $(\delta'_A - \delta'_W)^2$ terms, a relatively simple mathematical expression is obtained for the solubility of a crystalline inert solute in a binary alcohol + water mixture:

$$RT \ln \phi_A^{sat} = RT \{\phi_B^0 \ln (\phi_A^{sat})_B + \phi_W^0 \ln (\phi_A^{sat})_W$$

$$- 0.5[\ln (x_B^0 V_B + x_W^0 V_W) - \phi_B^0 \ln V_B - \phi_W^0 \ln V_W]\}$$

$$- RT\,\phi_B^0 (V_A/V_B)\,K_B[(\phi_B^0/V_B) + (\phi_W^0/V_W)]/\{1 + K_B[(\phi_B^0/V_B)$$

$$+ (\phi_W^0/V_W)]\} + RT\,\phi_B^0 (V_A/V_B)(K_B^*/V_B)/[1 + (K_B^*/V_B)]$$

$$- RT\,\phi_W^0 (V_A/V_W)\{K_{W1}[(\phi_B^0/V_B) + (\phi_W^0/V_W)]$$

$$+ 2\,K_{W1}\,K_{W2}[(\phi_B^0/V_B) + (\phi_W^0/V_W)]^2\}$$

$$\div \{1 + K_{W1}[(\phi_B^0/V_B) + (\phi_W^0/V_W)]$$

$$+ K_{W1}\,K_{W2}[(\phi_B^0/V_B) + (\phi_W^0/V_W)]^2\}$$

$$+ RT\,\phi_W^0 (V_A/V_W)\,[(K_{W1}^*/V_W) + 2\,(K_{W1}^*/V_W)$$

$$(K^*_{W2}/V_W)]/[1 + (K^*_{W1}/V_W) + (K^*_{W1}/V_W)$$

$$(K^*_{W2}/V_W)]\} + V_A \phi^0_B \phi^0_W (\delta'_B - \delta'_W)^2 \qquad \text{(Eqn. 17)}$$

which does not require a *priori* knowledge of the solute's enthalpy of fusion and melting point temperature. Elimination of the a^{solid}_A term from the predictive equation can lead to better solubility estimates, particularly in the case of high melting solutes as ΔC_P data are not readily available in the chemical literature. Moreover, the derived expression correctly describes the solubility in both pure self-associating solvents.

RESULTS AND DISCUSSION

Despite the complex appearance of Eqn. (17) its application to solubilities in alcohol + water solvent mixtures is relatively straightforward and is similar to numerical examples presented previously (for example, see McCargar and Acree [28]). The quantities $(\phi^{sat}_A)_B$ and $(\phi^{sat}_A)_W$ are calculated from measured mole fraction solubility of the solid in the pure solvents assuming that the excess molar volume (or alternatively the volume change upon mixing) is zero. These quantities, along with the molar volumes, modified solubility parameters, and assumed values for the equilibrium constants (K_B, K_{W1} and K_{W2}), are then used in Eqn. (17) to calculate ϕ^{sat}_A at each binary solvent composition. If desired, the entire procedure can be repeated until the "best" set of equilibrium constants is found.

The chemical literature contains only limited solubility data for crystalline solutes dissolved in binary alcohol + water mixtures. Many of the systems that were found were not suitable for testing the limitations and applications of Eqn. (17) because the solutes were either ionic in nature or had polar functional groups. Such solutes were likely to form solute-solvent complexes with one or both cosolvents. Several data sets had to be eliminated from consideration because of extremely large uncertainties in the measured values or because of questionable experimental procedures such as not using high purity chemicals, not maintaining a constant equilibration temperature, or using times believed to be too short for equilibrium to be attained.

After careful evaluation of published solubility data, we selected three data sets involving 4-chlorobiphenyl dissolved in binary methanol + water, ethanol + water and 1-propanol + water mixtures. [26] The three systems selected cover up to a 3×10^5-fold range in mole fraction solubilities. 4-chlorobiphenyl is considerably more soluble in alcohols than in water. Each system contains solubility data at six different binary compositions spanning the entire volume fraction range, as well as the measured 4-chlorobiphenyl solubility in both solvents. Accuracies of the 22 experimental solubilities used are believed to be as follows: 15 data points are accurate to within 30%, 5 data points have uncertainties between 30-90% and 2 of the reported values have uncertainties greater than 90%. Stated accuracies are based upon standard deviations of replicate measurements and the 95% confidence interval calculated by the reporting authors [26].

Table I provides a summarized comparison between Mobile Order predictions and experimental solubilities for 4-chlorobiphenyl dissolved in three binary alcohol + water solvent systems. Numerical values used in the predictions include molar volumes of $V_{Water} = 18.1$ cm^3 mol^{-1}, $V_{Methanol} = 40.7$ cm^3 mol^{-1}, $V_{Ethanol} = 58.7$ cm^3 mol^{-1} and $V_{Propanol} = 75.1$ cm^3 mol^{-1}, and modified solubility parameters of $\delta'_{Water} = 20.50$ MPa$^{1/2}$, $\delta'_{Methanol} = 19.25$ MPa$^{1/2}$, $\delta'_{Ethanol} = 17.81$ MPa$^{1/2}$ and $\delta'_{Propanol} = 17.29$ MPa$^{1/2}$ for the four pure solvents. A molar volume of $V_A = 162.3$ cm^3 mol^{-1} was assumed for the hypothetical sub-cooled liquid solute. This latter value was calculated *via* a group contribution method as $V_{Chlorobiphenyl} = V_{Biphenyl} + V_{Chlorobenzene} - V_{Benzene}$; where $V_{Biphenyl} = 149.4$ cm^3 mol^{-1}.[29] Computations show that an error of $\pm 10\%$ in $V_{Chlorobiphenyl}$ affects the predicted values by only 5% (or less).

Previous studies [1-6, 13] have shown that $K_B^* = 5.000$ cm^3 mol^{-1}, $K_{W1}^* = 8,000$ cm^3 mol^{-1} and $K_{W2}^* = 180$ cm^3 mol^{-1} are reasonable values for the stability constants for pure alcohols and for water, respectively. For computational simplicity we have assumed that the two stability constants involving each solvent's first electron pair is independent of binary solvent composition, *ie.*, $K_B = K_B^*$ and $K_{W1} = K_{W1}^*$. This assumption seems reasonable in light of the fact that both stability constants are fairly large and the computations are not too sensitive to the actual number value(s) assumed. "Computational insensitivity" can be rationalized in part as follows. First, the quantities $K_B[(\phi_B^0/V_B) + (\phi_W^0/V_W)]$ and (K_B^*/V_B) are both much larger than

TABLE I   Comparison Between the Experimental 4-Chlorobiphenyl Solubilities in Binary Alcohol (B) + Water (C) Solvent Mixtures and Predicted Values Based Upon Eqn. (17) of Mobile Order Theory

ϕ_W^0	$(x_A^{sat})^{exp,a}$	$(x_A^{sat})^{calc}$	$Deviation^b$
	Methanol (B) + Water (W)		
0.00	1.44×10^{-2}	$--$	$-$
0.20	1.21×10^{-3}	1.28×10^{-3}	$+0.05$
0.40	9.31×10^{-5}	1.13×10^{-4}	$+0.19$
0.60	6.66×10^{-6}	1.03×10^{-5}	$+0.43$
0.80	5.54×10^{-7}	9.90×10^{-7}	$+0.58$
0.90	2.53×10^{-7}	3.29×10^{-7}	$+0.26$
0.95	1.80×10^{-7}	1.98×10^{-7}	$+0.10$
1.00	1.27×10^{-7}	$-----$	$---$
	Ethanol (B) + Water (W)		
0.00	3.30×10^{-2}	$--$	$--$
0.20	3.83×10^{-3}	2.58×10^{-3}	-0.40
0.40	4.08×10^{-4}	1.98×10^{-4}	-0.72
0.60	2.53×10^{-5}	1.53×10^{-5}	-0.50
0.80	7.42×10^{-7}	1.22×10^{-6}	$+0.50$
0.90	2.74×10^{-7}	3.33×10^{-7}	$+0.19$
0.95	1.86×10^{-7}	2.10×10^{-7}	$+0.12$
1.00	1.27×10^{-7}	$-----$	$---$
	1-Propanol (B) + Water (W)		
0.00	4.13×10^{-2}	$-----$	$—$
0.20	6.68×10^{-3}	3.15×10^{-3}	-0.75
0.40	1.62×10^{-3}	2.34×10^{-4}	-1.93
0.60	2.86×10^{-4}	1.72×10^{-5}	-2.80
0.80	2.54×10^{-6}	1.31×10^{-6}	-0.66
0.90	3.68×10^{-7}	3.81×10^{-7}	$+0.04$
0.95	2.09×10^{-7}	2.13×10^{-7}	$+0.02$
1.00	1.27×10^{-7}	$-----$	$—$

[a] Experimental solubilities were reported in the literature[26] in units of moles/liter. 4—Chlorobiphenyl mole fraction solubilities were calculated using molar volumes of $V_{water} = 18.1$ cm^3 mol^{-1}, $V_{Methanol} = 40.7$ cm^3 mol^{-1}, $V_{Ethanol} = 58.7$ cm^3 mol^{-1} and $V_{Propanol} = 75.1$ cm^3 mol^{-1}
[b] Deviation $= \ln(x_A^{sat})^{calc} - \ln(x_A^{sat})^{exp}$.

unity. The two terms involving the alcohol's hydrogen-bonding contribution in Eqn. (17) thus mathematically cancel one another, leading to the following much simples predictive expression:

$$RT \ln \phi_A^{sat} = RT \{ \phi_B^0 \ln (\phi_A^{sat})_B + \phi_W^0 \ln (\phi_A^{sat})_W$$

$$- 0.5 [\ln (x_B^0 V_B + x_W^0 V_W) - \phi_B^0 \ln V_B$$

$$\phi_W^0 \ln V_W]\} - RT\,\phi_W^0\,(V_A/V_W)\{\,K_{W1}[(\phi_B^0/V_B)$$

$$+ (\phi_W^0/V_W)] + 2\,K_{W1}K_{W2}[(\phi_B^0/V_B) + (\phi_W^0/V_W)]^2\}/$$

$$\{1 + K_{W1}[(\phi_B^0/V_B) + (\phi_W^0/V_W)] + K_{W1}K_{W2}[(\phi_B^0 V_B)$$

$$+ (\phi_W^0/V_w)]^2\} + RT\,\phi_W^0\,(V_A/V_W)[(K_{W1}^*/V_W)$$

$$+ 2\,(K_{W1}^*/V_W)(K_{W2}^*/V_W)]/[1 + (K_{W1}^*/V_W)$$

$$+ (K_{W1}^*/V_W)(K_{W2}^*/V_W)] + V_A\phi_B^0\phi_W^0(\delta_B' - \delta_W')^2 \qquad \text{(Eqn. 18)}$$

Second, careful examination the above expression reveals that similar cancellation of water's two hydrogen-bonding terms occurs whenever $K_{W2}[(\phi_B^0/V_B) + (\phi_W^0/V_W)] \gg 1$ and $(K_{W2}^*/V_W) \gg 1$. In this special set of circumstances, Mobile Order theory predicts that the logarithm of the solute's volume fraction (or alternatively molar) solubility in a binary mixture is a simple volume fraction average of the logarithm of the solute's volume fraction (or alternatively molar) solubility in each pure solvent

$$\ln \phi_A^{\text{sat}} = \phi_B^0 \ln (\phi_A^{\text{sat}})_B + \phi_W^0 \ln (\phi_A^{\text{sat}})_W - 0.5\,[\ln(x_B^0 V_B + x_W^0 V_W)$$

$$- \phi_B^0 \ln V_B - \phi_W^0 \ln V_W] + V_A\phi_B^0\phi_W^0(\delta_B' - \delta_W')^2 (RT)^{-1} \text{ (Eqn. 19)}$$

plus terms of -0.5 $[\ln((x_B^0 V_B + x_W^0 V_W) - \phi_B^0 \ln V_B - \phi_W^0 \ln V_W]$ and $V_A\phi_B^0\phi_W^0(\delta_B' - \delta_W')^2$ $(RT)^{-1}$ to account for molecular size disparity and nonspecific interactions present in the binary solvent mixture, repsectively. Had the Flory-Huggins definition of solution ideality been assumed for the configurational entropy, rather than the Huyskens and Haulait-Pirson model, then the first correction would disappear. Except for the two correctional terms, Eqn. (19) is identical to the Log-Linear model suggested by Yalkowsky and coworkers [30–34] for describing the solubility of crystalline solutes in a wide range of binary aqueous-organic solvent systems. The fact that Mobile Order theory and the Log-Linear model share a common mathematical form suggests that many of the systems that have described successfully by the Log-Linear equation should also be describable by

Mobile Order theory whenever the simplifying approximations discussed above are realized.

Predictive expressions based upon Mobile Order theory are more versatile than the Log-Linear model, however, because stability constants are not necessarily solvent independent. In the case of K_{W2} one can put forth a reasonable argument to the contrary. Water's second hydroxylic proton has two possible "acceptor" sites. The probability of hydrogen-bonding with the second electron pair on the alcohol's oxygen atom versus hydrogen-bonding with the second electron pair on water's oxygen atom depends upon the relative strength of the two H-bonds to be formed (as would be reflected by the relative magnitude of the stability constants) and the concentration of each type of electron pair. While electron donor power of the alcohol and water molecules are weakened by the first-hydrogen bond there is no compelling theoretical reason and/or experimental evidence to support the idea that the second hydrogen-bond strengths are identical. In fact, one would expect different strengths because of both steric hinderance around the oxygen atom (alcoholic R-group versus water H-atom) and the electron donating abilities/tendencies of the functional groups covalently bonded to the oxygen atoms.

From an operational standpoint, Mobile Order theory treats the stability constants as "average value(s)." Actual numerical value(s) should depend to a large extent on the relative weights afforded the alcoholic oxygen and water oxygen contributions. These contributions should be solvent dependent. Predicted solubilities listed in Table I were calculated assuming a compositional dependence of $K_{W2} = K_{W2}^*$ $+ 200\,\phi_B^0 + 800\,\phi_B^0 \phi_W^0$. No attempt was made to optimize the mathematical function or the three coefficients used. The first coefficient was set equal to $K_{W2}^* = 180 \text{ cm}^3 \text{ mol}^{-1}$ in order to ensure that Eqn. (17) reduces to a correct thermodynamic description of the solubility behavior in pure water. The experimental uncertainty/error associated with the observed solubilities is too large to attempt meaningful determination of how the mixture K_{W2} might vary with binary solvent composition.

Careful examination of the last three columns in Table I reveals that Mobile Order theory does provide fairly reasonable (though by no means perfect) predictions for how the solubility of 4-chlorobiphenyl varies with binary solvent composition. Deviations are

reported in the last column as Deviation $= \ln(x_A^{sat})^{calc} - \ln(x_A^{sat})^{exp}$. With few exceptions, predicted values are within a three-fold deviation of measured saturation mole fraction solubilities. The deviation is admittedly larger than what was hoped for based upon our earlier studies [1–6] involving anthracene and pyrene solubilities in binary alkane + alcohol and alcohol + alcohol solvent mixtures. The 3×10^5-fold range in saturation mole fractions is considerably larger than the 3-fold to 9-fold range(s) noted in our earlier studies. Slightly better predictions could perhaps be obtained by adding stability constant(s) for formation of possible chlorobiphenyl-alcohol and/or chloro-biphenyl-water molecular complexes. The two benzene rings on the solute are a source of π-cloud electron density, which could conceivably interact with the hydroxylic protons on both cosolvents. At this time, however, we do not feel that the slight reduction in percentage deviation necessarily warrants the increased calculational complexity when one remembers that the experimental uncertainties of several of the experimental data points were $\pm$ 30–50%. Taking the much larger solubility range encompassed and the possibility of specific solute-solvent interactions into consideration, we find that Eqn. (17) is an acceptable (though by no means perfect) mathematical description of solute solubility behavior in the highly nonideal aqueous-alcohol solvent mixtures.

In fairness to Eqn. (17) we should not only compare predicted and measured solubilities as in Table I, but also compare predicted values to those derived from the more conventional thermodynamic treatments in our assessment of the applications and limitations of the basic Model Order theory. Such evaluations would eliminate any wrong conclusions that might be drawn from erroneous data points. Each model considered would show poor agreement between the predicted mole fraction solubility and any incorrect measured value. Fortunately, Li and Andren [35] have used the same three 4-chloro-biphenyl data sets in comparing the predictive abilities of the Log-Linear, Excess Free Energy, UNIFAC, Extended Regular Solution and Phenomenological models. Each solution model is discussed in detail elsewhere. [35] The authors reported differences between calculated and observed mole fraction solubilities as Deviation $= \ln(x_A^{sat})^{calc} - \ln(x_A^{sat})^{exp}$. Differences between predicted and experimental values are depicted in Figures 1 and 2 for Mobile Order theory

versus the Log-Linear, UNIFAC and Extended Regular Solution models. The latter three models were selected from the five studied by Li and Andren because each one contains very few adjustable curve-fit parameters. Examination of Figures 1 and 2 reveals that the predictive accuracy of Eqn. (17) is comparable to (and sometimes superior than) expressions derived from the three conventional solution models. For any given binary solvent system and binary solvent composition there is no a prior way of knowing which predictive expression will give the better estimation of 4-chlorobiphenyl solubility. All four models severely underpredict the observed solubility in the binary 1-propanol + water solvent system at $\phi^0_{Propanol} = 0.40$, suggesting that the measured value may be in error.

FIGURE 1 Deviations between observed mole fraction solubilities of 4-chlorobiphenyl dissolved in binary alcohol + water solvent mixtures and calculated values based upon Mobile Order theory [Eqn. (17)] and the Log-Linear model. The three alcohol cosolvents are methanol (■), ethanol (●) and 1-propanol (▲).
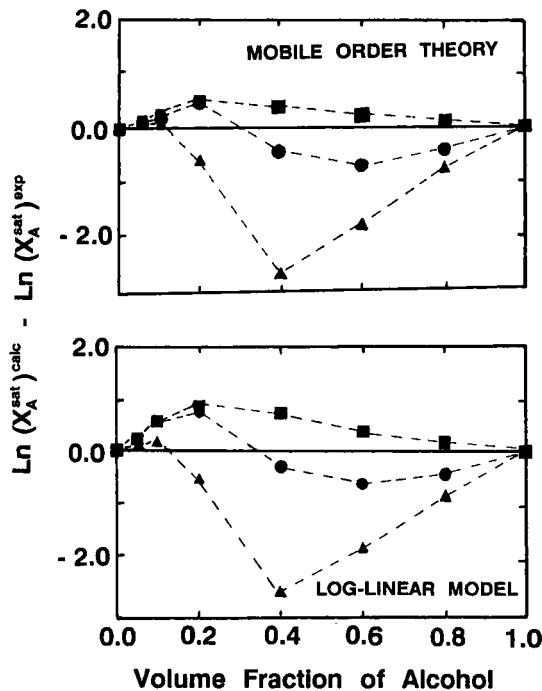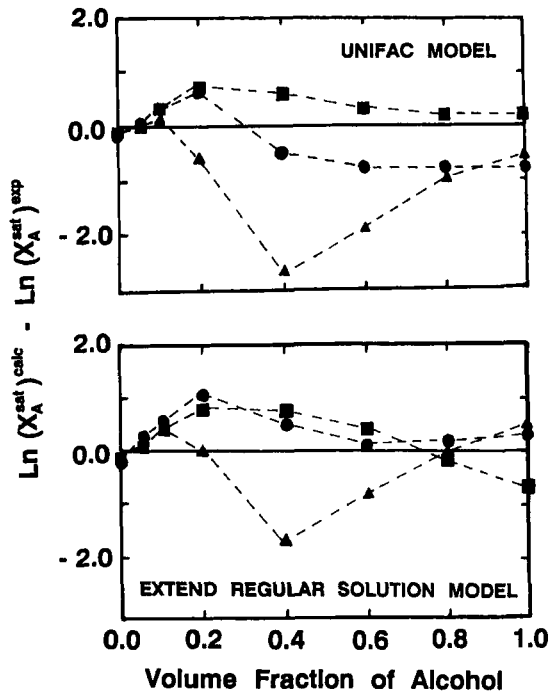
FIGURE 2 Deviation between observed mole fraction solubilities of 4-chlorobiphenyl dissolved in binary alcohol + water solvent mixtures and calculated values based upon the UNIFAC and Extended Regular Solution models. The three alcohol cosolvents are methanol (■), ethanol(●) and 1-propanol (▲).

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APPENDIX: GLOSSARY OF SYMBOLS

a_A^{solid} activity of the solid solute, defined as the ratio of the fugacity of the solid to the fugacity of the pure supercooled liquid.

ΔC_P difference between heat capacities of the solid and subcooled liquid solute, used in the computation of a_A^{solid}.

ΔH_A^{fus} molar enthalpy of fusion of the solid solute at its normal melting point temperature.

K_B, K_C — Mobile Order stability constants used to describe the formation of the homogeneous alcoholic hydrogen-bonded linear chains, where the concentration units are molarity.

K_{BC}, K_{CB} — Mobile Order stability constants used to describe the formation of the heterogeneous alcoholic hydrogen-bonded linear chains, where the concentration units are molarity.

K_{W1}, K_{W2} — First and second hydrogen-bonding stability constants for water, used in Order Theory in the calculation of the time that the hydroxylic proton is free from hydrogen-bonding in the binary alcohol + water mixture.

K_{W1}^*, K_{W2}^* — First and second hydrogen-bonding stability constants for water, used in Order Theory in the calculation of the time that the hydroxylic proton is free from hydrogen-bonding in pure water.

n_i — number of moles of component i.

T_{mp} — normal melting point temperature of the solute.

V_i — molar volume of component i.

x_i^0, x_j^0 — mole fraction compositions of the ij binary mixture, calculated as if the third component were not present.

x_A^{sat} — mole fraction solubility of the solute.

$(x_A^{sat})_i$ — mole fraction solubility of the solute in pure solvent i.

Greek letters

γ_{ih} — fraction of time that solvent i is not involved in hydrogen-bond formation.

δ_i — Scatchard-Hildebrand solubility parameter of component i.

δ_i' — modified solubility parameter of component i.

ϕ_B^0, ϕ_C^0 — ideal volume fraction compositions of the binary alcohol + alcohol solvent mixture, calculated as if the third component were not present.

ϕ_B^0, ϕ_W^0 — ideal volume fraction compositions of the binary alcohol (B) + water (C) solvent mixture, calculated as if the third component were not present.

ϕ_A^{sat} — ideal volume fraction solubility of the solute.

$(\phi_A^{sat})_i$ — ideal volume fraction solubility of the solute in pure solvent i.