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PREDICTION OF RETENTION IN GAS-LIQUID CHROMATOGRAPHY USING THE UNIFAC GROUP CONTRIBUTION METHOD

I. LOW-MOLECULAR-WEIGHT STATIONARY PHASES

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SUMMARY

The UNIFAC group contribution method and its free volume modified version were used to calculate thermodynamic activity coefficients for a number of solutes at infinite dilution in a range of non-polymeric gas-liquid chromatographic stationary phases. Specific retention volumes and partition coefficients were calculated and used to predict relative retentions and the order of elution of the solutes and these were compared with corresponding experimental values. For non-polar stationary phases, the elution orders were correctly predicted, even for closely related isomers, except with very close retention volumes, although the UNIFAC and experimental partition coefficients differed by up to 20-50%, depending on the system. For polar phases and systems with strong specific interactions such as hydrogen bonding, the predictions differed greatly from the experimental values. The method may be useful for correlating results for non-polar phases but its wider predictive use awaits further development of the UNIFAC methodology.

INTRODUCTION

In selecting a stationary phase for a particular analysis, the chromatographer is faced with a huge number of possibilities. A recent count showed in excess of 400 liquid phases for gas chromatography, to which must be added a range of solid adsorbents. Perhaps only a dozen or so are in common use although, when mixed stationary phases are considered, the number is multiplied many-fold¹. Despite the use of parameters such as Kováts retention indices or McReynold's constants for characterizing stationary phases, these often require a knowledge of some properties of the system and there are many occasions when a "trial and error" approach is needed, at least initially, to the selection of phases.

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Over the past 20 years or so, gas-liquid chromatography (GLC) has become a popular and well tested method for the measurement of thermodynamic properties of solutions² such as activity coefficients, enthalpies and free energies of mixing. The activity coefficient of a volatile solute at infinite dilution in a liquid stationary phase, γ_1^∞ , is given by

$$\gamma_1^\infty = 273.15 R/V_g^0 P_1^0 M_2 \quad (1)$$

where R is the gas constant, M_2 is the molecular weight of the stationary phase liquid, P_1^0 is the saturated vapour pressure of the solute at the column temperature and V_g^0 is the specific retention volume of the solute, *i.e.*, the retention volume per gram of stationary phase fully corrected to standard temperature and pressure. Similarly, the solute partition coefficient, K_r , can be calculated from

$$K_r = RT/\gamma_1^\infty V_2^0 P_1^0 \quad (2)$$

where V_2^0 is the molar volume of the stationary phase at the column temperature, T . A number of workers have demonstrated the utility of GLC in this area of study².

During the same time period, several techniques have been developed for predicting thermodynamic properties of liquid mixtures. Given the link between thermodynamics and GLC, it was of interest to determine whether retention on a particular stationary phase could be predicted in an accurate and reproducible manner, with a view to using the method to select a stationary phase for a given analysis or separation. One of the most useful of the methods is UNIFAC^{3,4}. This is a group contribution method that splits the molecules comprising the solution into a number of well defined groups. The thermodynamic activities of these groups are then summed using previously calculated and tabulated values of a selection of properties. Hence only relatively few parameters are needed and, as only pure component properties such as densities and molecular weights are needed, this makes the method particularly attractive as it may be used in systems where few or no experimental data are available, as in a new analysis.

Roth and Novak⁵ applied the original UNIFAC method to a number of systems and concluded that "... (it) can be used merely to give a rough estimation of relative retentions". Price and Ashworth⁶ found that a single result from GLC could be used to improve the predictive ability of UNIFAC for polymer solutions. In this paper, we present a systematic approach to a wider range of systems and also include the application of newer developments of the method. To test our techniques, high-quality thermodynamic results were required for comparison. Much of the earliest work to confirm that GLC was a valid technique for thermodynamic measurement involved squalane (2,6,10,15,19,23-hexamethyltetracosane) and dinonyl phthalate (bis-3,5,5-trimethylhexyl phthalate), so these phases were used as the basis of this work. Also considered are a number of other stationary phases covering a range of polarities. The work involving low-molecular-weight phases will be discussed here; that involving polymeric phases will be the subject of a future paper.

THE UNIFAC METHOD

UNIFAC is a group contribution technique, *i.e.*, it splits each molecule being considered into a number of functional groups such as methyl, methylene and carbonyl, and treats the solution as a mixture of these groups. The original method was developed by Fredenslund *et al.*⁴ for the correlation and prediction of vapour-liquid equilibrium although it has also been applied to a range of other properties^{7,8}. It involved the assumption of two contributions to the thermodynamic activity of a solvent in solution. The combinatorial (or entropic) part, a_1^C , is calculated using an expression derived from Staverman's statistical mechanical treatment⁹ as adapted by Abrams and Prausnitz¹⁰:

$$\ln a_1^C = \ln \varphi_1 + \varphi_2 + (zM_1q_1/2) [\ln (\theta_1/\varphi_1) - 1 - (\varphi_1/\theta_1)] \quad (3)$$

where M_1 is the solvent molecular weight, z is a "lattice coordination number", conventionally set to 10 to conform with recent practice^{6,11,12}, and φ_1 and θ_1 are the UNIFAC segment and surface area fractions, respectively, given for a weight fraction of solvent, W_1 by

$$\varphi_1 = W_1 r_1 / \sum_i W_i r_i; \quad \theta_1 = W_1 q_1 / \sum_i W_i q_i \quad (4)$$

For any molecule containing $n_k^{(i)}$ groups of type k and having molecular weight M_i , the molecular parameters r_i and q_i are found by summing all group volume and surface parameters R_k and Q_k which are listed in the literature¹², having been calculated from Van der Waals properties as given by Bondi¹³:

$$r_i = [\sum_k n_k^{(i)} R_k] / M_i; \quad q_i = [\sum_k n_k^{(i)} Q_k] / M_i \quad (5)$$

The second, residual (or enthalpic) contribution to the activity is defined in terms of inter-group interaction parameters which have been calculated by minimizing differences between UNIFAC and experimental vapour-liquid equilibrium results for a large number of binary systems. Each pair of groups, say j and k , has two parameters, ψ_{jk} and ψ_{kj} , which account for energetic interactions between the groups and are tabulated in the literature¹². The residual part of the activity, a_1^R , is given by

$$\ln a_1^R = \sum_k n_k^{(i)} [\ln \Gamma_k - \ln \Gamma_k^{(1)}] \quad (6)$$

where Γ_k is the group residual activity in the solution and $\Gamma_k^{(1)}$ is that in the pure liquid solvent. These may be calculated by summing the interactions over all pairs of groups in the solution:

$$\ln \Gamma_k = Q_k [1 - \ln (\sum_j \theta_j \psi_{jk}) - \sum_j (\theta_j \psi_{kj} / \sum_m \psi_{jm})] \quad (7)$$

The same equation can be used for $\Gamma_k^{(1)}$ with appropriate assignment of j and m .

These two contributions were found to be adequate for small-molecule solutions but, when working with polymer solutions, an extra contribution to the solvent activity arising from the well known free volume differences between polymers and solvents must be considered. As shown by Oishi and Prausnitz¹⁴, this may be done using Flory's expression¹⁵:

$$\ln a_1^{\text{FV}} = 3c_1 \ln [(v_1^{1/3} - 1)/(v^{1/3} - 1)] - c_1 \{[(v_1/v) - 1] (1 - 1/v_1^{1/3})^{-1}\} \quad (8)$$

where the parameter $3c_1$ is the number of external degrees of freedom. Oishi and Prausnitz¹⁴ gave expressions for the reduced volumes, v_i , of the solvent:

$$v_i = v_i/15.17 br_i$$

and v for the solution:

$$v = (\sum_i W_i v_i) / [15.17 b (\sum_i W_i r_i)]$$

where v_i is the specific volume of a component. By comparison with experimental data, they set the factors $c_1 = 1.1$ and $b = 1.28$.

The overall activity of the solvent in the solution is thus given by

$$\ln a_1 = \ln a_1^{\text{C}} + \ln a_1^{\text{R}} + \ln a_1^{\text{FV}} \quad (9)$$

RESULTS

Analytical GLC is usually performed with the solute being analysed effectively at infinite dilution. As a value of zero concentration cannot be used in the UNIFAC equations, a solute molar fraction of $1 \cdot 10^{-6}$ was used to simulate infinite dilution. The use of lower concentrations was found to have a negligible effect on the results. The UNIFAC activity of the solute was calculated using the above equations in a BASIC program written for the IBM PC and converted to activity coefficient by dividing by the molar fraction. Values of the specific retention volume and partition coefficient were calculated from eqns. 1 and 2 using this γ_1^∞ value and physical property data from the literature¹⁶.

The stationary phases considered here, *e.g.*, squalane, may be considered to be intermediate between the small molecules for which UNIFAC was originally developed and polymer systems for which the free volume treatment was developed. It was therefore of interest to determine which of the two treatments would yield better results, so both were used in this work. Values calculated from the original treatment will be designated "uni" and those from the later treatment as "uni-fv".

The predicted results were compared with experimental values in two ways. First, specific retention volumes were used to calculate relative retentions and the order of elution of the solutes. Second, the partition coefficients were used to construct plots so that the comparisons could be more easily visualized. As an illustration of the methodology, results for systems involving squalane will be described in detail and a summary of results for other phases will follow.

TABLE I
SPECIFIC RETENTION VOLUMES FOR SOLUTES IN SQUALANE AT 30°C

| Solute | V_g^0 ($\text{cm}^3 \text{g}^{-1}$) | | | Relative retention volume | | | Elution order | | |
|----------------------|---|-------|--------|---------------------------|------|--------|---------------|-----|--------|
| | Expt. | uni | uni-fv | Expt. | uni | uni-fv | Expt. | uni | uni-fv |
| Pentane | 105.6 | 125.7 | 100.2 | 2.5 | 2.2 | 2.0 | 4 | 3 | 3 |
| Hexane | 335.8 | 353.5 | 299.5 | 8.0 | 6.1 | 5.9 | 7 | 7 | 7 |
| Heptane | 1030.8 | 991.6 | 876.8 | 24.6 | 17.1 | 17.3 | 11 | 11 | 11 |
| Cyclohexane | 648.5 | 620.8 | 596.4 | 15.5 | 10.7 | 11.8 | 10 | 10 | 10 |
| Benzene | 483.3 | 523.9 | 474.9 | 11.6 | 9.0 | 9.4 | 8 | 8 | 9 |
| Diethyl ether | 82.4 | 74.0 | 57.4 | 2.0 | 1.3 | 1.2 | 2 | 2 | 2 |
| Acetone | 41.8 | 58.2 | 50.6 | 1 | 1 | 1 | 1 | 1 | 1 |
| Ethyl acetate | 183.9 | 219.8 | 197.5 | 4.4 | 3.8 | 3.9 | 5 | 5 | 5 |
| Dichloromethane | 82.3 | 141.2 | 123.7 | 1.9 | 2.4 | 2.5 | 3 | 4 | 4 |
| Chloroform | 249.7 | 276.6 | 249.4 | 6.0 | 4.8 | 4.9 | 6 | 6 | 6 |
| Carbon tetrachloride | 516.9 | 536.3 | 470.8 | 12.4 | 9.2 | 9.3 | 9 | 9 | 8 |

Squalane

Table I shows experimental V_g^0 results¹⁷⁻²³ for eleven solutes in squalane at 30°C together with the predicted values from both the UNIFAC treatments. Relative retentions were calculated using the lowest V_g^0 as a standard, in this instance that of acetone. Also shown is the order in which the solutes would elute under these conditions. The order is generally correct, with one or two exceptions where the V_g^0 values are close. Comparison in terms of the partition coefficients is given in Table II, which lists the deviation from the experimental results according to

$$\Delta K_r(\%) = 100 [K_r(\text{UNIFAC}) - K_r(\text{expt.})]/K_r(\text{expt.}) \quad (10)$$

so that negative values indicate that UNIFAC underestimates the partition coefficient.

TABLE II
PARTITION COEFFICIENTS FOR SOLUTES IN SQUALANE AT 30°C

| Solute | Partition coefficient | | | Deviation, ΔK_r (%) | |
|----------------------|-----------------------|-------|--------|-----------------------------|--------|
| | Expt. | uni | uni-fv | uni | uni-fv |
| Pentane | 93.9 | 111.9 | 89.2 | 16.0 | 2.4 |
| Hexane | 298.9 | 314.6 | 266.5 | 5.0 | -12.1 |
| Heptane | 1917.4 | 882.6 | 780.3 | -4.0 | -17.5 |
| Cyclohexane | 577.2 | 552.5 | 530.8 | -4.5 | -8.7 |
| Benzene | 430.1 | 466.6 | 422.7 | 7.8 | -1.8 |
| Diethyl ether | 76.6 | 65.8 | 51.0 | -16.4 | -50.2 |
| Acetone | 38.3 | 51.8 | 45.0 | 26.0 | 14.9 |
| Ethyl acetate | 167.3 | 195.6 | 174.4 | 14.5 | 4.1 |
| Dichloromethane | 76.3 | 125.6 | 110.1 | 39.3 | 30.7 |
| Chloroform | 223.9 | 246.1 | 221.9 | 9.0 | -1.0 |
| Carbon tetrachloride | 466.2 | 477.3 | 418.9 | 2.3 | -11.3 |

For the squalane system there is a wide variation in ΔK_r with deviations of up to 50% in the worst case, although the average deviation was around 10–15%.

For the other systems discussed in this paper, the tables will be simplified to aid interpretation. Relative retentions will be listed together with the V_g^0 of the reference component. Similarly, only the experimental partition coefficients and the deviations of the UNIFAC results will be listed. The original values can easily be calculated by other workers should this be required.

Tables III and IV show results for squalane stationary phases at 50, 60 and 70°C²⁴. Again, the elution order is predicted reasonably well except in the case of very close V_g^0 values. The partition coefficients for squalane at all temperatures are shown in Fig. 1, where the experimental values are plotted against the corresponding UNIFAC results so that, if the predictions were exact, all points would lie on the diagonal straight line. The agreement is good although the general trend is for UNIFAC to underestimate the results. There is no significant difference in comparing results from the original and free volume modified UNIFAC methods for squalane.

Dinonyl phthalate (DNP)

DNP is also a well studied stationary phase from a thermodynamic point of view and represents a moderately polar phase, in contrast to the non-polar nature of squalane. UNIFAC predictions are compared with experimental results^{17–24} in Tables

TABLE III

SPECIFIC RETENTION VOLUMES FOR SOLUTES IN SQUALANE AT 50, 60 AND 70°C

Experimental relative retentions were calculated using values for chloroform of 126.2, 92.07 and 69.13 cm³ g⁻¹ at 50, 60 and 70°C, respectively.

| Solute | Temperature (°C) | Relative retention volume | | | Elution order | | |
|---|---------------------|---------------------------|-----|--------|---------------|-----|--------|
| | | Expt. | uni | uni-fv | Expt. | uni | uni-fv |
| Hexane Heptane Cyclohexane Benzene Chloroform Carbon tetrachloride | 50 | 1.2 | 1.3 | 1.3 | 2 | 2 | 2 |
| | | 3.4 | 3.0 | 3.0 | 6 | 6 | 6 |
| | | 2.3 | 2.1 | 2.2 | 5 | 5 | 5 |
| | | 1.8 | 1.7 | 1.8 | 3 | 3 | 4 |
| | | 1 | 1 | 1 | 1 | 1 | 1 |
| | | 1.9 | 1.8 | 1.7 | 4 | 4 | 3 |
| Hexane Heptane Cyclohexane Benzene Chloroform Carbon tetrachloride | 60 | 1.2 | 1.2 | 1.2 | 2 | 2 | 2 |
| | | 3.2 | 2.8 | 2.8 | 6 | 6 | 6 |
| | | 2.3 | 2.0 | 2.1 | 5 | 5 | 5 |
| | | 1.8 | 1.7 | 1.7 | 3 | 3 | 3 |
| | | 1 | 1 | 1 | 1 | 1 | 1 |
| | | 1.9 | 1.8 | 1.7 | 4 | 4 | 4 |
| Hexane Heptane Cyclohexane Benzene Chloroform Carbon tetrachloride | 70 | 1.2 | 1.2 | 1.1 | 2 | 2 | 2 |
| | | 2.9 | 2.7 | 2.6 | 6 | 6 | 6 |
| | | 2.2 | 1.9 | 2.1 | 5 | 5 | 5 |
| | | 1.7 | 1.7 | 1.7 | 3 | 3 | 4 |
| | | 1 | 1 | 1 | 1 | 1 | 1 |
| | | 1.8 | 1.7 | 1.7 | 4 | 4 | 3 |

TABLE IV
PARTITION COEFFICIENTS FOR SOLUTES IN SQUALANE AT 50, 60 AND 70°C

| Solute | Temperature (°C) | Experimental K_r | Deviation, ΔK_r (%) | |
|----------------------|---------------------|-----------------------|-----------------------------|--------|
| | | | uni | uni-fv |
| Hexane | 50 | 148.9 | 2.6 | -6.5 |
| Heptane | | 402.9 | -5.3 | -20.0 |
| Cyclohexane | | 276.3 | -6.1 | -11.6 |
| Benzene | | 214.3 | 3.1 | -7.8 |
| Chloroform | | 118.2 | 5.9 | -5.7 |
| Carbon tetrachloride | | 229.5 | -0.1 | -16.0 |
| Hexane | 60 | 108.8 | 1.9 | -6.5 |
| Heptane | | 279.1 | -5.6 | -20.9 |
| Cyclohexane | | 198.5 | -6.5 | -12.6 |
| Benzene | | 157.2 | 0.9 | -10.7 |
| Chloroform | | 88.4 | 5.1 | -7.1 |
| Carbon tetrachloride | | 167.9 | -1.5 | -18.2 |
| Hexane | 70 | 81.9 | 0.3 | -21.1 |
| Heptane | | 198.5 | -5.9 | -21.9 |
| Cyclohexane | | 146.8 | -7.5 | -14.3 |
| Benzene | | 118.2 | -1.2 | -13.8 |
| Chloroform | | 67.9 | 3.6 | -9.5 |
| Carbon tetrachloride | | 124.7 | -2.1 | -19.4 |

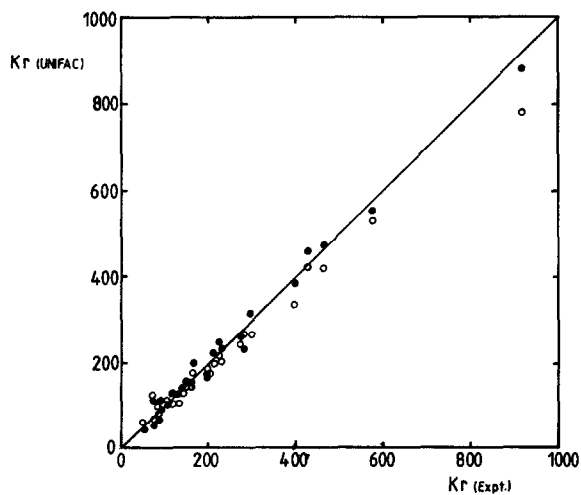


Fig. 1. Plot of experimental versus UNIFAC partition coefficients for solutes in squalane at 30, 50, 60 and 70°C. ●, uni; ○, uni-fv.

TABLE V

SPECIFIC RETENTION VOLUMES FOR SOLUTES IN DNP AT 30, 50, 60 AND 70°C

Experimental relative retentions were calculated using values for pentane of $57.3 \text{ cm}^3 \text{ g}^{-1}$ at 30°C and for hexane of 87.9, 63.8 and $47.6 \text{ cm}^3 \text{ g}^{-1}$ at 50, 60 and 70°C, respectively.

| Solute | Temperature (°C) | Relative retention volume | | | Elution order | | |
|----------------------|---------------------|---------------------------|-----|--------|---------------|-----|--------|
| | | Expt. | uni | uni-fv | Expt. | uni | uni-fv |
| Pentane | 30 | 1 | 1 | 1 | 1 | 1 | 1 |
| Hexane | | 3.2 | 2.7 | 2.9 | 4 | 4 | 4 |
| Heptane | | 9.3 | 7.3 | 8.2 | 9 | 10 | 10 |
| Cyclohexane | | 6.3 | 5.0 | 6.3 | 6 | 6 | 7 |
| Benzene | | 10.8 | 8.3 | 9.7 | 10 | 11 | 11 |
| Diethyl ether | | 1.5 | 1.3 | 1.3 | 2 | 2 | 2 |
| Acetone | | 2.7 | 2.1 | 2.4 | 3 | 3 | 3 |
| Ethyl acetate | | 7.2 | 5.3 | 6.1 | 7 | 7 | 6 |
| Dichloromethane | | 4.1 | 3.5 | 3.9 | 5 | 5 | 5 |
| Chloroform | | 11.4 | 6.2 | 7.2 | 11 | 8 | 8 |
| Carbon tetrachloride | 8.5 | 6.8 | 7.6 | 8 | 9 | 9 | |
| Hexane | 50 | 1 | 1 | 1 | 1 | 1 | 1 |
| Heptane | | 2.6 | 2.4 | 2.3 | 4 | 4 | 5 |
| Cyclohexane | | 2.0 | 1.8 | 1.9 | 2 | 2 | 2 |
| Benzene | | 3.2 | 2.9 | 2.8 | 6 | 6 | 6 |
| Chloroform | | 3.1 | 2.2 | 2.2 | 5 | 3 | 3 |
| Carbon tetrachloride | 2.5 | 2.4 | 2.3 | 3 | 4 | 5 | |
| Hexane | 60 | 1 | 1 | 1 | 1 | 1 | 1 |
| Heptane | | 2.6 | 2.4 | 2.3 | 4 | 4 | 5 |
| Cyclohexane | | 1.9 | 1.8 | 1.8 | 2 | 2 | 2 |
| Benzene | | 3.0 | 2.8 | 2.7 | 6 | 6 | 6 |
| Chloroform | | 2.9 | 2.2 | 2.3 | 5 | 3 | 3 |
| Carbon tetrachloride | 2.5 | 2.4 | 2.2 | 3 | 4 | 5 | |
| Hexane | 70 | 1 | 1 | 1 | 1 | 1 | 1 |
| Heptane | | 2.4 | 2.2 | 2.0 | 4 | 4 | 3 |
| Cyclohexane | | 1.9 | 1.7 | 1.8 | 2 | 2 | 2 |
| Benzene | | 2.9 | 2.7 | 2.6 | 6 | 6 | 6 |
| Chloroform | | 2.7 | 2.2 | 2.1 | 5 | 3 | 4 |
| Carbon tetrachloride | 2.4 | 2.3 | 2.1 | 3 | 5 | 5 | |

V and VI. Fig. 2 shows the graphical comparison and it is evident that there is much more scatter in the points and greater deviation of K_r than with squalane. The elution orders shown in Table V are generally correct, again with only one or two exceptions. It should be noted that the largest differences in the results, incorrect elution orders and the points lying furthest from the line in Fig. 2 all involve chloroform as the solute. This will be discussed in the following section. One feature of these results is that the free volume treatment underestimates K_r but gives superior predictions than the original treatment, which generally gives an overestimate.

There has been considerable interest in recent years in the use and properties of mixed stationary phases¹. Fig. 3 and Table VII show partition coefficients for three

TABLE VI

PARTITION COEFFICIENTS FOR SOLUTES IN DNP AT 30, 50, 60 AND 70°C

| Solute | Temperature (°C) | Experimental K_r | Deviation, ΔK_r (%) | | |
|----------------------|---------------------|-----------------------|-----------------------------|--------|------|
| | | | uni | uni-fv | |
| Pentane | 30 | 60.8 | 30.8 | -5.4 | |
| Hexane | | 192.0 | 19.5 | -3.1 | |
| Heptane | | 563.6 | 11.8 | -6.8 | |
| Cyclohexane | | 381.1 | 13.4 | 5.8 | |
| Benzene | | 659.4 | 9.9 | -5.8 | |
| Diethyl ether | | 96.3 | 16.9 | -17.1 | |
| Acetone | | 166.8 | 10.3 | -10.6 | |
| Ethyl acetate | | 448.9 | 3.1 | -16.3 | |
| Dichloromethane | | 255.7 | 19.4 | -1.0 | |
| Chloroform | | 701.3 | -28.9 | -52.4 | |
| Carbon tetrachloride | | 527.8 | -18.9 | -7.8 | |
| Hexane | | 50 | 98.3 | 16.3 | 4.7 |
| Heptane | | | 255.5 | 9.7 | -8.0 |
| Cyclohexane | 195.1 | | 7.4 | -0.6 | |
| Benzene | 307.2 | | 9.1 | -5.7 | |
| Chloroform | 301.5 | | -15.2 | -35.2 | |
| Carbon tetrachloride | 243.6 | | 14.3 | -4.6 | |
| Hexane | 60 | 73.2 | 14.8 | 3.9 | |
| Heptane | | 181.9 | 7.8 | -10.5 | |
| Cyclohexane | | 142.8 | 5.9 | -2.8 | |
| Benzene | | 218.5 | 8.8 | -6.4 | |
| Chloroform | | 214.6 | -13.7 | -34.0 | |
| Carbon tetrachloride | | 179.5 | 12.0 | -7.6 | |
| Hexane | 70 | 81.9 | -8.4 | -2.8 | |
| Heptane | | 132.1 | 6.3 | -12.9 | |
| Cyclohexane | | 105.5 | 5.7 | -3.6 | |
| Benzene | | 161.6 | 7.2 | -8.7 | |
| Chloroform | | 152.4 | -9.3 | -29.6 | |
| Carbon tetrachloride | | 131.9 | 11.9 | -7.9 | |

mixtures of squalane and DNP at 30°C (nominally 25, 50 and 75 mol-% although the actual concentrations from the experimental studies¹⁷⁻²³ were used). The results are similar to those for the pure component stationary phases, although ΔK_r for polar solutes increases as the amount of DNP in the mixture increases.

n-Hexadecane

n-Hexadecane was used as a stationary phase in the early days of GLC, although its use has largely been abandoned owing to its high volatility. However, accurate values of its retention properties are available²⁵ and these are compared with the UNIFAC predictions at 20, 30 and 40°C in Tables VIII and IX and in Fig. 4.

Fig. 4 clearly shows that UNIFAC considerably underestimates K_r in this phase

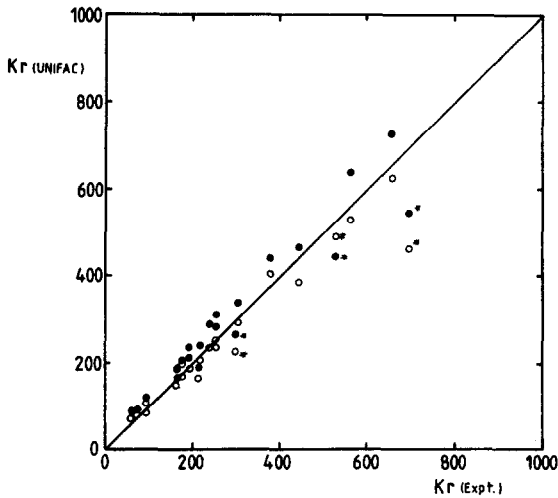


Fig. 2. Plot of experimental *versus* UNIFAC partition coefficients for solutes in DNP at 30, 50, 60 and 70°C. ●, uni; ○, uni-fv. The asterisks refer to chloroform results (see text).

and this is also shown by the values of ΔK_r in Table IX, where even the simple alkanes show deviations of 20–50%. In view of this it is perhaps surprising that, as shown in Table VIII, the elution order of the solutes considered is predicted exactly. For *n*-hexadecane, the original UNIFAC treatment gives better results, although these are considerably worse than with squalane or DNP.

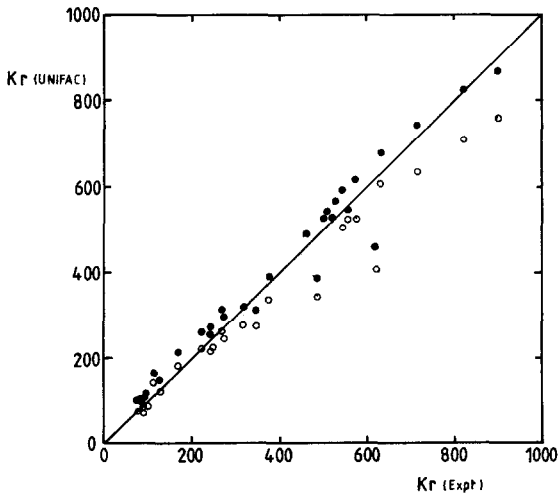


Fig. 3. Plot of experimental *versus* UNIFAC partition coefficients for solutes in mixtures of DNP and squalane at 30°C. ●, uni; ○, uni-fv.

TABLE VII

PARTITION COEFFICIENTS FOR SOLUTES IN MIXED STATIONARY PHASES OF SQUALANE AND DNP AT 30°C

| Mixture (mol-% squalane) | Solute | Experimental K_r | Deviation, ΔK_r (%) | |
|-----------------------------|----------------------|-----------------------|-----------------------------|--------|
| | | | uni | uni-fv |
| 25 | Pentane | 79.1 | 19.6 | -5.4 |
| | Hexane | 242.0 | 10.6 | -9.7 |
| | Heptane | 718.0 | 3.3 | -13.1 |
| | Cyclohexane | 462.0 | 5.7 | -0.3 |
| | Benzene | 604.2 | 6.4 | -4.6 |
| | Diethyl ether | 94.5 | 11.8 | -18.9 |
| | Acetone | 127.6 | 11.8 | -5.1 |
| | Ethyl acetate | 377.8 | 3.1 | -12.4 |
| | Dichloromethane | 224.1 | 13.2 | -2.5 |
| | Chloroform | 621.7 | -35.4 | -54.8 |
| | Carbon tetrachloride | 543.2 | 8.2 | -8.3 |
| | 50 | Pentane | 88.6 | 16.4 |
| Hexane | | 273.0 | 7.6 | -11.7 |
| Heptane | | 822.0 | -0.2 | -15.9 |
| Cyclohexane | | 522.0 | 0.8 | -4.6 |
| Benzene | | 576.0 | 6.3 | -4.3 |
| Diethyl ether | | 90.9 | 26.4 | -5.0 |
| Acetone | | 95.3 | 9.2 | -6.8 |
| Ethyl acetate | | 318.7 | 0.2 | -14.1 |
| Dichloromethane | | 170.4 | 19.4 | 6.0 |
| Chloroform | | 487.1 | -26.4 | -43.0 |
| Carbon tetrachloride | | 531.1 | 6.2 | -9.2 |
| 75 | | Pentane | 95.2 | 13.9 |
| | Hexane | 269.4 | 15.1 | -3.6 |
| | Heptane | 899.0 | -3.5 | -18.3 |
| | Cyclohexane | 561.0 | -2.6 | -7.4 |
| | Benzene | 512.0 | -5.6 | -4.1 |
| | Diethyl ether | 86.1 | 4.5 | -36.5 |
| | Acetone | 65.2 | 12.4 | -1.8 |
| | Ethyl acetate | 245.6 | 2.0 | -11.0 |
| | Dichloromethane | 118.4 | 27.5 | 16.5 |
| | Chloroform | 346.2 | -11.6 | -24.9 |
| | Carbon tetrachloride | 504.8 | 4.2 | -10.3 |

N-methylpyrrolidone (NMP)

NMP was selected as an example of a polar stationary phase and the results are compared in Fig. 5 and Table X. Only V_g^0 results have been published for this phase²⁶ so that comparisons will be made using this parameter. Fig. 5 shows a wide spread of results and very large deviations between the experimental and UNIFAC values. This is again confirmed by the ΔV_g^0 values calculated by substituting V_g^0 for K_r in eqn. 10, where values in excess of 200% are found. However, again the elution order is correctly predicted.

TABLE VIII

RELATIVE RETENTION VOLUMES FOR SOLUTES IN *n*-HEXADECANE AT 20, 30 AND 40°C

Experimental relative retentions were calculated using values for dichloromethane of 136.2, 98.5 and 74.4 cm³ g⁻¹ at 20, 30 and 40°C, respectively.

| Solute | Temperature (°C) | Relative retention volume | | | Elution order | | |
|----------------------|---------------------|---------------------------|-----|--------|---------------|-----|--------|
| | | Expt. | uni | uni-fv | Expt. | uni | uni-fv |
| Hexane | 20 | 5.1 | 2.7 | 2.6 | 3 | 3 | 3 |
| Heptane | | 17.0 | 7.9 | 8.0 | 7 | 7 | 7 |
| Cyclohexane | | 8.8 | 4.7 | 5.0 | 6 | 6 | 6 |
| Benzene | | 6.6 | 3.9 | 4.0 | 4 | 4 | 4 |
| Dichloromethane | | 1 | 1 | 1 | 1 | 1 | 1 |
| Chloroform | | 3.2 | 2.0 | 2.0 | 2 | 2 | 2 |
| Carbon tetrachloride | | 7.2 | 4.0 | 4.0 | 5 | 5 | 5 |
| Hexane | 30 | 4.5 | 2.5 | 2.5 | 3 | 3 | 3 |
| Heptane | | 14.3 | 7.0 | 7.1 | 6 | 6 | 6 |
| Cyclohexane | | 7.9 | 4.3 | 4.6 | 5 | 5 | 5 |
| Benzene | | 6.1 | 3.6 | 3.7 | 4 | 4 | 4 |
| Dichloromethane | | 1 | 1 | 1 | 1 | 1 | 1 |
| Chloroform | | 3.0 | 1.9 | 2.0 | 2 | 2 | 2 |
| Hexane | 40 | 4.1 | 2.4 | 2.3 | 3 | 3 | 3 |
| Heptane | | 12.2 | 6.3 | 6.4 | 7 | 7 | 7 |
| Cyclohexane | | 7.0 | 4.1 | 4.3 | 6 | 6 | 6 |
| Benzene | | 5.6 | 3.4 | 3.5 | 4 | 4 | 4 |
| Dichloromethane | | 1 | 1 | 1 | 1 | 1 | 1 |
| Chloroform | | 2.8 | 1.9 | 2.0 | 2 | 2 | 2 |
| Carbon tetrachloride | | 5.9 | 3.6 | 3.7 | 5 | 5 | 5 |

In the course of this work, several other polar stationary phases, *e.g.*, *N,N*-dibutyl-2-ethylhexamide, were considered but in each instance very large deviations were found, leading us to abandon the use of polar liquids.

Consideration of the results showed that the elution order could be predicted reasonably well by UNIFAC, so the method was applied to a number of closely related, isomeric hydrocarbon solutes in three stationary phases to assess the utility of UNIFAC in predicting the separation of this type of compound.

n-Heptadecane, di-*n*-octyl ether (DNOE) and di-*n*-octyl ketone (DOK)²⁷

The results for nine hydrocarbon solutes in *n*-heptadecane at 30°C are shown in Table XI and are similar (as would be expected) to those for *n*-hexadecane described above. Differences between the experimental and UNIFAC results are generally in the range 10–25%, with the free volume results being closer although the order of elution of even the five hexane isomers is correctly predicted by both treatments. The results for DNOE at 30°C shown in Table XII are similar in each respect, as are those shown in Table XIII for DOK at 50°C. Additionally, results were calculated for the same systems in each stationary phase at two other temperatures and were the same as those described here, so they have been omitted for brevity. In all instances, the order of

TABLE IX

PARTITION COEFFICIENTS FOR SOLUTES IN *n*-HEXADECANE AT 20, 30 AND 40°C

| Solute | Temperature (°C) | Experimental K_r | Deviation, ΔK_r (%) | |
|----------------------|---------------------|-----------------------|-----------------------------|--------|
| | | | uni | uni-fv |
| Hexane | 20 | 575.5 | -23.7 | -36.0 |
| Heptane | | 1926.5 | -38.4 | -47.3 |
| Cyclohexane | | 994.8 | -21.6 | -22.6 |
| Benzene | | 750.8 | -10.2 | -15.8 |
| Dichloromethane | | 113.0 | 35.6 | 31.2 |
| Chloroform | | 362.2 | -3.0 | -8.0 |
| Carbon tetrachloride | | 818.3 | -15.6 | -24.9 |
| Hexane | 30 | 380.2 | -23.0 | -35.4 |
| Heptane | | 1195.9 | -38.0 | -46.9 |
| Cyclohexane | | 660.8 | -23.8 | -24.9 |
| Benzene | | 509.8 | -14.3 | -19.5 |
| Dichloromethane | | 83.8 | 31.9 | 27.1 |
| Chloroform | | 252.0 | -5.0 | -10.2 |
| Carbon tetrachloride | | 547.3 | -17.1 | -26.4 |
| Hexane | 40 | 265.1 | -25.1 | -37.9 |
| Heptane | | 788.2 | -40.8 | -49.9 |
| Cyclohexane | | 455.7 | -26.5 | -27.8 |
| Benzene | | 360.0 | -19.2 | -24.8 |
| Dichloromethane | | 64.8 | 26.9 | 21.5 |
| Chloroform | | 183.1 | -8.5 | -14.0 |
| Carbon tetrachloride | | 384.6 | -20.6 | -30.2 |

elution is correctly predicted for all solutes even though the predicted retention volumes are considerably different from the experimental values. This is also illustrated in Fig. 6, where plots of $V_g^0(\text{UNIFAC})$ versus $V_g^0(\text{expt.})$ follow an almost linear relationship, although the values do not correspond exactly.

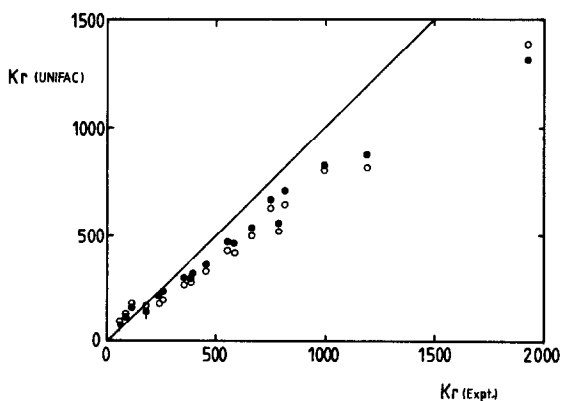


Fig. 4. Plot of experimental versus UNIFAC partition coefficients for solutes in *n*-hexadecane at 20, 30 and 40°C. ●, uni; ○, uni-fv.

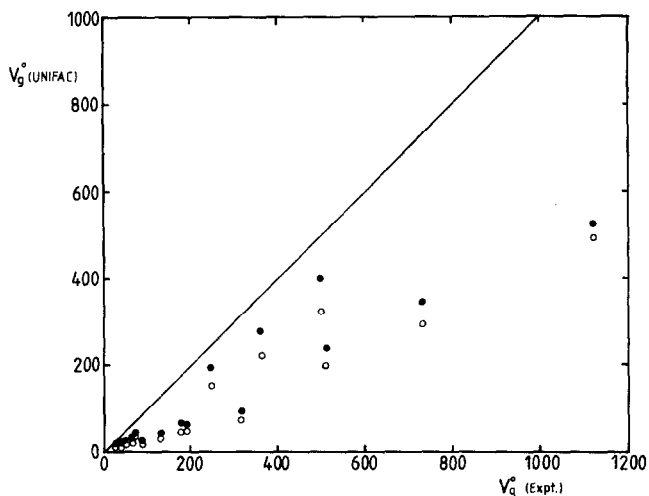


Fig. 5. Plot of experimental *versus* UNIFAC specific retention volumes for solutes in N-methylpyrrolidone at 50, 60 and 70°C. ●, uni; ○, uni-fv.

DISCUSSION

It is evident from the results that UNIFAC in its present form has limited use in the prediction of retention in chromatographic systems. The order of elution, even of closely related isomers, can be predicted well from the UNIFAC specific retention volumes except where the solute can form strong interactions such as hydrogen bonding with the stationary phase. However, the actual retention volumes show considerable discrepancies from the UNIFAC values so that, in agreement with Roth and Novak⁵, only approximations to the relative retentions could be obtained.

TABLE XI

RELATIVE RETENTION VOLUMES FOR SOLUTES IN *n*-HEPTADECANE AT 30°C

The experimental relative retentions were calculated using a value for pentane of 133.4 cm³ g⁻¹.

| Solute | Relative retention volume | | | Elution order | | | ΔV_g^0 (%) | |
|---------------------|---------------------------|--------|-----|---------------|--------|-----|--------------------|-------|
| | Expt. | uni-fv | uni | Expt. | uni-fv | uni | uni-fv | uni |
| Pentane | 1 | 1 | 1 | 1 | 1 | 1 | -13.9 | -3.4 |
| Hexane | 3.1 | 2.9 | 2.8 | 6 | 6 | 6 | -19.3 | -13.4 |
| 2-Methylpentane | 2.2 | 2.1 | 2.0 | 4 | 4 | 4 | -17.8 | -13.4 |
| 3-Methylpentane | 2.6 | 2.4 | 2.3 | 5 | 5 | 5 | -20.2 | -15.1 |
| 2,2-Dimethylbutane | 1.5 | 1.4 | 1.3 | 2 | 2 | 2 | -20.4 | -12.9 |
| 2,3-Dimethylbutane | 2.1 | 1.9 | 1.8 | 3 | 3 | 3 | -20.4 | -14.9 |
| Heptane | 9.8 | 8.5 | 7.9 | 9 | 9 | 9 | -25.3 | -22.1 |
| 2,4-Dimethylpentane | 4.4 | 4.0 | 3.8 | 7 | 7 | 7 | -22.0 | -17.1 |
| 3-Methylhexane | 7.3 | 6.4 | 5.9 | 8 | 8 | 8 | -24.8 | -21.9 |

TABLE XII

RELATIVE RETENTION VOLUMES FOR SOLUTES IN DI-*n*-OCTYL ETHER AT 30°C

The experimental relative retentions were calculated using a value for pentane of 132.8 cm³ g⁻¹.

| Solute | Relative retention volume | | | Elution order | | | ΔV_g^0 (%) | |
|---------------------|---------------------------|--------|-----|---------------|--------|-----|--------------------|-------|
| | Expt. | uni-fv | uni | Expt. | uni-fv | uni | uni-fv | uni |
| Pentane | 1 | 1 | 1 | 1 | 1 | 1 | -18.2 | -9.6 |
| Hexane | 3.1 | 2.9 | 2.8 | 6 | 6 | 6 | -23.3 | -18.7 |
| 2-Methylpentane | 2.2 | 2.1 | 2.0 | 4 | 4 | 4 | -22.2 | -16.6 |
| 3-Methylpentane | 2.6 | 2.4 | 2.2 | 5 | 5 | 5 | -22.2 | -20.3 |
| 2,2-Dimethylbutane | 1.5 | 1.4 | 1.3 | 2 | 2 | 2 | -24.3 | -18.3 |
| 2,3-Dimethylbutane | 2.1 | 1.9 | 1.8 | 3 | 3 | 3 | -24.7 | -20.3 |
| Heptane | 9.6 | 8.3 | 7.8 | 9 | 9 | 9 | -29.3 | -26.8 |
| 2,4-Dimethylpentane | 4.4 | 3.9 | 3.7 | 7 | 7 | 7 | -27.0 | -23.3 |
| 3-Methylhexane | 7.2 | 6.3 | 5.8 | 8 | 8 | 8 | -29.2 | -27.1 |

A considerable body of literature has shown that GLC is a valid method for measuring thermodynamic parameters², for example showing that results agreed within 1–2% with those extrapolated from static, equilibrium data^{17–23}. Thus, the disagreements found in this paper lie with the UNIFAC method.

Any group contribution method must necessarily be approximate owing to the arbitrary way in which the molecule is divided into groups. In deriving the group interaction parameters, a large number of results from small-molecule systems over a range of concentrations were used. Recent developments^{26,28} have obtained interaction parameters solely using infinite dilution results and it may be that, when more widely available, this new set of parameters would yield better results when applied to the work described here.

TABLE XIII

RELATIVE RETENTION VOLUMES FOR SOLUTES IN DI-*n*-OCTYL KETONE AT 50°C

The experimental relative retentions were calculated using a value for pentane of 55.9 cm³ g⁻¹.

| Solute | Relative retention volume | | | Elution order | | | ΔV_g^0 (%) | |
|---------------------|---------------------------|--------|-----|---------------|--------|-----|--------------------|-------|
| | Expt. | uni-fv | uni | Expt. | uni-fv | uni | uni-fv | uni |
| Pentane | 1 | 1 | 1 | 1 | 1 | 1 | -18.6 | -0.9 |
| Hexane | 2.8 | 2.6 | 2.5 | 6 | 6 | 6 | -22.8 | -10.7 |
| 2-Methylpentane | 2.0 | 1.9 | 1.9 | 4 | 4 | 4 | -22.4 | -8.3 |
| 3-Methylpentane | 2.3 | 2.2 | 2.0 | 5 | 5 | 5 | -23.5 | -11.7 |
| 2,2-Dimethylbutane | 1.5 | 1.3 | 1.3 | 2 | 2 | 2 | -25.4 | -11.6 |
| 2,3-Dimethylbutane | 2.0 | 1.8 | 1.7 | 3 | 3 | 3 | -25.5 | -13.6 |
| Heptane | 7.4 | 6.7 | 6.1 | 9 | 9 | 9 | -26.3 | -17.5 |
| 2,4-Dimethylpentane | 3.7 | 3.4 | 3.1 | 7 | 7 | 7 | -26.1 | -15.1 |
| 3-Methylhexane | 5.8 | 5.5 | 4.7 | 8 | 8 | 8 | -26.7 | -18.6 |

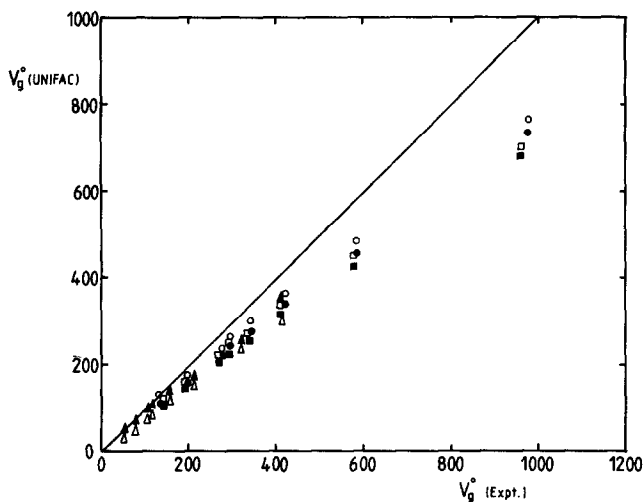


Fig. 6. Plot of experimental *versus* UNIFAC specific retention volumes for solutes in stationary phases. *n*-Heptadecane, 30°C: ●, uni; ○, uni-fv. Di-*n*-octylether, 30°C: ■, uni; □, uni-fv. Di-*n*-octyl ketone, 50°C: ▲, uni; △, uni-fv.

Even though activity coefficients could be predicted to within 1–2% for small-molecule solutions^{3,4}, even the systems consisting of mixed hydrocarbons considered here showed discrepancies of 20–50% and it is of interest to determine whether these could be ascribed to a particular part of the UNIFAC treatment. In general, although underestimating the retention volumes and partition coefficients, the free volume treatment gives better predictions but neither treatment gives results as good as in small-molecule solutions so that the a_1^{FV} term is clearly not a major source of error. Gottlieb and Herskowitz²⁹ suggested that an improved fit to experimental results can be obtained by treating c_1 as an empirically adjustable parameter. Similarly, Bekker *et al.*³⁰ achieved a better fit using a temperature-dependent b term in the free volume correction. However, from a predictive point of view, neither modification is useful for the current work.

For non-polar alkane solute–alkane stationary phase systems, all UNIFAC interaction parameters are zero so that the a_1^R term is also zero. However, there is a very small positive enthalpy of mixing in these systems³¹, so that this is one area in which UNIFAC departs from experiment. Other evidence for the inability of UNIFAC to account for the residual effects lies in the wide deviations found with the more polar systems, especially NMP, where retention was poorly predicted. In particular, the DNP–chloroform system was exceptional of those studied as hydrogen bonding is possible. Part of this undoubtedly arises from uncertainties in the published UNIFAC interaction parameters for some groups, particularly pertinent to the current discussion being the chlorine-containing groups with ketone or ester groups. Recently, new interaction parameters have been calculated treating NMP as a single group³², but when these were used in our work even larger differences were found. Study of the application of UNIFAC to polymer solutions has suggested that the expression for the residual activity may not be applicable owing to restricted conformations of the chain

preventing some groups from interacting³³. Similar effects may play a part in the relatively long-chain compounds used as stationary phases. The total contribution, apart from free volume effects, to the UNIFAC activity coefficient in the hydrocarbon systems arises from the combinatorial part, which is clearly not adequate in the systems described here. Some workers⁴ have suggested modifications to eqn. 3 for this term, but these were found to have relatively insignificant effects when used in our work.

In conclusion, reasonable predictions of retention can be made for non-polar stationary phases, but these should be treated with care. The method could possibly assist in the identification of isomers but is probably not superior to other techniques available. It had been hoped that retention could be predicted on a wide range of phases and that the predictions could be taken further so that, if a certain separation was required, the optimum weight of stationary phase or column length and efficiency could be estimated. Clearly, with the present refinements of UNIFAC this is not possible, but it is hoped that further development of the method will enable these aims to be achieved. In particular, the use of infinite dilution interaction parameters³⁴ seems a potentially profitable direction of research and this will be considered in the next paper in this series.

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