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UNIFAC model as a heuristic guide for estimating retention in reversed-phase liquid chromatography☆

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ABSTRACT

The utility of the UNIFAC activity coefficient determination method for understanding the magnitude of solute–solvent interactions in reversed-phase liquid chromatography (RPLC) is discussed. UNIFAC-computed partition coefficients for the transfer of various homologous series of solutes from aqueous mixtures of methanol, acetonitrile and tetrahydrofuran to hexadecane, octane, butane and benzene were used to investigate the effects of the carbon number, the type of functional group of the solutes, the composition of the mobile phases, the chain length of alkyl-bonded stationary phases and temperature on retention in reversed-phase liquid–liquid partition chromatography. Although UNIFAC is not accurate enough to be useful for the quantitative determination of retention in RPLC, it is useful in explaining a wide variety of issues of general importance in RPLC.

INTRODUCTION

The UNIFAC (*UNI*QUAC *f*unctional group *a*ctivity *c*oefficient) model is an activity coefficient determination scheme that has found very general utility in chemical engineering [1]. Its major use is for the prediction of vapour–liquid [2] and liquid–liquid equilibria [3]. There have been a number of studies on the application of UNIFAC for the determination of retention in gas and liquid chromatography [4–11]. Recently we have shown how generally applicable UNIFAC is as a heuristic guide for understanding the magnitude of solute–solvent interactions in gas chromatography and normal- and reversed-phase liquid chromatography [12].

Because UNIFAC is a functional group-oriented method, it is broadly applicable in a predictive sense. So far 50 different "main" groups have been defined and the relevant interaction parameters made available [13]. Hence, in principle, the activity coefficients in any mixture of species consisting of molecules containing these functional groups can be computed. This makes the UNIFAC method far more powerful in terms of its generality than other approaches, such as those based on the separation of cohesive energy densities, which have found considerable utility in chromatography [14–16]. As we have shown, UNIFAC is not accurate enough, at this stage of its development, to be useful for the quantitative prediction of retention [12,17]. Because chromatography is able to distinguish between two types of solute molecules that differ

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☆ Dedicated to Professor Taesub Oh on the occasion of his 65th birthday.

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in the strength of their interactions with the mobile and stationary phases by only a few calories per mole, there is as yet no general predictive method that suffices for use in chromatography. Nonetheless, UNIFAC is sufficiently accurate to be useful for the prediction of the relative retention, the relative strengths of solvents and other important chromatographic properties [7,8,12].

There have been only a few studies on the application of UNIFAC to predicting retention in reversed-phase liquid chromatography (RPLC) [9–11]. Petrovic *et al.* [9] have shown that the UNIFAC model can be used for the calculation of changes in solute retention with alterations in mobile phase composition and for a rough estimation of absolute retention indices, assuming that the retention of a solute is due to liquid–liquid partition and that the activity coefficient of the solute in the stationary phase and the phase ratio are constant. They also studied the selectivity of separation in RPLC by utilizing calculated activity coefficients of the solutes in the mobile phases and measured capacity factors on ODS silica stationary phases with varying coverages [10]. They observed that a strictly linear relationship exists between the experimentally determined selectivity factor and the calculated selectivity factor in the mobile phase and that the relative retention on the stationary phase is independent of the mobile phase strength and the silica coverage. However, they did not calculate directly the activity coefficients of analytes in the stationary phase. Recently, Dasko [11] applied UNIFAC to the assessment of retention in RPLC by directly computing activity coefficients of solutes in model stationary and mobile phases. However, it has not been systematically explored how generally applicable UNIFAC is as a guide to understanding the magnitude of solute–solvent interactions in RPLC. The purpose of this paper is to show how it can be applied to and explain a wide variety of issues of general importance in RPLC such as the effects of the carbon number and the type of functional groups of homologous series of solutes, the type and volume composition of organic modifiers in the aqueous mobile phase, the chain length of alkyl-bonded stationary phases and temperature on retention.

THE UNIFAC METHOD

UNIFAC [2] combines the UNIQUAC model of solutions [18] and the so-called analytical solution of group (ASOG) concept [19]. The UNIQUAC (*uni*versal *qua*si-chemical) is an approximate model of liquid mixtures developed by application of Guggenheim's quasi-chemical lattice model of liquid mixtures [20] through the use of a component's local area fraction as the main concentration variable. In essence, this approach is a simple alternative to the highly unrealistic random mixing model which is the basis for regular solution theory. The ASOG approach is based on the idea that a solution can be viewed as a mixture of independent functional groups of all the components of a solution, and assumes that the contribution that any functional group makes to the activity coefficient of a molecule is independent of any other functional group in that molecule, that is, the free energy of interaction of one species with a second is assumed to be the additive sum of independent functional group contributions. Thus, in principle, the ASOG method can be made more realistic by simply redefining the set of functional groups to contain a larger and more complex group of units until the set includes all possible molecules. Activity coefficients in both binary and multi-component liquid mixtures are computed by virtue of structural parameters and binary group-interaction parameters characterizing the energy of mutual interaction of functional groups present in the mixture. The structural parameters [18] are derived from the Van der Waals surface areas and volumes of the functional groups [21]. The interaction parameters are derived from banks of experimental phase equilibrium data [22].

Recently, two different modified UNIFAC methods, which show substantially improved accuracy for prediction of γ^{∞}, have been reported [23,24]. However, the two modified UNIFAC methods use six interaction parameters between two interacting groups, whereas only two parameters are used in the original version of UNIFAC, hence the flexibility of the modified methods is substantially reduced. In addition, the number of available group interaction parameters in the modified UNIFAC methods is

smaller than in the original version of UNIFAC. More recently Bastos *et al.* [25] developed a new set of UNIFAC parameters based on solely infinite dilution activity coefficient (γ^{∞}) data. It is well known that the very large errors in the predicted γ^{∞} values for non-polar solutes in associating solvents are mainly due to errors in group interaction parameters. This is a consequence of the fact that the parameters in the original version of UNIFAC were derived primarily from data at high concentrations [17]. Thus, in principle, the use of infinite dilution interaction parameters should improve the accuracy of prediction. However, it was observed that the use of infinite dilution interaction parameters does not improve the predictive accuracy and gives even worse predictions than the original UNIFAC [8,26]. Therefore, the original UNIFAC method [2,22] was utilized in this work.

CALCULATIONS

All calculations were performed on an IBM-compatible personal computer using programs written in GWBASIC. The double-precision option was employed in order to improve computational accuracy. For the present calculations the original UNIFAC model [2] and parameters for vapour–liquid equilibria recently revised by Hansen *et al.* [13] were employed. For the test of the temperature dependence of retention, the modified UNIFAC by Larsen *et al.* [24] was used. This version of modified UNIFAC uses temperature-dependent group interaction parameters and has a better built-in temperature dependence than the original UNIFAC, thus allowing for the simultaneous prediction of vapour–liquid equilibria and enthalpies of mixing. In the original UNIFAC the interaction parameters are assumed to be independent of temperature and hence cannot be successfully used for the test of temperature dependence.

RESULTS AND DISCUSSION

There have been a number of studies on retention mechanisms in RPLC and three main theories have evolved. These include the solvophobic theory of Horváth and co-workers [27,28] in which retention is thought to occur through an adsorption rather than partitioning process, the statistical mechanical partitioning model of Martire and Boehm [29] and the interphase partitioning model of Dill and co-workers [30–32]. The last two models argue for and demonstrate both theoretically and experimentally that partitioning is the relevant model of RPLC retention. Although chromatographic retention cannot be well modelled by liquid–liquid partitioning [32], a pure partitioning model is adopted in this work for the sake of simplicity. The values of the partition coefficient can be used for the assessment of retention as the capacity factor is closely related to the partition coefficient [27]. We may neglect the effect of the organic solvent that partitions into the stationary phase. This is a good approximation for methanol and acetonitrile mixtures with water if hexadecane is used as the stationary phase. However, 2-propanol and tetrahydrofuran are fairly miscible with hexadecane [33]. Even with a considerable amount of organic modifier present in hexadecane, modelling of the stationary phase as pure hexadecane is still a good approximation because the change in the activity coefficient of the solute caused by the presence of an organic modifier in hexadecane is very small [34] and thus does not alter the partition coefficient appreciably. However, Yonker *et al.* [35,36] have shown that the stationary phase in aqueous organic mobile phases is solvated not only by association of the organic modifier with bonded organic moieties but also by adsorption of water on residual silanol groups on the silica substrate. We model the stationary phase as hexadecane solvated by organic modifiers and water when the composition of the solvated stationary phase is known.

The partition coefficient can be calculated from known values of infinite dilution activity coefficients (γ^{∞}) of the solute of interest in both phases [37–39]:

$$K = (\gamma_m^{\infty} V_m / \gamma_s^{\infty} V_s) \quad (1)$$

where V denotes the molar volume and the subscripts m and s indicate the mobile and stationary phase, respectively. Molar volumes of the mobile and stationary phases are computed

as sum of mole fraction-weighted molar volumes for all the components present in each phase.

Effect of carbon number

Most chromatographers are familiar with the Martin equation, which states that in many forms of chromatography the logarithm of the partition coefficient (K) and therefore the logarithm of the capacity factor (k') are a linear function of the number of methylene groups within a homologous series of solutes:

$$\log K \text{ (or } \log k') = A + Bn \quad (2)$$

where n denotes the homologue number. Agreement with this equation is so generally accepted that it is frequently used as the basis for estimating column dead volumes in GC and RPLC [40]. The Kováts retention index is also based largely on the observed compliance with the Martin equation. Similarly, Smith's scheme for establishing a retention index in RPLC relies in part on the linearity between log k' and n [41,42].

Assuming that the stationary phase is represented by hexadecane, partition coefficients between hexadecane and aqueous mixtures of organic solvents (40 vol.%) for various homologous series of solutes were computed and are plotted against n in Fig. 1. As can be seen, in all instances the computed partition coefficients are essentially linear functions of n. UNIFAC produces the desired qualitative results.

Calculated partition coefficients between hexadecane and methanol–water mixtures for n-alkylbenzenes and 1-alkanols are compared with measured values [43] in Fig. 2. The predicted values are generally in reasonable agreement with the measured values. The errors in the predicted values are greater for 1-alkanols than n-alkylbenzenes. The larger errors for alcohols may be speculated to be due to the incorrect interaction parameters between hydroxyl groups and water because of the possible dissociation of alcohols in water, as was thought to be so for phenols [10]. It is not likely, however, that a dissociation reaction is main cause of the incorrect interaction parameters for n-alkanols, as dissociation constants for n-alkanols are very small. A more likely explanation of this problem is that most of the data on which UNIFAC parameters are based were obtained at high concentrations (mole fraction > 0.05), and thus the discrepancy between the measured and computed activity coefficients of a component in the mixture is greatest in the infinite dilution region [24,26,44]. This is because the infinite dilution region is generally where the activity coefficient is most strongly dependent on composition. Nevertheless, the trend in the variation of log K with n is linear and in agreement with the linear variation of measured log K with n.

Plots of experimental log k' *vs.* n for alkylbenzenes in water–acetonitrile mixtures of different

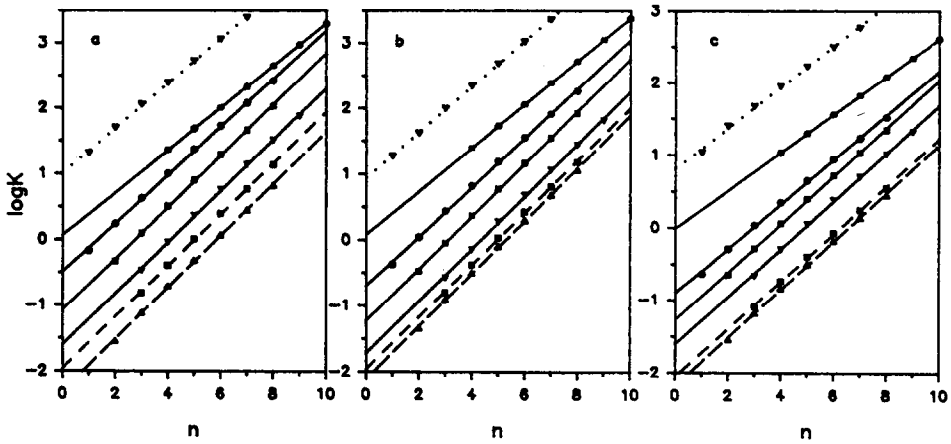

Fig. 1. Plots of calculated log K for transfer of homologous solutes from organic solvent–water (40:60, v/v) mixture to hexadecane *vs.* n at 298.15 K. (a) Methanol; (b) acetonitrile; (c) tetrahydrofuran. ● = n-Alkanes; ▼ = n-alkylbenzenes; ■ = 2-ketones; ▲ = 1-alkanols; ○ = n-alkyl acetates; ▽ = n-alkylnitriles; □ = nitroalkanes.

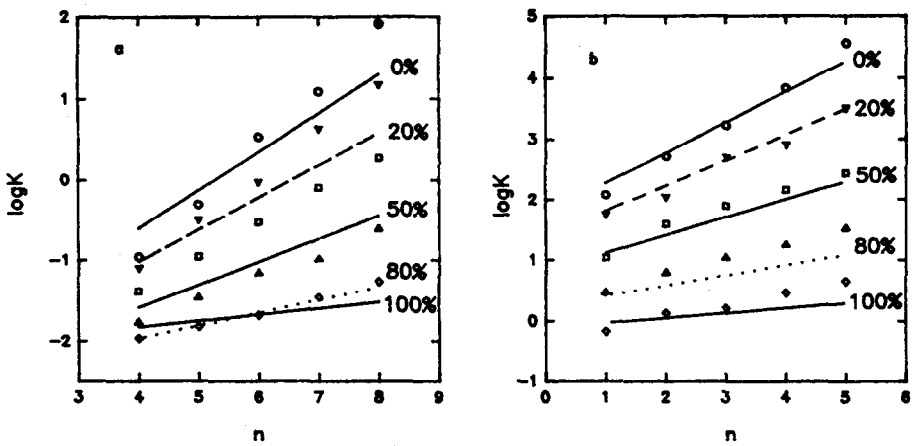

Fig. 2. Comparison of calculated (lines) and measured (symbols) log K values of (a) 1-alkanols and (b) n-alkylbenzenes for transfer from aqueous methanol mixtures to hexadecane *vs.* n at 298.15 K. ○ = 0%; ▽ = 20%; □ = 50%; △ = 80%; ◇ = 100% methanol.

composition are shown in Fig. 3 together with those for UNIFAC-computed log K values. The trends in these two sets of plots are both linear. For methylene group selectivity, which increases with decreasing content of organic solvent, the predictions by UNIFAC are also in agreement with experimental observations, as shown in Fig. 3.

Effect of mobile phase composition

Mobile phase composition effects are very important in LC. The exact form of the relationship between k' and the volume fraction of strong solvent in RPLC has been the subject of much debate. A linear relationship between log k' and volume percentage is thought to be more accurate for methanol–water mixtures than for mixtures of other solvents [34]. Other workers, on the basis of lattice theories [45] and simple regular solution theory [46], have advocated quadratic relationships. The displacement model of Geng and Regnier [47,48] argues for a linear relationship between log k' and the logarithm of the molar concentration of the modifier. The use

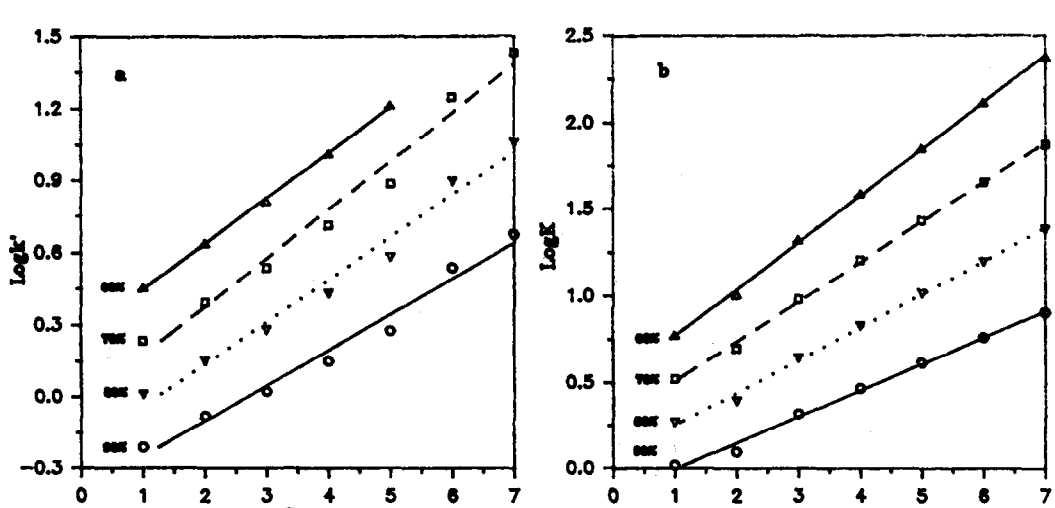

Fig. 3. Plots of (a) experimental log k' and (b) calculated log K of n-alkylbenzenes for transfer from aqueous acetonitrile mixtures to hexadecane *vs.* n at 298.15 K. Experimental k' data on an ODS column are from ref. 64.

of empirical parameters such as the ET(30) scale to correlate retention in RPLC have been discussed at length [49,50].

We can model mobile phase effects in RPLC by use of the UNIFAC approach by assuming as above that retention process in RPLC is pure partitioning. Plots of log K *vs.* composition for judiciously selected solutes chosen to span a wide range of properties (dipolarity, hydrogen bond donor and acceptor strength) are shown in Fig. 4. Note that the solid lines are those connecting the end-points and not least-squares lines. Clearly the plots are not precisely linear but there appears to be more curvature for the acetonitrile mixtures than the methanol mixtures. It can be seen that UNIFAC can predict elution sequences. For example, UNIFAC predicts that the elution sequence in RPLC would be butylamine < 1-butanol < 2-butanone < butyronitrile < butyl acetate < pentane with methanol–water as mobile phase, as is invariably observed in RPLC when there is no contribution to retention from strong adsorption of hydrogen-bonding solutes on the residual surface silanol groups of silica.

Dorsey and Dill [32] have persuasively shown in their development of interphase partition theory of retention that although there are some deviations from partitioning due to molecular organization in the stationary phase, the relevant model for RPLC retention is partitioning rather than adsorption and the relationship between retention (log k') and volume fraction of organic solvent (φ_0) is quadratic in nature. Schoenmakers and co-workers [46,51] have shown that log k' varies quadratically with φ_0 according to the equation

$$\log k' = A\varphi_0^2 + B\varphi_0 + C \quad (3)$$

Other investigators have disputed this quadratic dependence and argued that retention can be described by the linear relationship [52–54]

$$\log k' = \log k'_w - S\varphi_0 \quad (4)$$

where k'_w is the k' value in 100% water and S is a parameter related to the solvent strength of the pure organic solvent. As can be seen Fig. 4, plots of log K *vs.* volume fraction of organic solvent for non-polar and non-hydrogen-bonding solutes such as *n*-pentane and *n*-propylbenzene are linear in aqueous mixtures of all three organic solvents. The same plots for polar and hydrogen-bonding solutes are curved and the extent of curvature seems to increase with increasing polarity and hydrogen-bonding capability. This is in

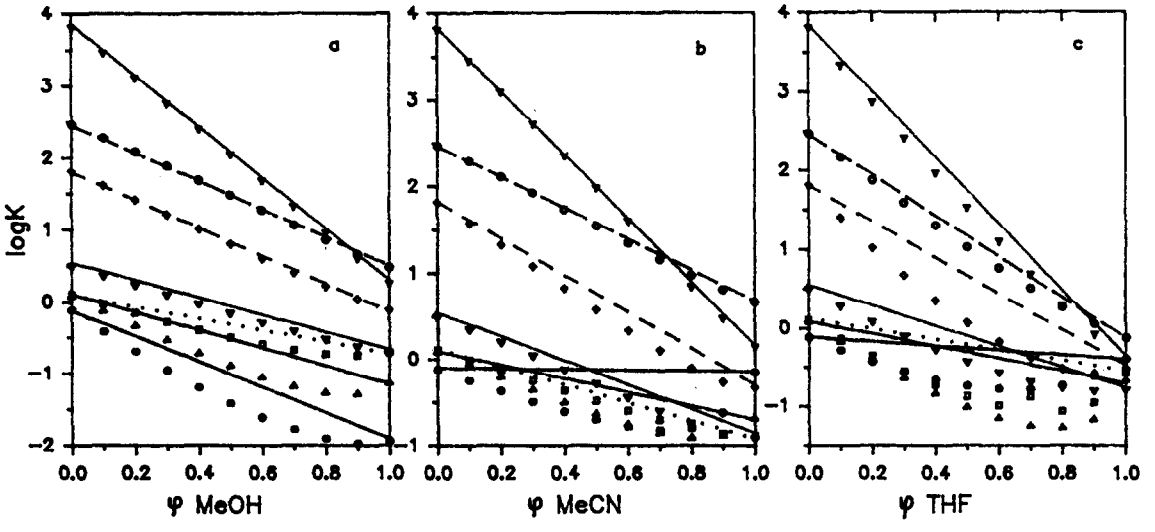

Fig. 4. Plots of calculated logarithm of hexadecane–aqueous mixture partition coefficients (K) of various solutes *vs.* volume fraction of (a) methanol, (b) acetonitrile and (c) tetrahydrofuran at 298.15 K. ○ = *n*-Pentane; ▽ = *n*-propylbenzene; □ = 2-butanone; △ = 1-butanol; ◇ = *n*-butyl acetate; ● = *n*-butylamine; ▼ = butyronitrile.

TABLE I

REGRESSION ANALYSIS OF EFFECT OF VOLUME FRACTION ON HEXADECANE–AQUEOUS METHANOL PARTITION COEFFICIENTS

The data are the results of regressing the log K *vs.* volume fraction of the organic solvent in the aqueous mixture. The number of data points is 11 in all regressions.

Solute	Log k'_w [a]	S^a	r^a	A^b	B^b	C^b	r^b
Pentane	2.48	−2.01	0.9999	−0.01	−2.00	2.47	1.0000
n-Propylbenzene	3.78	−3.57	0.9999	−0.04	−3.53	3.78	1.0000
2-Butanone	−0.33	−0.88	0.9675	0.79	−1.67	0.21	0.9969
1-Butanol	−0.77	−1.38	0.9521	1.47	−2.85	−0.55	0.9930
n-Butyl acetate	1.35	−1.96	0.9995	0.18	−2.14	1.38	0.9999
Butyronitrile	1.10	−1.24	0.9988	0.20	−1.44	0.13	0.9998
n-Butylamine	−0.61	−1.91	0.9741	1.56	−3.47	−0.37	0.9989

[a] Based on eqn. 4.
[b] Based on eqn. 3.

fact what is observed for these solutes in RPLC. Schoenmakers and co-workers [46,51] have shown that log k' varies non-linearly with φ_0 if k' data are collected over a sufficiently wide range of φ_0 values. The extent of curvature becomes more pronounced with type of organic solvent in the order methanol < tetrahdrofuran < acetonitrile. This order is the reverse of that for the degree of association of the organic solvents with water (acetonitrile < tetrahydrofuran < methanol) [55,56]. The prediction by UNIFAC is in agreement with these experimental observations. In Tables I–III are listed the coefficients of the quadratic expression (eqn. 3) and of the linear expression (eqn. 4) for UNIFAC-predicted log K together with correlation coefficients (r). In agreement with experimental observations [46,51], the retention of non-polar solutes is well described by the linear relationship whereas that of polar and associating solutes is better described by the quadratic expression. The implication of these results is that in gradient elution

TABLE II

REGRESSION ANALYSIS OF EFFECT OF VOLUME FRACTION ON HEXADECANE–AQUEOUS ACETONITRILE PARTITION COEFFICIENTS

The data are the results of regressing the log K *vs.* volume fraction of the organic solvent in the aqueous mixture. The number of data points is 11 in all regressions.

Solute	Log k'_w [a]	S^a	r^a	A^b	B^b	C^b	r^b
Pentane	2.48	−1.88	0.9999	−0.06	−1.83	2.47	1.0000
n-Propylbenzene	3.79	−3.72	0.9999	−0.17	−3.58	3.77	1.0000
2-Butanone	−0.25	−1.15	0.9995	0.13	−1.25	−0.23	0.9999
1-Butanol	−0.64	−1.29	0.9943	0.56	−1.74	−0.59	0.9992
n-Butyl acetate	1.36	−2.43	0.9998	0.17	−2.57	1.38	0.9999
Butyronitrile	0.13	−1.57	0.9999	−0.02	−1.55	0.12	0.9999
n-Butylamine	−0.47	−0.91	0.9681	0.97	−1.69	−0.38	0.9961

[a] Based on eqn. 4.
[b] Based on eqn. 3.

TABLE III

REGRESSION ANALYSIS OF EFFECT OF VOLUME FRACTION ON HEXADECANE–AQUEOUS TETRAHYDROFURAN PARTITION COEFFICIENTS

The data are the results of regressing the log K *vs.* volume fraction of the organic solvent in the aqueous mixture. The number of data points is 11 in all regressions.

Solute	Log k'_w [a]	S [a]	r [a]	A [b]	B [b]	C [b]	r [b]
Pentane	2.43	−2.76	0.9993	0.45	−3.12	2.47	1.0000
n-Propylbenzene	3.72	−4.41	0.9996	0.56	−4.85	3.77	1.0000
2-Butanone	−0.37	−1.51	0.9725	1.58	−2.77	−0.23	0.9909
1-Butanol	−0.73	−1.75	0.9799	1.55	−2.99	−0.59	0.9995
n-Butyl acetate	1.20	−2.94	0.9900	1.85	−4.42	1.38	1.0000
Butyronitrile	0.04	−1.60	0.9916	0.91	−2.33	0.12	0.9999
n-Butylamine	−0.53	−0.80	0.9190	1.51	−2.01	−0.39	0.9988

[a] Based on eqn. 4.
[b] Based on eqn. 3.

optimum gradients are convex rather than linear, as shown by Schoenmakers *et al.* [51].

Effect of length of bonded stationary phase chains

The effects of the chain length of bonded alkyl phases were studied early in the development of RPLC [57–61]. It has been observed that methylene group selectivity increases with increasing chain length of non-monomeric alkyl-bonded phases [58,59]. Others [60,61], however, have shown that the selectivity is almost independent of bonded alkyl chainlength when measured on monomeric stationary phases. To see how UNIFAC can explain these observations, log K for *n*-alkanes and *n*-alkylbenzenes between aqueous organic mixtures and hexadecane, octane, butane (hypothetical supercooled liquid) and benzene, which simulate hexadecyl-, octyl-, butyl- and phenyl-bonded stationary phases, respectively, were computed and regressed *vs.* n. The resulting slopes are listed in Table IV. The slope of the plot of log K *vs.* n for *n*-alkanes (methylene group selectivity) increases in the order hexadecane < octane < butane,

TABLE IV

SLOPES OBTAINED BY LINEAR REGRESSION OF LOG K OF *n*-ALKANES AND *n*-ALKYLBENZENES AGAINST CARBON NUMBER

K = Partition coefficients for transfer from organic solvent–water (40:60, v/v) mixtures to each stationary phase liquid at 298.15 K.

Compounds	Stationary phase	Methanol	Acetonitrile	Tetrahydrofuran
n-Alkanes	Butane	0.386	0.392	0.324
	Octane	0.347	0.353	0.285
	Hexadecane	0.324	0.331	0.262
	Benzene	0.353	0.360	0.291
n-Alkylbenzenes	Butane	0.406	0.411	0.346
	Octane	0.367	0.372	0.307
	Hexadecane	0.344	0.349	0.284
	Benzene	0.373	0.378	0.313

which is opposite to the experimental observation [58,59]. This may be due to the failure of UNIFAC to predict accurately the γ^{∞} values of *n*-alkane solutes in *n*-alkane solvents. Table V lists calculated the γ_m^{∞} values for *n*-alkanes in methanol–water mixture (40:60, v/v) and γ_s^{∞} in butane, octane and hexadecane, along with selectivity factors in the mobile phase (α_m) and stationary phase (α_s). The γ^{∞} values for *n*-alkanes in methanol–water (40:60, v/v) increase sharply with increasing carbon number. In butane, γ_s^{∞} for *n*-alkanes decreases with increasing carbon number (slope = −0.059, correlation coefficient = 0.987), whereas in octane it increases with increasing carbon number of up to 8 and then decreases, and in hexadecane it increases monotonously with increasing carbon number (slope = 0.054, correlation coefficient = 0.990). This makes the slopes of plots of log *K* for *n*-alkanes increase in the order hexadecane < octane < butane. Experiments indicate that the γ^{∞} values for *n*-pentane to *n*-heptane in *n*-octane decrease slightly [62] whereas those for *n*-pentane to decane in hexadecane increase with increasing carbon number [63]. The causes of the failure of UNIFAC to predict γ^{∞} values for these simple systems of alkanes in alkanes have already been discussed in detail elsewhere [17]. However, it should be noted that in Table V the variation in the selectivities in the stationary phases is very small (factors of 1.15, 1.36 and 1.51 in octane, butane and hexadecane, respectively) compared with that in the mobile phase (factor of 62). This is in agreement with the experimental observation of very small differences in α_s between octylsilica and octadecylsilica with aqueous methanol (1.9%) [60].

For *n*-alkylbenzenes a similar trend is observed but the methylene group selectivity is higher than that for *n*-alkanes. This is in agreement with the observation that the presence of π-electrons enhances the selectivity [64].

Temperature dependence of retention

Recently, Dorsey and co-workers [65,66] showed in their studies of the temperature dependence of retention in RPLC that Van 't Hoff plots are not linear if retention data are measured over a wide temperature range (−5 to 80°C). In water–1-propanol (95:5) the curved Van 't Hoff plot for the retention of benzene on an ODS silica column were fitted by a second-degree polynomial. In order to see whether UNIFAC can predict this temperature dependence, a Van 't Hoff plot for benzene was prepared using UNIFAC-based log *K* values in the same mobile phase on hexadecane, and compared with the plot for log *K* values derived from experimental *k'* values measured on an ODS column in Fig. 5. The modified UNIFAC by Larsen *et al.* [24] was used for comparison as this version has a much better built-in temperature dependence and a better accuracy of predictions of γ^{∞} than the original UNIFAC [22]. We

TABLE V

VALUES OF γ^{∞} AND SELECTIVITY FACTORS FOR *n*-ALKANES IN METHANOL–WATER (40:60, V/V), BUTANE, OCTANE AND HEXADECANE AT 298.15 K

Values in parentheses are selectivity factors relative to decane in the mobile phase (α_m) and model stationary phases (α_s). Selectivity factors were calculated using the equations $\alpha_m = \gamma_{m2}/\gamma_{m1}$ and $\alpha_s = \gamma_{s2}/\gamma_{s1}$. By definition, solute 2 is more retained.

n-Alkane	Methanol–water (40:60, v/v)	Butane	Octane	Hexadecane
Butane	169 (137)	1.00 (0.66)	0.86 (1.14)	0.59 (1.56)
Pentane	405 (57)	0.98 (0.67)	0.93 (1.05)	0.67 (1.37)
Hexane	941 (24)	0.94 (0.70)	0.97 (1.01)	0.74 (1.24)
Heptane	2139 (11)	0.88 (0.75)	0.99 (0.99)	0.80 (1.15)
Octane	4786 (4.8)	0.81 (0.81)	1.00 (0.98)	0.85 (1.08)
Nonane	10 572 (2.2)	0.73 (0.90)	0.99 (0.99)	0.89 (1.03)
Decane	23 116	0.66	0.98	0.92

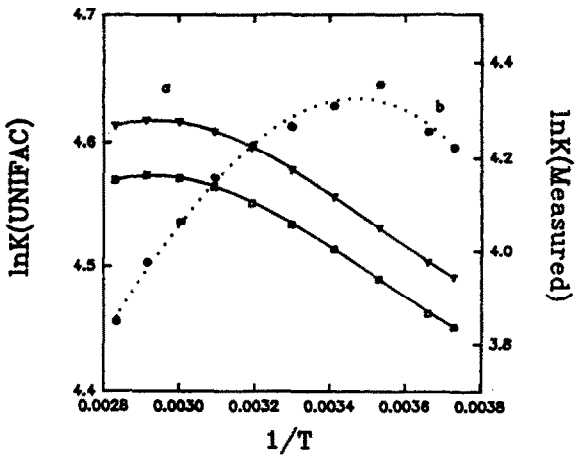

Fig. 5. Van 't Hoff plots for (a) calculated (solid lines) and (b) measured (dotted line) log K of benzene for transfer from water–1-propanol (95:5) to a model stationary phase composed of hexadecane, 1-propanol and water (composition in mole fraction: ▽ = 0.45:0.45:0.1; □ = 0.6:0.3:0.1) and to an ODS silica (●).

therefore expected that UNIFAC should, at least, be able to predict the same trend as observed in experiments even if it cannot quantitatively reproduce the experiment. The prediction by UNIFAC is curved, as are the experimental values, but the temperature at which a distinct change in slope occurs is different from that observed experimentally [*ca.* 50°C (UNIFAC) *vs.* 20°C (ref. 66)]. The change in slope in the Van 't Hoff plot is an indication of the hydrophobic effect operating in the system of a strongly hydrogen-bonded mobile phase and a non-polar alkyl-bonded phase [67–69]. Even the modified UNIFAC of Larsen *et al.* [24], which uses temperature-dependent group interaction parameters, is not able to predict temperature dependence accurately.

CONCLUSIONS

Although UNIFAC is not accurate enough for the quantitative prediction of retention in RPLC, it is useful in explaining a variety of issues of general importance in RPLC such as the effects of the carbon number, the type of functional group of the solutes and the composition of the mobile phase on retention in reversed-phase liquid–liquid partition chromatography. Even with a number of modifications applied to the original UNIFAC to improve its predictive accuracy for γ^{∞}, predictions of retention by UNIFAC are still not accurate enough to be useful for developing a computer-based retention prediction scheme [8]. Among several versions of the UNIFAC method, the modified UNIFAC method of Weidlich and Gmehling [23] has been shown to give the best prediction of γ^{∞} with an accuracy of *ca.* 5% and was thus been able to predict retention in GLC with similar accuracy [5]. However, it does not have group interaction parameters for water. If group interaction parameters for water which could predict γ^{∞} to within 5% in water-containing systems are obtained, it would be possible to develop a computer program to predict retention in RPLC.

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