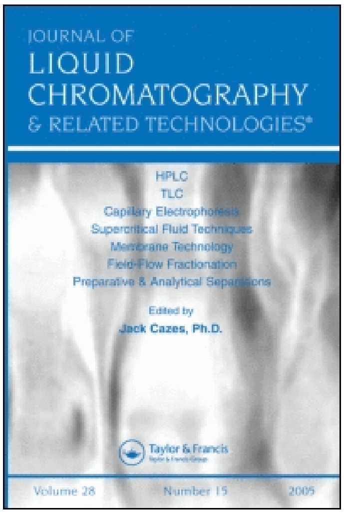

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William E. Acree Jr.[a]; J. Howard Rytting[a]
[a] Pharmaceutical Chemistry Department, The University of Kansas, Lawrence, Kansas

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A THERMODYNAMIC MODEL FOR LIQUID-LIQUID CHROMATOGRAPHY WITH A BINARY MOBILE PHASE

William E. Acree, Jr. and J. Howard Rytting
Pharmaceutical Chemistry Department
The University of Kansas
Lawrence, Kansas 66045

ABSTRACT

A simple model which previously led to successful predictive equations for gas-liquid partition coefficients on mixed stationary phases has been slightly modified to include liquid-liquid partitioning. Predictive expressions are developed for distribution coefficients determined from liquid-liquid chromatographic studies using a binary mobile phase. Limitations of the method are briefly discussed.

INTRODUCTION

Liquid-Liquid Chromatography (LLC) is a very powerful technique for chemical separations. This technique has not been applied to analytical determinations as frequently as the more modern method of gas-liquid chromatography. Recent improvements in column technology and instrumental design have led to a renewed interest in LLC. The desirable experimental features include; small (μl) samples, relatively short analysis times, a large selection of possible partitioning systems, and the ability to use nonvolatile solutes. Theoretically, there exist numerous combinations of binary immiscible phases which can be used in LLC. The number grows even larger if one considers the ternary (or higher order multicomponent) systems which can be mixed to form two immiscible liquid phases.

The ability to conveniently work at very low solute concentrations offers possibilities to determine thermodynamic properties through equations developed by Locke and Matire[1-2]. In this paper, we extend the considerations of Locke and Matire to include thermodynamic studies using a binary solvent as the mobile phase. In many instances the derived equations should provide an indication of phase compositions needed to achieve desired elution characteristics. Similar expressions developed specifically for gas-liquid chromatography have been shown to be beneficial in the selection of mixed stationary phases and in the study of associations complexes between the solute and one of the solvent components[3,4].

Relationship Between Solute Retention and Thermodynamic Properties.

The partitioning of a solute between two immiscible liquid phases provides the physical basis for liquid-liquid chromatography. As such, it is often convenient to define an experimental distribution coefficient as the ratio of solute concentration in each phase:

$$K_R = \frac{\text{concentration of solute in stationary phase}}{\text{concentration of solute in mobile phase}} \qquad (1)$$

For LLC it has been shown that solute retention volume (V_R) is related to the distribution coefficient through

$$V_R = \nu_m + K_R \nu_S \qquad (2)$$

where ν_S is the volume of the stationary liquid in the column and ν_m is the interstitial volume occupied by the mobile phase. To express retention measurements in a manner independent of experimental parameters, Littlewood *et al.*[5], suggested specific retention volume (V_g):

$$V_g = \frac{K_R}{\rho_S} \qquad (3)$$

where ρ_S is the density of the stationary phase.

The mathematical derivation of equation (2) assumes normal LLC operating conditions, and if one further requires liquid-

liquid partitioning to be the sole retention mechanism, then retention measurements can be related to thermodynamic quantities. The activity coefficient of a solute relative to Raoult's law, $\gamma_3^{\ell}(T,P)$, in a binary solution is defined by:

$$RT \ln \gamma_3^{\ell}(T,P) = \mu_3^{\ell}(T,P) - \mu_3^{o,\ell}(T,P) - RT \ln X_3^{\ell} \qquad (4)$$

where $\mu_3^{o,\ell}(T,P)$ is the chemical potential of pure liquid solute at T and P, $\mu_3^{\ell}(T,P)$ is the solute chemical potential in the solution, and X_3^{ℓ} is the mole fraction of solute.

In liquid-liquid chromatography the condition for thermodynamic equilibrium is

$$\mu_3^{s}(T,P) = \mu_3^{m}(T,P) \qquad (5)$$

in which $\mu_3^{s}(T,P)$ and $\mu_3^{m}(T,P)$ are the solute chemical potentials in the stationary and mobile phases respectively. Substitution of equation (5) into equation (4) with rearrangement yields:

$$\mu_3^{o,m}(T,P) - \mu_3^{o,s}(T,P) = RT \ln \frac{\gamma_3^{s}\, X_3^{s}(T,P)}{\gamma_3^{m}\, X_3^{m}(T,P)} \qquad (6)$$

since both $\mu_3^{o,m}(T,P)$ and $\mu_3^{o,s}(T,P)$ represent the chemical potential of pure liquid solute at T and P, $(\lim_{X_3 \to 1} \gamma_3^{i} = 1)$, their difference is zero. For simplicity we have elected to choose the column pressure (P) as our reference and interested readers are referred to an article by Locke and Matire if another reference state is preferred. In very dilute solutions the experimental distribution coefficient is expressed more conveniently as:

$$K_R = \frac{X_3^{s}\bar{V}_m^{o}}{X_3^{m}\bar{V}_s^{o}} \qquad (7)$$

where $\bar{V}_i^{o}$ is the molar volume of pure liquid phase <u>i</u>. Combination of equations (6) and (7) give:

$$\ln K_R^{o} = \ln \frac{\gamma_3^{m,\infty}(T,P)\ \bar{V}_m^{o}}{\gamma_3^{s,\infty}(T,P)\ \bar{V}_s^{o}} \qquad (8)$$

the superscript $\underline{\infty}$ denoting values at infinite dilution. Expressed in terms of specific retention volume, equation (8) becomes

$$\ln V_g = \ln \frac{\gamma_3^{m,\infty}(T,P)\ \bar{V}_m^o}{\gamma_3^{s,\infty}(T,P)\ M_s} \tag{9}$$

in which M_s is the molecular weight of the stationary phase. These simple mathematical relationships enable a priori predictions of distribution coefficients and retention volumes for any system in which the activity coefficients are known or can be estimated from solution theories.

The Nearly Ideal Binary Solvent (NIBS) Approach to Liquid-Liquid Partition Coefficients in Non-Complexing Systems.

The Nearly Ideal Binary Solvent (NIBS) approach developed by Bertrand and co-workers has been shown to be quite successful in predicting heats of solution[6], gas-liquid partition coefficients[3], and solubilities[7,8] in systems containing only nonspecific interactions. Using a simple mathematical model for the excess Gibbs free energy of a multicomponent system:

$$\Delta\bar{G}^{mix} = RT \sum_{i=1}^{N} (X_i \ln \phi_i) + \Delta\bar{G}^{fh} \tag{10}$$

$$\Delta\bar{G}^{fh} = \left(\sum_{i=1}^{N} X_i\ \bar{V}_i^o\right) \sum_{\text{all pairs}} \phi_i \phi_j A_{ij} \tag{11}$$

Acree and Bertrand developed a zero-parameter equation (Equation VV, reference 7) which predicts solubilities in 35 systems of non-specific interactions containing naphthalene, stannic iodide, iodine and benzil as solutes with an average deviation of 2.2% and a maximum deviation of 25%. This maximum deviation occurs in a system (Benzil-Benzene + Cyclohexane) in which complex formation has been suggested and if this system is excluded from calculations, the maximum deviation becomes 6%. The success of this model is even more remarkable if one realizes the mole fraction solubility of benzil changes by a factor of 14 in the carbon tetrachloride + n-hexane system[8].

Using the following thermodynamic definitions

$$\Delta\bar{G}^{fh} = RT \sum_{i=1}^{N} X_i \ln\gamma_i^{fh} \tag{12}$$

$$\ln\gamma_i^{fh} = \ln\,(a_i/\phi_i) - (1 - \frac{\bar{V}_i^o}{\bar{V}_M^o}) \qquad (13)$$

$$(\gamma_i^{fh})^\infty = \lim_{X_i \to o} \gamma_i^{fh} \qquad (14)$$

$$\gamma_3^\infty = (\gamma_3^{fh})^\infty \frac{\bar{V}_3^o}{\bar{V}_{solvent}^o} \exp\,(1 - \frac{\bar{V}_3^o}{\bar{V}_{solvent}^o}) \qquad (15)$$

the activity coefficient for a solute (relative to Flory-Huggins entropy) at infinite dilution in binary solvent mixtures (components 1 and 2)

$$\ln(\gamma_3^{fh})^\infty = \phi_1^o \ln(\gamma_3^{fh})^\infty_{x_1=1} + \phi_2^o \ln(\gamma_3^{fh})^\infty_{x_2^o=1} - \bar{V}_3^o\,(X_1^o\bar{V}_1^o + X_2^o\bar{V}_2^o)(RT)^{-1}\,\Delta\bar{G}_{12}^{fh} \qquad (16)$$

where,

$$\phi_1^o = \frac{X_1^o\bar{V}_1^o}{X_1^o\bar{V}_1^o + X_2^o\bar{V}_2^o} \quad \text{and} \quad X_1^o = \frac{X_1}{X_1+X_2} \qquad (17)$$

is shown to depend on a weighted average of the solute activity coefficient in each of the pure solvents $(\gamma_3^{fh})^\infty_{x_1=1}$, $(\gamma_3^{fh})^\infty_{x_2=1}$ and a contribution due to the "unmixing" of the solvent pair by the presence of the solute. Enhancement of the unmixing term by a large solute molecule can lead to predictions of maxima or minima in the thermodynamic properties of the solute.

Although the NIBS approximations for solute activity coefficients in binary solvent mixtures cannot be rigorously extended to liquid-liquid partitioning in systems of practical importance, expressions developed for "model" systems may possess predictive applicability[9]. The simplest system to consider involves the partitioning of a solute between two "completely" immiscible liquid phases where only nonspecific interactions are permitted. The mobile phase consists of a binary mixture of inert solvent molecules (completely immiscible with the stationary phase at all binary compositions) and the stationary phase is such that the solute activity coefficients at infinite dilution $\gamma_3^{s,\infty}$ remains constant. The combinations of equations (8), (15) and (16) then gives:

$$\ln K_R^o = \phi_1^o \ln\ (K_R^o)_{x_1^o=1} + \phi_2^o \ln\ (K_R^o)_{x_2^o=1} - \bar{V}_3^o (X_1^o \bar{V}_1^o + X_2^o \bar{V}_2^o)(RT)^{-1} \Delta\bar{G}^{fh}(T,P) \qquad (18)$$

With this equation retention volumes in pure solvents can be used to calculate solute distribution coefficients at infinite dilution in the pure solvents. These values can be combined with the excess free energy of the binary solvent mobile phase to predict solute distribution coefficients. The predictive ability of this equation will depend to a large extent on the complexity of the system under investigation. It is anticipated that this approach will provide reasonably accurate approximations for simple systems containing only nonspecific interactions and will fail in systems having either specific solute-solvent or solvent-solvent interactions. The extension of equation (18) to systems involving complexation between the solute and one component of the binary mobile phase should be similar to methods employed in gas-liquid chromatography to study association complexes.

Experimental LLC partition coefficinets were unavailable for comparison, but similar expressions based on mole fractions have been applied by Buchowski and Teperek[10] to infinite dilution partition coefficients of benzoic acid and o-nitroaniline in systems benzene + cyclohexane--water and isooctane + bromoform--water. This general approach if proven successful, will offer new possibilities to study association phenomenon for nonvolatile solute molecules.

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