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THERMODYNAMIC MODEL FOR SUPERCRITICAL FLUID CHROMATOGRAPHY

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SUMMARY

The possibility to apply a thermodynamic model to supercritical fluid chromatography (SFC) is investigated. Thermodynamics can be used to characterize the (mobile) phases used in SFC, as well as for the description and ultimately the prediction of retention behaviour. The solubility parameter, as obtained from a thermodynamic equation of state, has been used for characterization purposes. An equation which describes retention in terms of thermodynamic functions is derived. This equation enables the prediction of the effect of pressure or density on the retention behaviour. Since the interactions of solutes with the stationary phase are not taken into account, the retention data can be calculated only relative to some arbitrary pressure. Close agreement between experimental and calculated data is observed, and illustrated with representative examples. Some practical conclusions are drawn.

INTRODUCTION

Supercritical fluid chromatography (SFC) was demonstrated as early as 1962¹. Since then successful experiments have been reported at more or less regular intervals (for reviews see, *e.g.*, refs. 2-4). However, the amount of work published on SFC over the two decades of its existence has been very modest in comparison to that on other chromatographic techniques. Undoubtedly, the spectacular growth of first gas chromatography (GC) and then high-performance liquid chromatography (HPLC) has tempered the interest in SFC. The instrumental problems associated with SFC have also limited its development, although the advance of modern HPLC instrumentation has brought SFC more within reach^{5,6}.

Van Wasen *et al.*³ identified a third reason for the relatively slow development of SFC. They noticed a lack of physicochemical knowledge, which obstructs the understanding of the technique. Although they discussed many of the physical parameters involved in SFC separations, there appears to be no quantitative model to predict or even describe the observed retention behaviour. Several models have been proposed with little success, as reviewed in refs. 4 and 7. According to Randall⁷ the solubility-parameter approach of Giddings and co-workers⁸⁻¹⁰ is the most promising. However, many of the obstacles that prevent such a model from being of

quantitative use in HPLC¹¹ are no less valid for SFC. The solutions typically encountered in SFC cannot be expected to behave in a "regular" way and the stationary phases will not be (bulk) liquids. An additional problem is the requirement of solubility-parameter data for the solutes and the phases at elevated pressures and temperatures. The "merits" of the solubility-parameter concept in chromatography can be summarized as follows (*cf.*, ref. 11):

it is very useful as a means to characterize chromatographic phases and solutes, *i.e.*, as a quantitative measure of "polarity"

it is useful to describe retention, but only in qualitative or semi-quantitative terms

it cannot be used to predict retention.

Hence, in this paper the solubility parameter is used for characterization purposes only.

For the quantitative description and for the prediction of retention behaviour in SFC a different approach will be followed. The aim of this paper is to investigate the potential of a thermodynamic model for this purpose. A rigorous theoretical model will be described, which relates the capacity factor to thermodynamic quantities. In order to use this model in practice an equation of state is required. Given the exploratory character of this work, no constraints were placed on the complexity of the equation of state and on the number of coefficients involved. In the following paragraphs I will first introduce an empirical generalized equation of state, and use it for the characterization of pure substances, *i.e.*, SFC mobile phases. Then the treatment is extended to include mixtures, so that the description and the prediction of SFC retention behaviour becomes possible. The goals of the project can be expressed in terms of the following two questions:

(1) is a thermodynamic model useful for (a) the characterization of phases and solutes, and (b) the description and (c) the prediction of retention behaviour in SFC?

(2) which assumptions are needed about the SFC system, and can these assumptions be justified by the results obtained with the model?

The validity of the present model will be tested with some selected literature data.

Three-parameter corresponding states

The principle of corresponding states implies that the intensive properties of different compounds will be identical when compared at identical values of the reduced pressure and temperature¹². The reduced properties are defined by the ratio between the actual and critical parameters. In this form of the principle of corresponding states, two parameters (the critical pressure, P_c , and temperature, T_c) are required to allow calculation of the thermodynamic properties of any compound from a suitable equation of state. Many such equations have been formulated, based on arguments that range from purely theoretical to almost entirely empirical (see, *e.g.*, ref. 13, Ch. 3). Roughly speaking, the more complex the equation is and the more coefficients it involves, the better it can be made to describe a large number of experimental (p , V , T) data. Another way to increase the accuracy of the equation is the inclusion of a third parameter in the principle of corresponding states. Such a parameter is the acentric factor, ω , defined by Pitzer and Curl¹⁴ to account for the non-spherical force fields of molecules. The acentric factor is obtained from the va-

pour pressure of a pure substance at $T = 0.7T_c$. In terms of three parameters, the principle of corresponding states may be formulated as follows: two substances will behave identically if their reduced pressures, $p_R = p/p_c$, their reduced temperatures, $T_R = T/T_c$, and their acentric factors are equal.

The Lee and Kesler equation

For the calculations reported here the generalized three-parameter equation of Lee and Kesler¹⁵ has been used exclusively. The analytical form of this equation is given in Appendix A. Lee and Kesler's equation is mathematically quite complex. However, it has many attractive features¹⁶:

It covers a wide range of reduced pressures ($0 < p_R < 10$) and temperatures ($0.3 < T_R < 4$).

All coefficients in the equation (see Table AI) are independent of the substances involved, for pure components as well as for mixtures.

It gives accurate results for a wide variety of substances.

In essence, the Lee and Kesler equation can be described as

$$Z = f(V_R, T_R, \omega) \quad (1)$$

in which Z is the compressibility factor defined as

$$Z = \frac{pv}{RT} = \frac{p_R V_R}{T_R} \quad (2)$$

where R is the gas constant and v the molar volume. V_R is a reduced volume defined by:

$$V_R = \frac{p_c v}{R T_c} \quad (3)$$

Note that V_R does not equal v/V_c !

The function f in eqn. 1 involves as many as twelve constants. Although the function f itself does not change, there are two sets of such constants (see Table AI). One set is used to calculate the properties of a so-called simple fluid (identified by the superscript o) and the other set refers to a reference fluid (superscript r), for which n -octane was arbitrarily selected by Lee and Kesler.

Eqn. 1 has to be solved for V_R by a numerical procedure. This should be done for the simple fluid as well as for the reference fluid, yielding Z^o and Z^r , respectively. The actual value for the compressibility factor, Z , of the real fluid can then be found from

$$Z = Z^o + \frac{\omega}{\omega^r} (Z^r - Z^o) \quad (4)$$

in which ω^r is another constant, the 25th.

Properties of pure substances

The simplest information that can be obtained from the Lee and Kesler equa-

tion are the p , V , T data of pure substances. Of particular interest for SFC is the mobile phase density as a function of pressure and temperature. Once Z has been calculated, the density, ρ , is easily obtained from

$$\rho = \frac{Mp}{ZRT} \quad (5)$$

where M is the molecular weight of the substance.

It has been shown by Tijssen *et al.*¹⁷ that the solubility parameter, δ , can also readily be obtained from a thermodynamic equation of state. The appropriate equation is:

$$\delta^2 = - \frac{RT_c}{v} \left[\frac{(H - H^*)}{RT_c} + T_R \right] \quad (6)$$

In this equation the term $(H - H^*)/RT_c$, known as the residual enthalpy function or enthalpy departure, can be found from tables given by Lee and Kesler¹⁵ or from an analytical equation given in Appendix A. According to Bagley *et al.*¹⁸, an extra term should be added to the right-hand side of eqn. 6 to account for the change in the number of degrees of freedom of the substance relative to an ideal gas. Experimentally¹⁸ it was found that

$$\delta_T^2 = \delta^2 + \frac{3}{2} \cdot \frac{RT}{v} \quad (7)$$

where the subscript T = total. Under SFC conditions the density and hence the molar volume may vary substantially. Hence the correction of eqn. 7 cannot be neglected.

Properties of mixtures; the pseudo-critical method

To calculate the properties of mixtures from the equation of Lee and Kesler, the so-called pseudo-critical method may be used (see ref. 12, p. 146 *et seq.*). In this method a set of critical parameters (in this case p_c , T_c and ω) is estimated for the mixture. Thenceforth the mixture is treated as a pure substance. This has the great advantage that all the parameters in Table AI remain unaltered and that no binary or other interaction parameters are needed for the mixture. Although there does not seem to be a sound theoretical foundation for the pseudo-critical method, its usefulness is clearly illustrated by the accuracy that can be achieved in the description of many mixtures (see, *e.g.*, refs. 16 and 19).

It then remains to establish a set of rules to relate the critical parameters of mixtures to those of the pure constituents. Several different sets of rules have been extensively tested in the present study. The best results were obtained with the rules which Plöcker *et al.*¹⁹ developed especially for use in combination with the Lee and Kesler equation. For a binary mixture, the full set of rules is given in Appendix B.

To estimate the critical properties of a mixture from these rules the properties of the pure components need to be known, plus a binary interaction parameter, κ_{12} , which is dependent on the two constituents of the binary mixture (see eqn. B5). The fact that such a parameter is required forms the main disadvantage of this set of

rules. Although more complicated mixtures (ternary, etc.) do not require any higher interaction factors, the rules imply that one extra parameter is needed. Fortunately, Plöcker *et al.*¹⁹ suggested the presence of a correlation between κ_{ij} and the dimensionless quantity

$$r = \frac{T_{c,2} v_{c,2}}{T_{c,1} v_{c,1}} \quad (8)$$

for different classes of mixtures. Many experimental data are available for hydrocarbon-hydrocarbon mixtures. These can accurately be summarized by:

$$\kappa_{12} = -6 \cdot 10^{-4} r^2 + 0.042 r + 0.94 \quad (9)$$

For carbon dioxide-hydrocarbon mixtures, which are currently of most interest for SFC, the experimental data are scarce and limited to r values up to about 13 (*n*-decane). An estimate can be found from:

$$\kappa_{12} = 0.9 + 0.02 r \quad (10)$$

Eqns. 9 and 10 were estimated from the graphical representation of the data by Plöcker *et al.*¹⁹. An extensive literature search did not reveal any additional data on the particular interaction parameter κ_{12} .

Two further aspects of the parameter κ_{12} should be noted. First, the value of κ_{12} has a considerable effect upon the outcome of calculations using Lee and Kesler's equation. It has been suggested, therefore, that even a rough estimate of κ_{12} will usually be better than setting $\kappa_{12} = 1$ (ref. 19). Secondly, however, it appears from work done by Plöcker *et al.* (ref. 19, Fig. 2) that the influence of the κ_{12} value diminishes when the temperature is increased towards T_c . In other words, for calculations concerning SFC, the value of κ_{12} does not appear to be all that critical.

Fugacities; SFC retention data

An equation for the fugacity coefficient of a pure substance can readily be obtained from Lee and Kesler's equation by performing the appropriate integration. The resulting equation is given in Appendix A (eqn. A5). The fugacity coefficient of component 2 in a binary mixture can then be found from (ref. 12, p. 146)

$$\ln \varphi_2 = \ln \varphi_m + (1 - x_2) \left(\frac{\partial \ln \varphi_m}{\partial x_2} \right)_{p,T} \quad (11)$$

where φ_m is the fugacity coefficient of the mixture and x_2 , is the mole fraction of component 2.

In chromatography it is good practice to work at high dilutions, in the range where the amount of sample injected does not affect retention. Therefore, the parameter of interest is

$$\ln \varphi_2^\infty = \lim_{x_2 \downarrow 0} (\ln \varphi_2) \quad (12)$$

where the superscript ∞ indicates infinite dilution. Eqn. 11 can be solved analytically if we establish equations for the partial derivatives vs. x_2 for the pseudo-critical properties (eqns. B1–B8) and then combine these into a total differential equation^{12,19}. In this paper, a more rigorous numerical procedure has been followed. First the fugacity coefficient is obtained for a small value of x_2 , using Appendix B and eqn. A5. x_2 is then divided by 2 and the procedure is repeated. The two values for $\ln \varphi_m$ yield a direct numerical estimate for $\ln \varphi_2$ from eqn. 11. The procedure is then repeated for ever decreasing values of x_2 , until the estimate for $\ln \varphi_2$ (which then equals $\ln \varphi_2^\infty$) remains constant to well within the desired accuracy.

The fugacity coefficient then found can be related to distribution data by using the following rigorous equation (ref. 12, pp. 170, 171)

$$K_x = \frac{x_2^{\text{stat}}}{x_2^{\text{mob}}} = \frac{\varphi_2^\infty p}{p_2^\infty \varphi_2^\infty \cdot \exp \frac{p}{p_2^\infty} \int \frac{v_2^\infty}{RT} dp} \quad (13)$$

where K_x is the distribution coefficient over the two chromatographic phases in terms of mole fractions, p_2^∞ is the saturated vapour pressure of component 2, φ_2^∞ its fugacity coefficient in the stationary phase at saturation and v_2^∞ its (liquid) molar volume and the superscripts stat and mob refer to the stationary and mobile phases. K_x is related to the chromatographic capacity factor, k , by

$$k = K_x \cdot \frac{n^{\text{stat}}}{n^{\text{mob}}} \quad (14)$$

where n is the total number of moles of each phase.

Some reasonable assumptions should now be made in order to obtain a more manageable equation. If it is assumed that the stationary phase is non-compressible and that the solubility of the mobile phase in the stationary phase is negligible even at elevated pressures, then v_2^∞ will be independent of the pressure. The integral in eqn. 13 is then easily solved. Moreover, as there is no interest in very volatile solutes in SFC, p_2^∞ can be neglected with respect to p . With p_2^∞ , φ_2^∞ and n^{stat} constant and finally realizing that n^{mob} is proportional to the mobile phase density, ρ , we obtain

$$\ln k = \ln \varphi_2^\infty + \ln (p/\rho) - \frac{v_2^\infty p}{RT} + \ln k_p \quad (15)$$

where k_p is a constant. Since φ_2^∞ , p and v_2^∞ can all be obtained from the Lee and Kesler equation, the above is a very simple equation from which k can be calculated once the constant k_p has been established, *i.e.*, once the retention at some arbitrary pressure is known. Hence, eqn. 15 does not yield a quantitative *a priori* estimate for capacity factors in SFC, but it does provide a quantitative description of the pressure and density dependence of the retention.

In prediction of the value of k_p , there is only one factor that causes problems, *i.e.*, the stationary phase fugacity coefficient at saturation, φ_2^∞ . For liquid stationary phases, this coefficient may be tackled with an equation of state, although polar liquids should be approached carefully¹⁹. However, liquid stationary phases are of little or no value in SFC, where one is forced to rely on polymers of very high

molecular weight, solid adsorbents or chemically bonded phases. A discussion on the interactions involved in such systems is beyond the scope of this paper.

Review of assumptions and approximations

At this point it is worthwhile to review the various assumptions and approximations involved in the derivation of eqn. 15 and in the calculation of the parameters required therein.

(1) The Lee and Kesler equation is entirely empirical. It is designed to describe a large number of experimental data as accurately as possible. Nevertheless, any application of such an equation is a potential source of error.

(2) Values for the critical parameters and the acentric factors of substances have been extensively tabulated. However, frequently there are no experimental data available, in which case an estimate should be made^{1,3}.

(3) The equations given in Appendix B, used to obtain the pseudo-critical parameters for mixtures, as well as the pseudo-critical method itself can only be approximately correct.

(4) The stationary phase is assumed to behave as an incompressible fluid.

(5) The mobile phase is assumed not to dissolve in the stationary phase, *i.e.*, not to such an extent that it would influence retention.

(6) The vapour pressure of the solutes is negligible in comparison to the operating pressure.

(7) The pressure drop over the column is neglected. This condition does not conflict with the use of capillary columns in SFC⁴. For packed columns the pressure drop may be significant, so that an experimental or a mathematical correction may be required.

RESULTS AND DISCUSSION

The following sections present some results obtained from the calculation procedures described above. First, it is demonstrated that useful data can be generated to characterize the behaviour of the SFC mobile phase under various conditions. Thereafter, the calculation procedure for the pressure and density dependence of SFC retention data will be tested on some literature data. For convenience, these data have been taken from one source, a review by Van Wasen *et al.*³. Literature data from other sources have been recalculated with comparable success. Finally, the possibilities to analyse high-molecular-weight solutes with SFC will be investigated on the basis of the present model.

Essentially all the information required to perform the calculations consists of the critical pressures and temperatures, as well as the acentric factors of the substances. These are summarized in Table I.

Characterization of SFC mobile phases

Carbon dioxide is by far the most attractive mobile phase for SFC from a practical point of view. The well known pressure-density diagram for CO₂ can readily be produced from the Lee and Kesler equation. Eqn. 6 also permits the construction of a plot of the solubility parameter against the (reduced) pressure for various (reduced) temperatures. This is shown in Fig. 1. For T_R values lower than 1 there are

TABLE I
CRITICAL PROPERTIES OF SUBSTANCES USED IN THE CALCULATIONS¹³

Substance	p_c (atm)	T_c ($^{\circ}K$)	ω
Carbon dioxide	72.8	304.2	0.225
Methanol	79.9	512.6	0.559
Ethanol	63.0	516.2	0.635
1-Propanol	51.0	536.7	0.624
2-Propanol	47.0	508.3	0.773*
Ethene	55.0	491.0	0.278
<i>n</i> -Pentane	33.3	469.6	0.251
Naphthalene	40.0	748.4	0.302
<i>n</i> -Decane	20.8	617.6	0.490
<i>n</i> -Hexadecane	14	717	0.742
<i>n</i> -Eicosane	11.0	767	0.907
Squalane	8.5*	888*	0.750*
Ethane	48.2	305.4	0.098

* Estimated (see ref. 13, Ch. 2).

two stable forms of CO_2 , the gaseous state (G) and the liquid state (L). For $T_R \geq 1$, there is a unique value for the solubility parameter for each combination of pressure and temperature. Note that for $T_R = 1$, *i.e.*, at the critical temperature of carbon dioxide, there is a sudden jump in the solubility parameter at the critical point (p_R

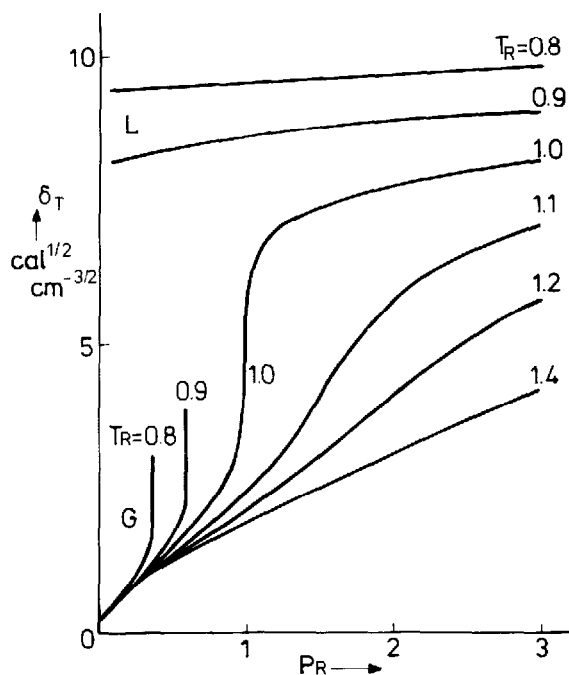


Fig. 1. The solubility parameter of carbon dioxide (eqn. 7) as a function of the reduced pressure for various reduced temperatures.

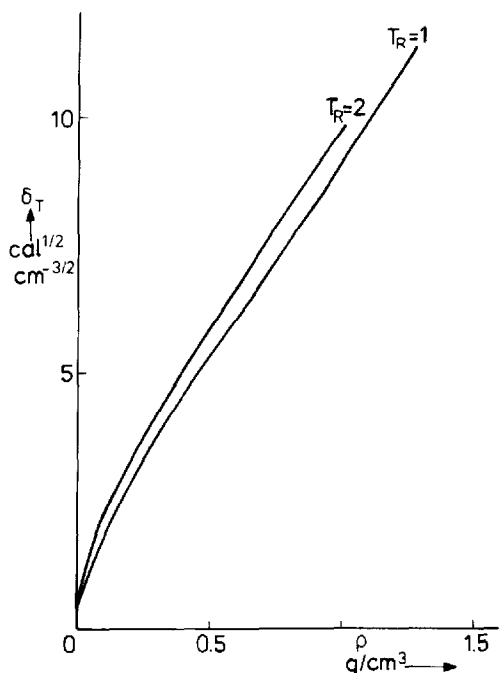


Fig. 2. The solubility parameter of carbon dioxide (eqn. 7) as a function of density for two different reduced temperatures.

= 1), when the derivative $d\delta_T/d\rho$ becomes very large. Hence, it will be very difficult to control solubility in the direct vicinity of the critical point. However, when the temperature is increased, this drastic change in δ_T is soon replaced by a smoother transition between a gas-like phase ($\delta_T < 1$) and a liquid-like phase ($\delta_T > 7$), as is seen from the curve for $T_R = 1.1$.

In Fig. 2 the solubility parameter is plotted against the density for carbon dioxide at two different temperatures. Two conclusions can be drawn. First, the solubility parameter varies very regularly with the mobile phase density; over a large range the relationship is almost linear. Secondly, the temperature appears to have a very minor effect on the δ_T vs. ρ curve. Note that the two temperatures are far apart, *i.e.*, *ca.* 30 and 330°C. Of course, this observation does little more than underline the existing notion that it is the mobile phase density, not the pressure, that controls retention in SFC. Although it may seem from Fig. 2 that the temperature is of little practical importance in SFC, one should realize that the pressure required to obtain a given density is at the same time a strong function of temperature. The relationship between SFC retention data and mobile phase density will be discussed later.

Finally, in Fig. 3 the versatility of the present approach is illustrated. This figure shows the variation of the solubility parameter during a hypothetical programmed SFC analysis, in which the pressure, temperature and composition all change at the same time. A program has been chosen in which p varies from 1 to 201 atm and T from 50 to 250°C, both linearly with time. Moreover, a linearly increasing amount of various organic "modifiers" (in terms of mole fractions) is added to carbon

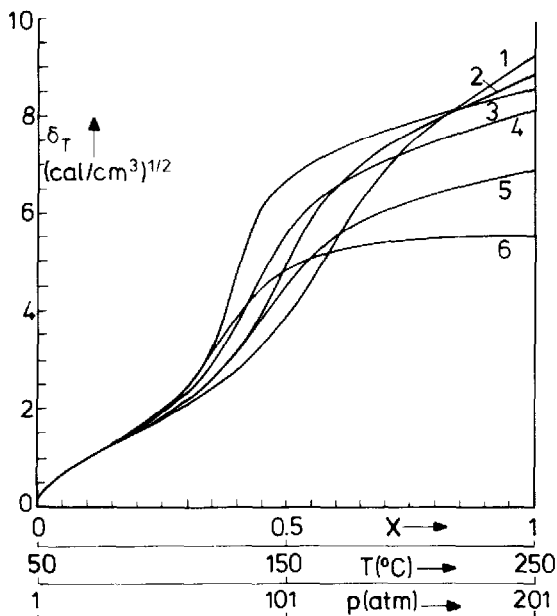


Fig. 3. Variation of the mobile phase solubility parameter (eqn. 7) with time during a programmed SFC analysis. Linear program: pressure 1 to 201 atm; temperature 50 to 250°C; mole fraction of modifier 0 to 1. Modifiers: 1 = methanol; 2 = ethanol; 3 = 1-propanol; 4 = 2-propanol; 5 = ethene; 6 = *n*-pentane.

dioxide. An extra source of error may have been introduced because eqn. 10 has been used for all mixtures, including those containing alcohols, whereas strictly speaking it is valid only for hydrocarbon-carbon dioxide mixtures.

It is seen that a wide variation of solubility parameter vs. time curves can be generated using different modifiers. However, much of this variation may also be generated by selecting different *p*-*T* programs, using the same modifier for all programs or even pure CO₂. Nevertheless, organic modifiers may prove useful because (a) higher values for δ_T can be realized than with CO₂ alone and (b) the same value for δ_T does not necessarily imply that two different mobile phases should yield exactly the same retention behaviour¹¹.

Description of SFC retention data

In Fig. 4 the calculated retention for naphthalene at three different temperatures with CO₂ as the mobile phase is plotted against pressure (a), against the mobile phase density (b) and against the logarithm of the latter (c). The experimental data shown in Fig. 4a were taken from ref. 3. The stationary phase used for the experiments was an RP-8 (chemically bonded *n*-octylsilyl) material. Note, however, that this is irrelevant for the application of eqn. 15. The anchor point needed to obtain a value for k_p in eqn. 15 was taken at $\log k = 1.5$ for $p = 60$ atm at all temperatures.

Fig. 4a is a good illustration of the potential of the calculation procedure. Eqn. 15 appears to describe the shape of the experimental curves very well. However, some discrepancies remain between theory and experiment. The greatest deviations are observed at high pressure, where retention is very low and experimental error, e.g.,

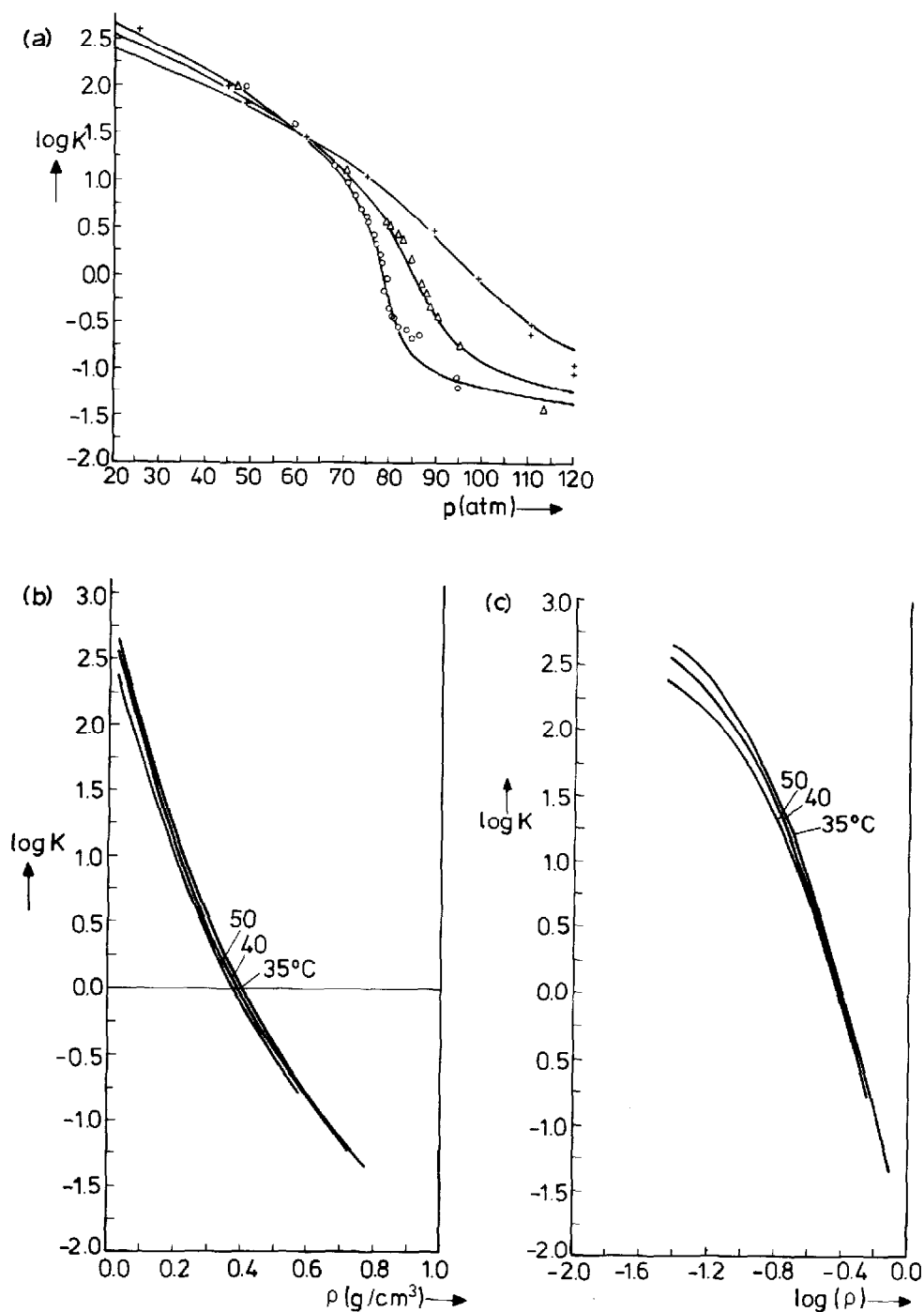


Fig. 4. Calculated retention for naphthalene at three different temperatures plotted vs. pressure (a), mobile phase density (b) and the logarithm of the density (c). Anchor points: $\log k = 1.5$ for $p = 60$ atm (all temperatures). Experimental data points: O, 35°C; Δ , 40°C; +, 50°C.

in the determination of the true hold-up volume of the reversed-phase column, may well play a role.

The accuracy of eqn. 15 depicted in Fig. 4a makes it feasible to extrapolate experimental retention data towards higher and lower pressures. In principle, only one experimental data point at some arbitrary pressure is required to predict retention at other pressures or under programmed pressure conditions. The latter, however, will require a numerical integration process²⁰, because of the complex variation of retention with pressure.

With respect to the possibilities for programmed elution, Fig. 4b is more relevant. In this figure the regular but non-linear behaviour of retention ($\log k$) with mobile phase density is shown. Since this is essentially a replot of Fig. 4a, a new comparison with experimental data is not necessary. It is worth noticing the remarkable resemblance of Fig. 4b with the typical plots of $\log k$ vs. the volume fraction of organic modifier in reversed-phase chromatography (RPLC; refs. 20 and 21). Hence, if the suggestion²² is followed to vary density (rather than pressure) linearly with time in SFC programmed analysis, a situation is obtained that is comparable to the use of linear (volume fraction) gradients in RPLC. The curves in Fig. 4b can be described quite accurately with a quadratic relationship, as a result of which ana-

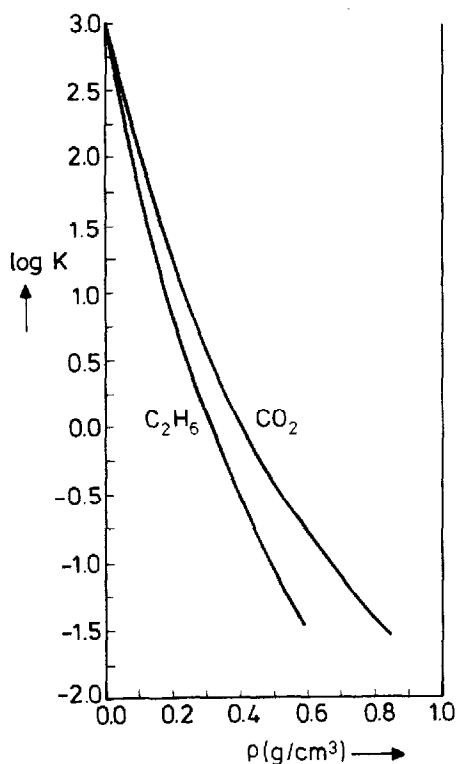


Fig. 5. Calculated retention data for naphthalene at 40°C using two different mobile phases, carbon dioxide and ethane. Anchor points: $\log k = 3$ for $p = 1$ atm (both curves).

lytical equations are available to predict retention when a linear density gradient is applied²⁰. It even appears that the analogy between RPLC and SFC can be taken one step further to include the applicability of concave gradients in mobile phase composition²¹ and mobile phase density²², respectively.

In Fig. 4c $\log k$ is plotted vs. the logarithm of the mobile phase density. It was suggested by Van Wasen *et al.*³ that such plots would yield straight lines. However, it is clear from Fig. 4c that a straight line is not obtained. Rather, the non-linear part of the curve is shifted from the high-density part of the curves in Fig. 4b to the low-density range in Fig. 4c. Hence, a linear relationship can be obtained over a limited range of densities by plotting $\log k$ against either density or against its logarithm, for the low- and high-density ranges respectively.

In Fig. 5 the influence of the mobile phase is investigated. Since in GC the influence of the carrier gas on retention is negligible, the same value for $\log k$ at $p = 1$ atm should be assumed. Somewhat arbitrarily, $\log k = 3$ was assumed for both mobile phases. The present model yields different values for k when different mobile phases are used. This is in agreement with experimental observations, *cf.*, ref. 3.

Finally, in Fig. 6, an attempt is made to expand the scope of the present calculation scheme towards high-molecular-weight solutes, since these are expected to be of particular interest for the practical application of SFC. For this purpose an artificial series of *n*-alkanes was assumed. Because very similar molecules can be obtained from a polymerization of ethene, such a series is not entirely hypothetical. In order to perform these calculations, estimates have to be made for the critical properties, as well as for the anchor points needed for the calculations. This, of course, introduces additional uncertainties. Moreover, we stretch the limits of applicability of the Lee and Kesler equation because $p_R > 10$, as well as of eqn. 10, which strictly is not applicable to molecules larger than *n*-decane. In view of all these ap-

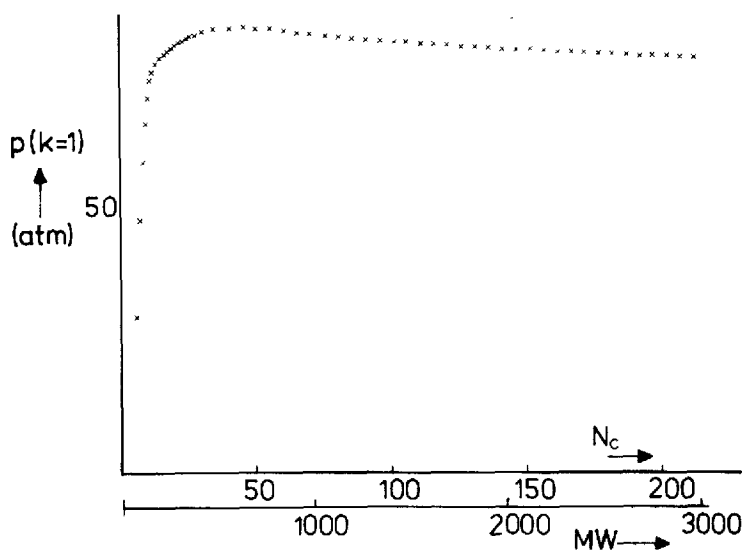


Fig. 6. Pressure required to obtain $k = 1$ for members of a homologous series of *n*-alkanes, calculated from eqn. 15 using Appendix B. Temperature = 35°C.

proximations, Fig. 6 should be seen as indicative of the retention behaviour of large molecules in SFC, but should otherwise be approached with circumspection. The rules used to obtain the necessary input data for the calculations are summarized in Appendix C.

Fig. 6 suggests that when the pressure is increased very large molecules may be eluted, but that individual hydrocarbons will be much harder to separate. In other words, selectivity decreases with increasing pressure, a conclusion formulated earlier by Peaden and Lee⁴. In Fig. 6 it seems that for very high carbon numbers the elution order may be reversed. Although this may not be entirely impossible, *e.g.*, a reversal of the elution order of 1,2-dimethylnaphthalene and *n*-decylnaphthalene has been reported by Rijnders²³, the reason for this observation may well be the approximate character of the calculations.

CONCLUSIONS

We are now in a position to answer the questions posed in the Introduction of this paper.

(1) A thermodynamic model appears to be highly useful for SFC. It permits: the characterization of mobile phases by means of their solubility parameters; the formulation of a rigorous equation, which yields a description of retention in terms of thermodynamic functions; prediction of the effect of pressure or density changes on the retention.

(2) The assumptions made to arrive at the present model appear to be justified by the results of the calculations. Hence, in the range of pressures (densities) of interest for SFC it appears that: the stationary phase can be assumed to behave as a non-compressible fluid; the solubility of the mobile phase in the stationary phase does not vary with the pressure.

Furthermore, the results of the calculations performed so far can be summarized as follows.

(3) The variation of retention ($\log k$) with pressure yields rather complicated curves.

(4) The relationship between $\log k$ and mobile phase density can be described by a quadratic function, inviting a comparison between the influence of density in SFC and the volume fraction of organic modifier in RPLC.

(5) Plotting $\log k$ against the logarithm of the mobile phase density does not yield a straight line, unless a limited range of (high) densities is considered.

(6) The selectivity of the SFC system, as estimated for a series of *n*-alkanes, appears to decrease with increasing pressure.

The thermodynamic model described in this paper forms a framework for the study of retention and selectivity in SFC. By using this model the number of experiments required for an investigation of the behaviour of different mobile and stationary phases can be drastically reduced. However, additional experimental SFC data are still needed. Absolute values cannot be predicted because of the inability of the present model to deal with interactions occurring in the stationary phase. A further disadvantage of the method is that it requires rather complex algebraic equations to be solved. Although this is easily done by computer, it is very difficult to envisage the effect of a particular parameter, without actually performing the calculation.

Therefore, further research on the application of thermodynamics to SFC should focus on the possibilities to simplify the present calculation scheme. This may include the use of simple equations of state, possibly one that is valid only over a limited range (notably $p_R > 1$ and $T_R > 1$), and the introduction of sensible approximations in both the model and the computations. Ideally, the outcome should be an analytical equation for SFC retention as a function of pressure and temperature.

APPENDIX A

The Lee and Kesler equation of state

The generalized three-parameter equation of state as described by Lee and Kesler¹⁵ reads as follows

$$Z = \frac{p_R V_R}{T_R} = 1 + \frac{B}{V_R} + \frac{C}{V_R^2} + \frac{D}{V_R^3} + \frac{c_4}{T_R^3 V_R^2} \left(\beta + \frac{\gamma}{V_R^2} \right) \exp \left(\frac{-\gamma}{V_R^2} \right) \quad (\text{A1})$$

where

$$B = b_1 - \frac{b_2}{T_R} - \frac{b_3}{T_R^2} - \frac{b_4}{T_R^3} \quad (\text{A2})$$

$$C = c_1 - \frac{c_2}{T_R} + \frac{c_3}{T_R^3} \quad (\text{A3})$$

$$D = d_1 + \frac{d_2}{T_R} \quad (\text{A4})$$

TABLE AI
COEFFICIENTS IN THE LEE AND KESLER EQUATION A1

Taken from ref. 15.

Coefficient	Simple fluid (<i>o</i>)	Reference fluid (<i>r</i>)
b_1	0.1181193	0.2026579
b_2	0.265728	0.331511
b_3	0.154790	0.027655
b_4	0.030323	0.203488
c_1	0.0236744	0.0313385
c_2	0.0186984	0.0503618
c_3	0	0.016901
c_4	0.042724	0.041577
d_1	0.155488×10^{-4}	0.48736
d_2	0.623689×10^{-4}	0.0740336
β	0.65392	1.226
γ	0.060167	0.03754
ω^r		0.3978

The constants in these equations each have two values, for the simple fluid and for the reference fluid. They are listed in Table AI.

From eqn. A1 two other thermodynamic quantities can be derived¹⁵ that are relevant to the present work: the fugacity coefficient of a pure substance

$$\ln \phi = \ln \frac{f}{p} = Z - 1 - \ln Z + \frac{B}{V_R} + \frac{C}{2V_R^2} + \frac{D}{5V_R^5} + E \quad (\text{A5})$$

where f = fugacity, and the enthalpy departure:

$$\frac{H - H^*}{RT_c} = T_R \left(Z - 1 - \frac{b_2 + \frac{2b_3}{T_R} + \frac{3b_4}{T_R^2}}{T_R V_R} - \frac{c_2 - \frac{3c_3}{T_R^2}}{2T_R V_R^2} + \frac{d_2}{5T_R V_R^5} + 3E \right) \quad (\text{A6})$$

In both eqns. A5 and A6, E is defined as:

$$E = \frac{c_4}{2T_R^3 \gamma} \left\{ \beta + 1 - \left(\beta + 1 + \frac{\gamma}{V_R^2} \right) \exp \left(- \frac{\gamma}{V_R^2} \right) \right\} \quad (\text{A7})$$

APPENDIX B

Rules for the critical properties of binary mixtures^{15,19}

In the following equations the two components of the binary mixture are denoted by the subscripts 1 and 2, i refers to both components and m to the mixture. The exponent η is an empirical constant, for which a value of 0.25 should be taken¹⁹. κ_{12} is a binary interaction parameter (see main text for details). The critical parameters for the mixture can be estimated if the following equations are applied in the given order:

$$Z_{c,i} = 0.2905 - 0.085 \omega_i \quad (\text{B1})$$

$$v_{c,i} = \frac{Z_{c,i} RT_{c,i}}{p_{c,i}} \quad (\text{B2})$$

$$v_{c,12} = \frac{(v_{c,1}^{1/3} + v_{c,2}^{1/3})}{8} \quad (\text{B3})$$

$$v_{c,m} = x_1^2 v_{c,1} + 2x_1 x_2 v_{c,12} + x_2^2 v_{c,2} \quad (\text{B4})$$

$$T_{c,12} = \kappa_{12} \sqrt{T_{c,1} T_{c,2}} \quad (\text{B5})$$

$$T_{c,m} = \frac{1}{v_{c,m}^{\eta}} (x_1^2 v_{c,1}^{\eta} T_{c,1} + 2x_1 x_2 v_{c,12}^{\eta} T_{c,12} + x_2^2 v_{c,2}^{\eta} T_{c,2}) \quad (\text{B6})$$

$$\omega_m = x_1 \omega_1 + x_2 \omega_2 \quad (\text{B7})$$

$$p_{c,m} = \frac{Z_{c,m} R T_{c,m}}{v_{c,m}} \quad (\text{B8})$$

APPENDIX C

Estimate of parameters for higher alkanes

Estimates for the critical pressure and volume can be obtained from Lydersen's method (ref. 13, Ch. 2). Since the boiling point of very large n -alkanes cannot be established, we have to rely on the Forman and Thodos method²⁴ to estimate T_c . The equations used, in which n_c is the number of carbon atoms, are

$$A_T = 2 \times 14,368 + (n_c - 2) \times 13.678 \quad (\text{C1})$$

$$B_T = 2 \times 11,453 + (n_c - 2) \times 6.262 \quad (\text{C2})$$

$$T_c = \frac{8 A_T^{3/2}}{27 B_T^{4/3} R} \quad (\text{C3})$$

where R is the gas constant (82.05)

$$p_c = \frac{M}{(0.227 n_c + 0.34)^2} = \frac{2 + 14 n_c}{(0.227 n_c + 0.34)^2} \quad (\text{C4})$$

where M is the molecular weight

$$V_c = 40 + 55 n_c \quad (\text{C5})$$

$$Z_c = \frac{p_c V_c}{R T_c} \quad (\text{C6})$$

$$\omega = \frac{0.2905 - Z_c}{0.085} \quad (\text{C7})$$

The anchor points are taken at $p = 1$ atm, using:

$$\ln k_{p=1} = 0.4 n_c - 2 \quad (\text{C8})$$

REFERENCES

- 1 E. Klesper, A. H. Corwin and D. A. Turner, *J. Org. Chem.*, 27 (1962) 700.
- 2 E. Klesper, *Angew. Chem.*, 90 (1978) 785.
- 3 U. van Wasen, I. Swaid and G. M. Schneider, *Angew. Chem.*, 92 (1980) 585.
- 4 P. A. Peaden and M. L. Lee, *J. Liquid Chromatogr.*, 5 (suppl. 2) (1982) 179.
- 5 D. R. Gere, R. Board and D. McManigill, *Anal. Chem.*, 54 (1982) 736.
- 6 H. H. Lauer, D. McManigill and R. D. Board, *Anal. Chem.*, 55 (1983) 1370.
- 7 L. G. Randall, *Separ. Sci. Technol.*, 17 (1982) 1.
- 8 J. C. Giddings, M. N. Myers, L. McLaren and R. A. Keller, *Science*, 162 (1968) 67.
- 9 J. C. Giddings, M. N. Myers and J. W. King, *J. Chromatogr. Sci.*, 7 (1969) 276.
- 10 J. J. Czubyrt, M. N. Myers and J. C. Giddings, *J. Phys. Chem.*, 74 (1970) 4260.
- 11 P. J. Schoenmakers, H. A. H. Billiet and L. de Galan, *Chromatographia*, 15 (1981) 205.
- 12 J. M. Prausnitz, *The Molecular Thermodynamics of Fluid-phase Equilibria*, Prentice Hall, Englewood Cliffs, 1969.
- 13 R. C. Reid, J. M. Prausnitz and T. K. Sherwood, *The Properties of Gases and Liquids*, McGraw-Hill, New York, 3rd ed., 1977.
- 14 K. S. Pitzer and R. F. Curl, *J. Amer. Chem. Soc.*, 77 (1955) 3427.
- 15 B. I. Lee and M. G. Kesler, *AIChE J.*, 21 (1975) 510.
- 16 L. Oellrich, U. Plöcker, J. M. Prausnitz and H. Knapp, *Chem.-Ing.-Tech.*, 49 (1977) 955.
- 17 R. Tijssen, H. A. H. Billiet and P. J. Schoenmakers, *J. Chromatogr.*, 122 (1976) 185.
- 18 E. B. Bagley, T. P. Nelson, S.-A. Chen and J. W. Barlow, *Ind. Eng. Chem. Fundam.*, 10 (1971) 27.
- 19 U. Plöcker, H. Knapp and J. M. Prausnitz, *Ind. Eng. Chem. Prod. Res. Develop.*, 17 (1978) 324.
- 20 P. J. Schoenmakers, H. A. H. Billiet, R. Tijssen and L. de Galan, *J. Chromatogr.*, 149 (1978) 519.
- 21 P. J. Schoenmakers, H. A. H. Billiet and L. de Galan, *J. Chromatogr.*, 185 (1979) 179.
- 22 J. C. Fjeldsted, W. P. Jackson, P. A. Peaden and M. L. Lee, *J. Chromatogr. Sci.*, 21 (1983) 222.
- 23 G. W. A. Rijnders, *Chem.-Ing.-Techn.*, 42 (1970) 890.
- 24 J. C. Forman and G. Thodos, *AIChE J.*, 4 (1958) 356.