Comment on "Thermochemical Investigations of Associated Solutions: Calculation of Solute-Solvent Equilibrium Constants from Solubility Measurements"

In an earlier article, Acree et al.¹ extended the basic nearly ideal binary solvent 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:

$$RT \left[\ln (a_A^{\text{solid}} / \phi_{A_1}^{\text{sat}}) - 1 + \bar{V}_A \left(\frac{\phi_{A_1}^{\text{sat}}}{\bar{V}_A} + \frac{\phi_B}{\bar{V}_B} + \frac{\phi_C}{\bar{V}_C} \right) \right] =$$

$$(1 - \phi_A^{\text{sat}})^2 [\phi_B^0 (\Delta \bar{G}_A^{\text{fh}})_B^* + \phi_C^0 (\Delta \bar{G}_A^{\text{fh}})_C^* -$$

$$\bar{V}_A (X_B^0 \bar{V}_B + X_C^0 \bar{V}_C) - \Delta \bar{G}_{BC}^{\text{fh}}] \quad (3)$$

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

$$\phi_A^{\text{sat}} = \phi_{A_1}^{\text{sat}} + \phi_{AC} \bar{V}_A / (\bar{V}_A + \bar{V}_C) =$$

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

where

$$\phi_C = \phi_{C_1} + \phi_{AC} \bar{V}_C / (\bar{V}_A + \bar{V}_C) \quad (5)$$

The various terms are defined elsewhere.¹

Following the publication of this earlier paper, several individuals wrote asking me to prove that eq 18 from Acree et al. (eq 6 below), describing the chemical potential of the *uncomplexed* solute (μ_{A_1}) relative to the pure liquid (μ_A^*), can be mathematically rearranged to eq 28 from Acree et al.¹ (eq 7 below) for the stoichiometric component A:

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

$$\bar{V}_A [\phi_B (1 - \phi_{A_1}) A_{A_1B} + \phi_{C_1} (1 - \phi_{A_1}) A_{A_1C_1} +$$

$$\phi_{AC} (1 - \phi_{A_1}) A_{A_1AC} - \phi_B \phi_{C_1} A_{BC_1} -$$

$$\phi_B \phi_{AC} A_{BAC} - \phi_{C_1} \phi_{AC} A_{C_1AC}] \quad (6)$$

$$\mu_A - \mu_A^* = RT \left[\ln \phi_{A_1} + 1 - \frac{\bar{V}_A}{\bar{V}_{\text{solution}}} \right] + \bar{V}_A (1 - \phi_A)^2$$

$$[\phi_B^0 A_{A_1B} + \phi_C^0 A_{A_1C_1} - \phi_B^0 \phi_C^0 A_{BC_1}] \quad (7)$$

The often requested derivation, though perhaps not obvious, is relatively straightforward and is given below.

The A_{A_1AC} and A_{C_1AC} binary interaction parameters involving the AC complex

$$A_{A_1AC} = \bar{V}_C^2 (\bar{V}_A + \bar{V}_C)^{-2} A_{A_1C_1} \quad (8)$$

$$A_{C_1AC} = \bar{V}_A^2 (\bar{V}_A + \bar{V}_C)^{-2} A_{A_1C_1} \quad (9)$$

and the A_{BAC} parameter, not defined in the original paper,

$$A_{BAC} = \frac{\bar{V}_A A_{A_1B}}{\bar{V}_A + \bar{V}_C} + \frac{\bar{V}_C A_{BC_1}}{\bar{V}_A + \bar{V}_C} - \frac{\bar{V}_A \bar{V}_C A_{A_1C_1}}{(\bar{V}_A + \bar{V}_C)^2} \quad (10)$$

are substituted directly into eq 18 of Acree et al.¹ (eq 6 above). Through grouping of like terms and rearrangements

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

$$\bar{V}_A \left[\phi_B (1 - \phi_{A_1}) A_{A_1B} + \phi_{C_1} (1 - \phi_{A_1}) A_{A_1C_1} + \right.$$

$$\frac{\phi_{AC} (1 - \phi_{A_1}) \bar{V}_C^2 A_{A_1C_1}}{(\bar{V}_A + \bar{V}_C)^2} - \phi_B \phi_{C_1} A_{BC_1} -$$

$$\frac{\phi_B \phi_{AC} \bar{V}_A A_{A_1B}}{\bar{V}_A + \bar{V}_C} - \frac{\phi_B \phi_{AC} \bar{V}_C A_{BC_1}}{\bar{V}_A + \bar{V}_C} +$$

$$\frac{\phi_B \phi_{AC} \bar{V}_A \bar{V}_C A_{A_1C_1}}{(\bar{V}_A + \bar{V}_C)^2} - \frac{\phi_{C_1} \phi_{AC} \bar{V}_A^2 A_{A_1C_1}}{(\bar{V}_A + \bar{V}_C)^2} \Big] =$$

$$\bar{V}_A \left[\phi_B (1 - \phi_A) A_{A_1B} - \phi_B \phi_{C_1} A_{BC_1} + \right.$$

$$\phi_{C_1} (1 - \phi_{A_1}) A_{A_1C_1} + \frac{\phi_{AC} (1 - \phi_{A_1}) \bar{V}_C A_{A_1C_1}}{\bar{V}_A + \bar{V}_C} - \frac{\phi_{AC} \phi_{C_1} \bar{V}_A A_{A_1C_1}}{\bar{V}_A + \bar{V}_C} - \frac{\phi_{AC}^2 \bar{V}_A \bar{V}_C A_{A_1C_1}}{(\bar{V}_A + \bar{V}_C)^2} \quad (11)$$

one obtains eq 28 from Acree et al.¹ (eq 7 above)

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

$$\bar{V}_A (1 - \phi_A)^2 [\phi_B^0 A_{A_1B} + \phi_C^0 A_{A_1C_1} - \phi_B^0 \phi_C^0 A_{BC_1}] \quad (12)$$

where $\phi_B = (1 - \phi_A) \phi_B^0$ and $\phi_C = (1 - \phi_A) \phi_C^0$. Similarly, eqs 19 and 20 from Acree et al.¹ for the chemical potentials of components B and C₁ can be shown to be identical to those obtained through differentiation of eq 26 from Acree et al.¹

References and Notes

1. Acree, W. E., Jr.; McHan, D. R.; Rytting, J. H. *J. Pharm. Sci.* **1983**, *72*, 929-934.

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