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CRITERIA FOR THE USE OF MIXED SOLVENTS IN GAS-LIQUID CHROMATOGRAPHY

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SUMMARY

Recent investigations have shown that, for a stationary phase composed of a binary (A + S) mixture, the infinite dilution solute partition coefficient in the mixture, K_R , is given by

$$K_R = \varphi_A K_{R(A)}^0 + \varphi_S K_{R(S)}^0$$

where $K_{R(A)}^0$ and $K_{R(S)}^0$ represent the corresponding partition coefficients in pure A and S, respectively, and φ is a volume fraction. This equation has been shown to apply to all cases quantitatively reported in the literature and applies equally to systems wherein charge transfer, hydrogen bonding or no specific interactions are postulated.

The equation and its consequences also establish criteria for the analytical usefulness of mixed phases in gas-liquid chromatography (GLC). For a two-component solute mixture, no advantage is gained by employing a mixed liquid phase. For three or more components, a mixed phase may or may not be useful, depending on the α values for each solute pair with each of the pure liquid phases. For solutes and stationary phases for which the above equation is valid, it is also possible to predict the optimum composition at which the resolution of all components will be maximized. The method is described and both theoretical and practical examples are given. The procedure is so straightforward that it offers considerable possibilities for improvement in the range of solvent selectivity available in GLC.

INTRODUCTION

Despite the considerable volume of published retention data, it is still not readily possible to make more than a qualitative or semi-quantitative estimate of the effectiveness of a single solvent for a desired analytical application; furthermore, conventional solution theory offers little prospect of anything better than a rough guess of retention values. Thus, the problem of predicting the behaviour of a mixture of solvents, and of choosing the optimum composition, has appeared almost intractable. For these reasons, mixed solvents are little used in practice although their potential advantages have been discussed¹⁻⁵.

In a series of recent papers⁶⁻¹⁰ we have shown that, in fact, both the practical and theoretical aspects of retention by a mixed solvent are considerably simpler than has been supposed. In addition, we have shown that for every gas-liquid chromatographic (GLC) system so far described in the literature in sufficient detail to allow the necessary calculations (*ca.* 400), one simple general equation prevails, *viz.*

$$K_R = \varphi_A K_{R(A)}^0 + \varphi_S K_{R(S)}^0 \quad (1)$$

where K_R is the infinite dilution partition coefficient between the liquid mixture (A + S), of volume fraction composition φ_A , and the gas phase, and $K_{R(A)}^0$ and $K_{R(S)}^0$ are the corresponding values for pure A and pure S. Eqn. 1 may be put alternatively as

$$K_R = K_{R(S)}^0 + \varphi_A (K_{R(A)}^0 - K_{R(S)}^0) \quad (2)$$

from which we see that a plot of K_R against φ_A will be linear.

Since, as we have shown, eqn. 1 is completely general, even where chemical complexing has been postulated to occur, it follows that as long as $K_{R(A)}^0$ and $K_{R(S)}^0$ are known, K_R for a given solute can be calculated for any mixture composition. We thus have a basis to evaluate theoretically, from the comprehensive literature tabulations of retention data for pure phases, the GLC performance of binary solvent mixtures for many solutes. This paper illustrates the simplicity and success of this proposition.

THEORY

For any pair of solutes (1 and 2) whose retention behaviour is described by eqn. 1, the relative retention, α , is defined by

$$\alpha = K_{R1}/K_{R2} = [\varphi_A \Delta K_{R1}^0 + K_{R(S)1}^0] / [\varphi_A \Delta K_{R2}^0 + K_{R(S)2}^0] \quad (3)$$

where $\Delta K_R^0 = K_{R(A)}^0 - K_{R(S)}^0$.

Alternatively, we may write

$$\varphi_A = [K_{R(S)1}^0 - \alpha K_{R(S)2}^0] / [\alpha \Delta K_{R2}^0 - \Delta K_{R1}^0] \quad (4)$$

Consider now the simplest analytical problems. It is self-evident that, according to eqn. 1, no two-component solute mixture can ever be separated better by a mixture of solvents than by one or other of the pure solvents alone. Thus, the minimum realistic problem involves a three-component solute mixture.

We illustrate the approach to be adopted by taking the hypothetical case of a four-component mixture. Fig. 1a shows plots of K_R against φ_A which are drawn such that (i) α for solute components X and W is always 2, (ii) the plot for solute Z crosses all others over the range $\varphi_A = 0-1$, (iii) solutes Y and W have $\alpha = 1$ (un-

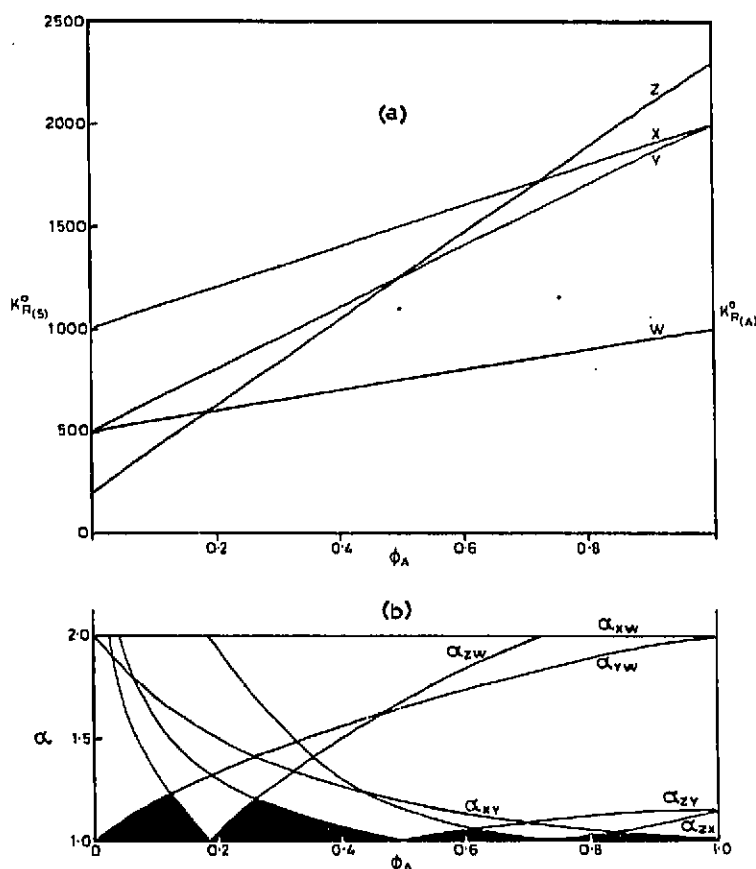


Fig. 1. (a) Plots of K_R vs. ϕ_A for four hypothetical solutes, W, X, Y, and Z. (b) Plots of α vs. ϕ_A for the four solutes of Fig. 1a. Optimum column composition for separation occurs at $\phi_A = 0.12$.

separable) at $\phi_A = 0$ (*i.e.*, $\phi_S = 1$) and solutes X and Y have $\alpha = 1$ at $\phi_A = 1$ (*i.e.*, $\phi_S = 0$). Fig. 1b illustrates the variation of α as a function of ϕ_A , for all six pairs of solutes. For convenience we retain the convention of $\alpha \geq 1$, *i.e.*, when retention inversion occurs as indicated by line crossings in Fig. 1a, we invert the K_R ratio. Thus, where no crossing occurs the plot is continuous, whereas, when crossing does occur, we have an approximately V-shaped plot. To illustrate the use of this diagram, those regions of α values which can actually be attained in practice are filled in. We need now only to look at the several "windows" to define precisely the optimum mixture composition for use. All that is required, as a first consideration, is to find that window having the highest value of α , which, in this case, is that peaking at $\alpha = 1.23$ at $\phi_A = 0.12$. This value of course corresponds to the minimum for the system, *i.e.*, for the most difficultly separable pair. We can now go farther, since the theoretical plate requirement equation¹¹ allows the calculation of effective column length. For instance, if we assume a very large capacity factor k , N_{req} is given by $36(a/a-1)^2$ for complete resolution, so at $\alpha = 1.23$, N_{req} is 900. At 1 mm theoretical plate height, a 90-cm column is thus needed. Finally, of course, we can now refer back to Fig. 1a,

at the appropriate ϕ_A , and identify the order of elution, in this case, Z, W, Y, X. The calculation described thus provides all the relevant information to define column construction and performance, a most acceptable situation.

To proceed from this point it is convenient to recognise some simplifying factors:

- (a) V-shaped plots can be drawn as triangles for our present purposes;
- (b) it is better to use eqn. 4 than eqn. 3, and to evaluate ϕ_A at fixed values of α ;
- (c) although in principle we should evaluate α for every pair of solutes in a mixture, the majority can usually be neglected since their α values are so large. It is worth noting that at reasonably high capacity factors (k) the number of theoretical plates (N) required for separation¹¹ are:

α	1.05	1.10	1.20	1.30
N	16,000	4400	1300	675

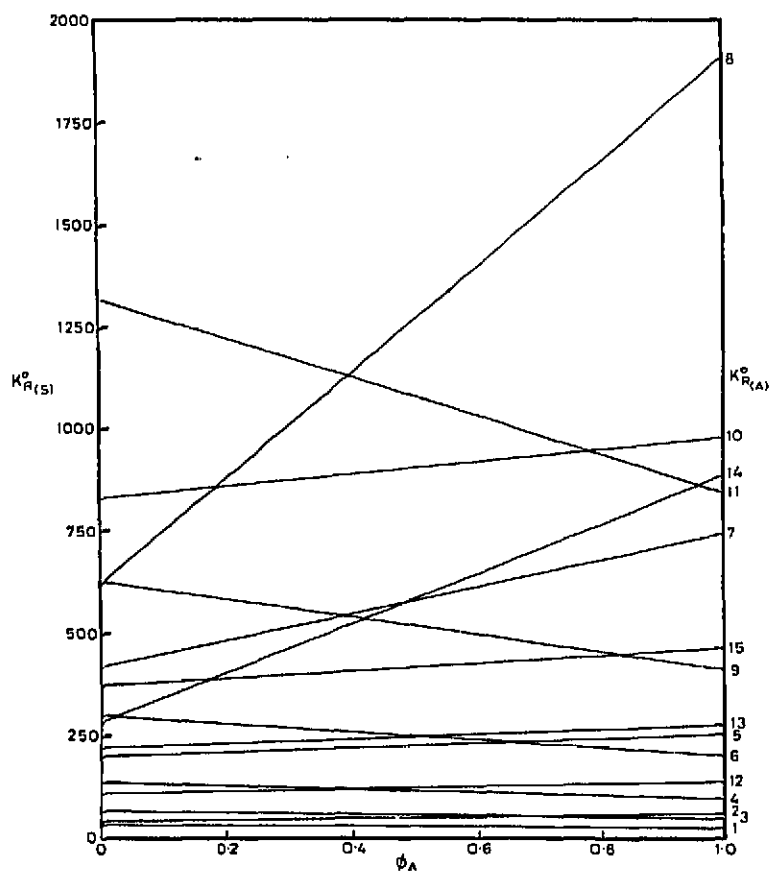


Fig. 2. Plots of K_R vs. ϕ_A for the 15 solutes of Table I. Temperature: 100°; solvent (S): squalane; additive (A): di-*n*-nonyl phthalate.

TABLE I
SOLUTES AND K_R^0 DATA FOR FIG. 2

No.	Solute	$K_{R(S)}^0$	$K_{R(A)}^0$
1	<i>n</i> -Hexane	33.7	24.5
2	Benzene	41.2	58.6
3	<i>n</i> -Heptane	67.2	49.0
4	<i>n</i> -Octane	140	97.1
5	Ethylbenzene	200	254
6	<i>n</i> -Nonane	301	202
7	Ethoxybenzene	416	745
8	Acetophenone	618	1906
9	<i>n</i> -Decane	630	414
10	<i>n</i> -Butylbenzene	830	980
11	<i>n</i> -Undecane	1315	847
12	Toluene	108	138
13	<i>p</i> -Xylene	221	276
14	Benzaldehyde	281	884
15	<i>n</i> -Propylbenzene	372	462

Thus, any pair of solutes having an α value above 1.30 over the whole range of ϕ_A can be ignored.

We now proceed to illustrate the foregoing principles in practice. Fig. 2 illustrates plots according to eqn. 1 of $K_{R(A)}^0$ and $K_{R(S)}^0$ data⁸ for fifteen solutes, where A is di-*n*-nonyl phthalate and S is squalane. The plots, it must be emphasised, were

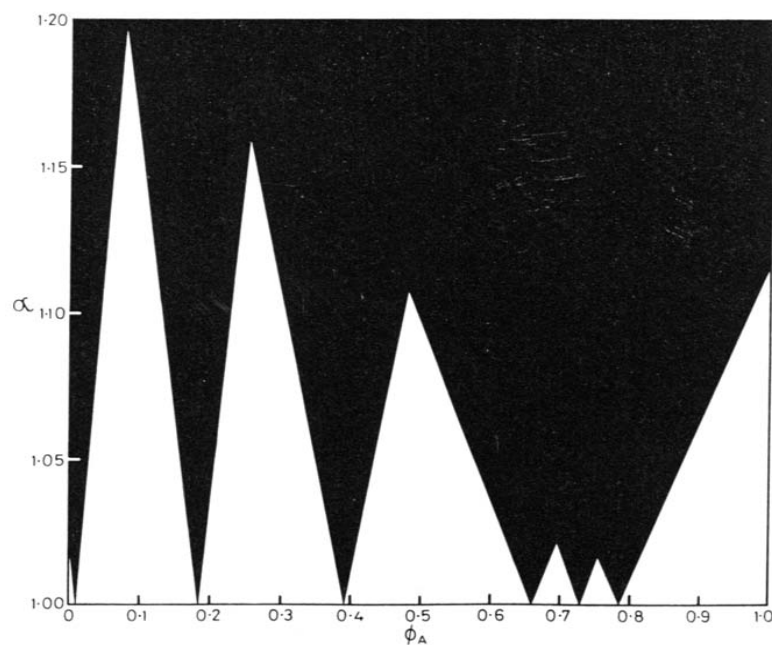


Fig. 3. Window diagram for solutes 1-11 of Table I. Optimum column composition occurs at $\phi_A = 0.075$.

drawn merely by linearly connecting the known values of $K_{R(A)}^0$ and $K_{R(S)}^0$ for each solute. The solutes, identified in Table I, were selected as (i) representing a variety of chemical types, (ii) presenting some difficulty of separation with the pure liquid solvents, and (iii) showing a number of crossings in the range $\phi_A = 0-1$.

First, let us consider the analytical problem of separating solutes 1-11 in Table I. The plot of α versus ϕ_A for these is shown in Fig. 3, where the windows have been left open, and the inaccessible regions shaded. We see that there are six available windows, but that the one occurring at $\phi_A = 0.075$ will be the best to use in practice. Although the overall analysis time would be slightly longer than it would in the next best window ($\phi_A = 0.255$) at equal column length and loading, this would be more than offset by the extra column length required for complete separation in the second window due to its much lower α value. Fig. 4 shows the predicted complete resolution of all 11 components with a column of $\phi_A = 0.0755$ and the appropriate number of theoretical plates.

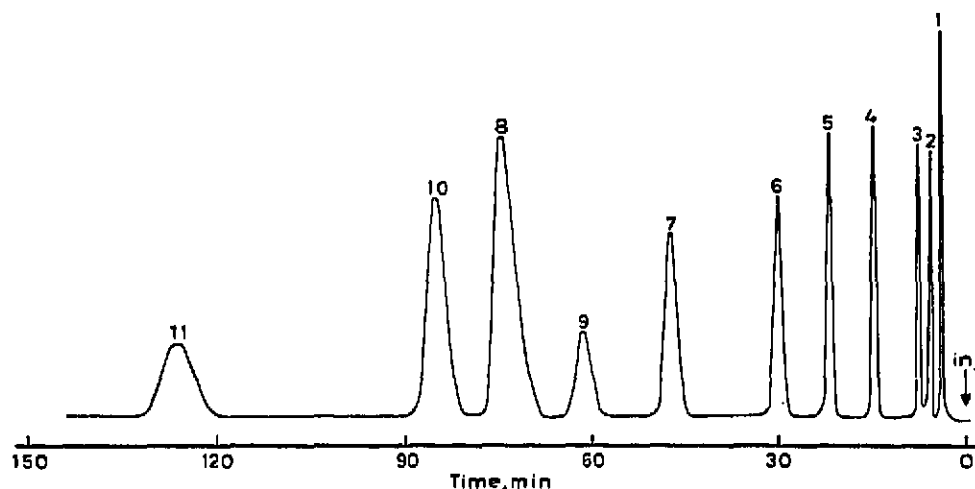


Fig. 4. Chromatogram of solutes 1-11 of Table I. Temperature: 100° ; ϕ_A : 0.0755; column: 1/8 in. \times 12 ft. stainless steel; support: Chromosorb G AW DMCS (60-80 mesh); column pressure drop: 20 p.s.i.g.

The foregoing discussion illustrates the criteria of choice in this method: The primary criterion is that the mixture giving the highest α is the most suitable; the secondary criterion is that where two or more windows offer reasonably similar values of α , the one of lower α may provide the shortest overall analysis time. However, since it is obvious that as we increase the number of components to be separated we must expect the number of windows to increase and to provide, in general, lower α , this second criterion is liable only to be important for mixtures of few components. We illustrate this situation by considering the window diagram for the full 15-component mixture. Fig. 5 shows that we now have fourteen windows. All but three are valueless since the α available is less than that for pure di-*n*-nonyl phthalate (DNNP). Of the other three, that at $\phi_A = 0.075$ is unquestionably the best.

Fig. 6 illustrates a group of chromatograms obtained with a series of columns

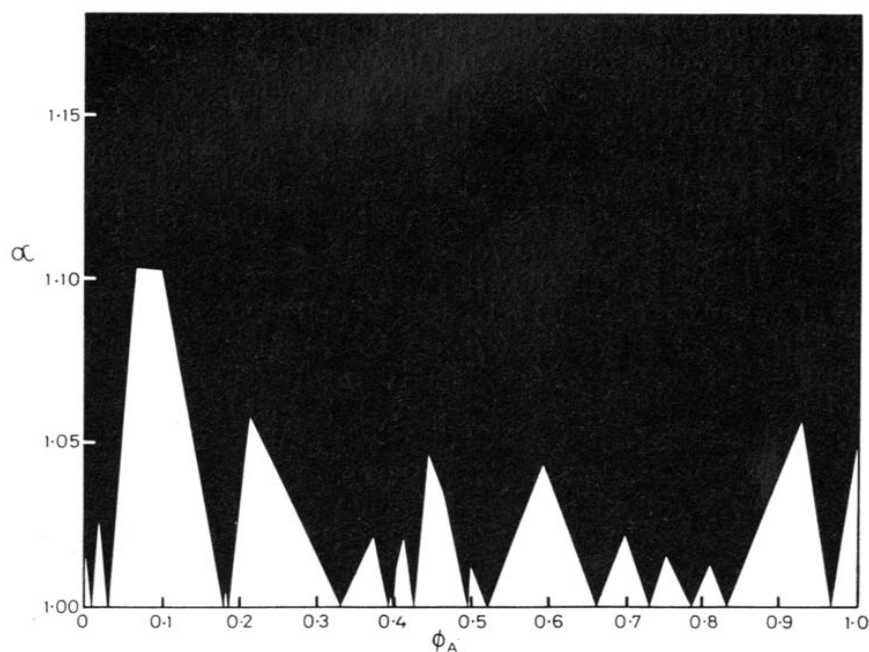


Fig. 5. Window diagram for all solutes of Table 1. Optimum column composition occurs at $\phi_A = 0.075$.

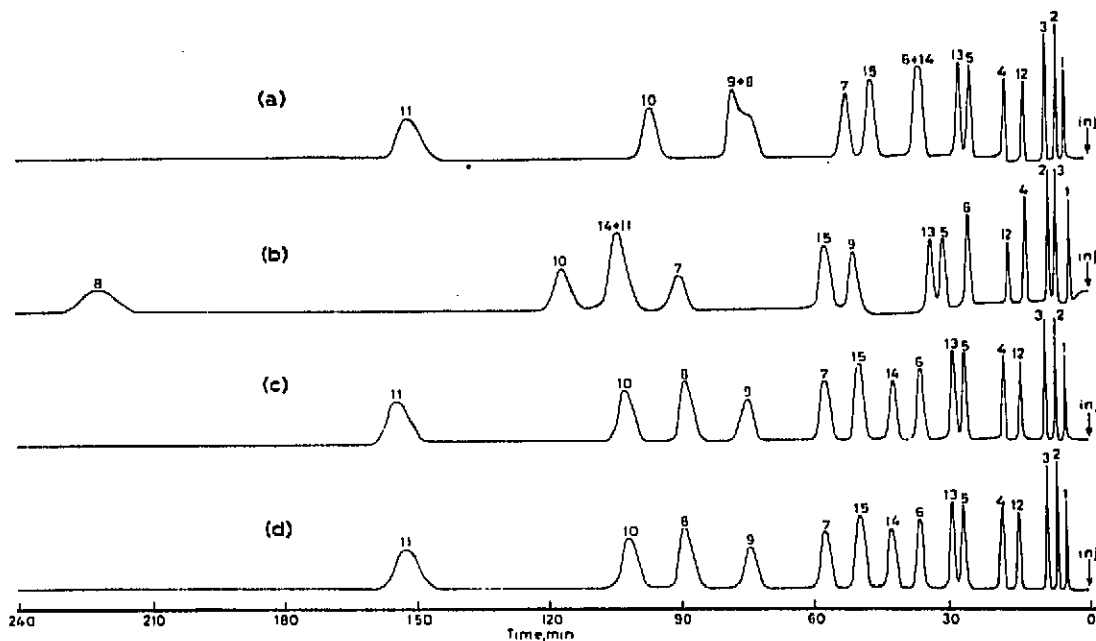


Fig. 6. (a) Chromatogram of 15-component mixture on pure squalane ($\phi_A = 0$). Column pressure drop: 15 p.s.i.g.; other conditions as in Fig. 4. (b) Chromatogram of 15-component mixture on pure DNNP ($\phi_A = 1$). Other conditions as in Fig. 6a. (c) Chromatogram of 15-component mixture on squalane + DNNP ($\phi_A = 0.0755$). Other conditions as in Fig. 6a. (d) Chromatogram of 15-component mixture on mechanically mixed packing corresponding to $\phi_A = 0.0755$. Other conditions as in Fig. 6a.

all of the same length, containing the same volume of stationary phase, and operated at the same flow-rate and temperature, which quantitatively verify the above discussion. Fig. 6a shows the 15-component mixture on pure squalane, whilst Fig. 6b shows the analysis with pure DNNP. In each can be seen clear cases of failure to resolve certain pairs. In fact, as Fig. 2 shows, solutes 8 and 9 cannot be resolved on pure squalane, while solutes 11 and 14 would require phenomenal column lengths for complete separation with pure DNNP. Fig. 6c illustrates the complete resolution of all 15 components with a column of $\phi_A = 0.0755$.

An important practical aspect of the theory referred to earlier⁶⁻¹⁰ is that the retention characteristics of the mixed (A + S) solvent are simply the volume fraction averaged characteristics of the separate solvents (*cf.* eqn. 1). Thus, from a purely practical point of view, a mechanical mixture of (support + A) with (support + S), can be used as effectively as a packing of (support + mixed A + S). Fig. 6d establishes the accuracy of this proposition, since it was obtained with a column identical in every respect to that used to generate Fig. 6c, except that the packing was made up simply by mixing the appropriate amounts of a squalane packing and a DNNP packing. The slight differences in retention result from the use of a commercial instrument lacking the necessary precision for reproduction of flow-rate.

We of course recognise that in the chromatograms shown, analysis times are particularly long. Naturally, having identified an appropriate mixture composition, one would then proceed to apply the well-known principles of minimum time analysis¹¹.

DISCUSSION

It is evident that the procedure we have described above is quantitatively successful in that the predictions made are quite precisely confirmed. As has been indicated, in addition to evaluation of optimum solvent compositions, column lengths and flow-rates can be calculated ahead via some representative *H versus \bar{u}* plot and the theoretical plate requirement equation¹¹. Thus, all operating conditions for a given analysis based on binary solvents can be specified with a minimum of experimentation, and all this from information relating to pure solvent behaviour. Thus, the enormous compilations of retention data for pure solvents can be turned to immediate use. The simplicity of this procedure, and the highly increased analytical power that will derive from an ability to handle multi-component solvents in such simple fashion, strongly suggests the possibility that in future, in contrast to the present, mixed solvents will dominate GLC analysis.

We have here dealt with solvent systems of two components, but it is evident that this is in no way a restriction, and our procedure could readily be extended to handle three or more solvent components. Further, the number of solutes to be handled offers no real problem, since the nature of the calculations involved is so elementary that even a simple computer could handle complex solvent and solute mixture data. This offers new perspectives for the analysis of volatile materials.

Finally, it is worth pointing out that although all our calculations have been presented in terms of partition coefficients, eqn. 1 can readily be put in terms of specific retention volumes and solvent densities. Even relative retention data can be used, provided absolute values of partition coefficients or specific retention volumes are known for one component.

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