

CHROMSYMP. 1961

## Use of chromatographic retention measurements to obtain solubilities in a liquid or supercritical fluid mobile phase

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### ABSTRACT

A thermodynamic analysis is given of the relationship between the capacity factor in high-performance liquid chromatography (HPLC) and supercritical fluid chromatography (SFC) and the solubility of the solute in the mobile phase. The analysis shows that in certain circumstances, where particular assumptions are valid, there is a simple inverse relationship between the two quantities. In these circumstances the proportionality constant has a fixed value for a particular column, temperature and solute, and is independent of the mobile phase. Furthermore, the logarithm of the constant is approximately linearly related to the inverse of the absolute temperature over a limited temperature range. Some experimental studies are then described which show that practical conditions exist where these relationships are valid. It is shown that the same equation-of-state, with the same parameters, can be used to predict quantitatively both supercritical fluid solubilities and the temperature dependence of retention in SFC. Experimental results illustrate the inverse relationship between solubility and retention where the same column was used in both SFC and HPLC. Results are also given for the variation of the proportionality constant with temperature. The various ways in which these relationships could be used to measure solubilities are discussed and examples of experimental measurements are given for some methods.

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### INTRODUCTION

The degree of retention of a solute in supercritical fluid chromatography (SFC), as measured by the capacity factor,  $k'$ , is at least qualitatively inversely related to the solvating power of the mobile phase for that solute: the more soluble it is in the mobile phase, the less it will be retained. The relationship has been used qualitatively and also to obtain quantitative information related to solubilities for both liquids and supercritical fluids. In one study chromatographic retention has been used to obtain pressure thresholds for the solubilities of various compounds at different temperatures<sup>1</sup>. In another, the relative solvating power of supercritical CO<sub>2</sub> compared with that of hexane has been discussed in terms of the differences in retention when the two

fluids were used as mobile phases<sup>2</sup>. A preliminary study has been carried out of solute fugacities in a stationary phase in SFC, with a view to obtaining by chromatography solute fugacities or enhancement factors (relating to solubilities) in a supercritical fluid<sup>3</sup>. High-performance liquid chromatography (HPLC) is used to obtain hydrophobicity constants, and also solubilities of organic electrolytes have been estimated using HPLC retention data to obtain parameters in the modified Hildebrand–Scott equation<sup>4</sup>. Normal-phase HPLC has been used to obtain oil–water partition coefficients, and “ideal solubilities” have been calculated from the ratios<sup>5</sup>.

In this paper it will be argued that in some situations at constant temperature, solubility of solid solutes in the mobile phase can be inversely proportional to  $k'$ . When this is the case, chromatographic retention can be used to measure solubilities relatively rapidly in both liquids and supercritical fluids. The relationship between the two quantities is investigated theoretically and experimentally, before discussing the various routes for obtaining solubilities from chromatographic retention measurements. These measurements could provide an important source of solubility data, particularly for supercritical fluids, and the studies are very much in the tradition of the use of chromatography for obtaining physical and chemical data, in which Professor Giddings has been a pioneer.

#### THERMODYNAMIC ANALYSIS

Thermodynamic analyses of the type given below have appeared previously in a number of publications. However, it is necessary to detail a treatment of this type, which is directly relevant to the present situation, in order to identify the assumptions which must be made to arrive at the eventual simple equation. In general we must allow for the fact that the solubility and chromatographic experiments will be carried out at different pressures,  $p_s$  and  $p_c$ , respectively. This will not be the case for supercritical fluid experiments, where solubilities refer to a particular pressure, and the corresponding retention measurements must be made at the same pressure. But it will be the case for liquids, where pressures of the order of 100 bar are needed to pass the mobile phase through the column in HPLC, whereas solubilities are usually and most easily done at low (atmospheric) pressure. For both types of mobile phase, pressure is decreasing along the column though much less so for SFC. For HPLC the arguments below refer to one point in the column, but for SFC pressure is assumed to be constant along the column, and this subject is discussed later as an experimental problem.

We begin by discussing the situation for chromatography. At equilibrium at constant pressure and temperature, equating the chemical potentials of the solute in both phases gives

$$\mu_m^{\ominus} + \int_0^{p_c} V_m dp + RT \ln a_m = \mu_{st}^{\ominus} + \int_0^{p_c} V_{st} dp + RT \ln a_{st} \quad (1)$$

where  $\mu_m^{\ominus}$  and  $\mu_{st}^{\ominus}$  are the standard chemical potentials of the solute in the mobile and stationary phases, respectively, and refer to infinite dilution and standard pressure. In all cases, but importantly in the case of a supercritical fluid, the state at the standard

pressure of 1 atm is a hypothetical and ideal one, where the activity coefficient, defined as being unity in the limit of zero pressure, is also unity in the standard state.  $V_m$  and  $V_{st}$  are the partial molar volumes at infinite dilution of the solute,  $a_m$  and  $a_{st}$  are the activities of the solute in the corresponding phases,  $R$  is the molar gas constant and  $T$  is the temperature. Rearrangement of eqn. 1 gives

$$\mu_m^\ominus - \mu_{st}^\ominus + \int_0^{p_c} (V_m - V_{st})dp = RT \ln (a_{st}/a_m) \quad (2)$$

If we assume that chromatography is carried out under conditions which approximate to infinite dilution, the activities can be replaced in eqn. 2 by the concentrations divided by standard concentrations,  $c_m/c_m^\ominus$  and  $c_{st}/c_{st}^\ominus$ . The standard concentrations are shown as different, in general, for the two phases, as will necessarily be the case for adsorption chromatography, where  $c_{st}^\ominus$  will be a surface concentration. For partition chromatography the standard concentrations will usually be identical amounts of solute per unit volume. Analytical chromatography is normally carried out at very low dilution and, if it is not the case, is observable as a distortion of the chromatographic peak shape and a variation of the degree of retention with the amount of solute injected. The ratio of these concentrations is related to  $k'$  by

$$k' = rc_{st}/c_m \quad (3)$$

where  $r$  is the stationary to mobile phase ratio, which in the simplest case of partition chromatography, when the standard concentrations in the two phases are identical, will be the ratio of the volumes of the two phases. For adsorption chromatography or a bonded stationary phase  $r$  will involve an area-to-volume ratio.  $r$  will be a constant for a particular chromatographic column. Substitution of eqn. 3 into eqn. 2, with the activities replaced by concentration ratios, gives the following expression:

$$\mu_m^\ominus - \mu_{st}^\ominus + \int_0^{p_c} (V_m - V_{st})dp = RT \ln (k'c_m^\ominus/rc_{st}^\ominus) \quad (4)$$

We now consider solubility and a saturated solution of the solute in the mobile phase. Discussion is restricted to conditions where the solid solutes remain as solids in the presence of the mobile phase, *i.e.* do not form a solute-rich liquid phase, and the solids are assumed not to absorb the mobile phase, and thus the chemical potential of the solute can be considered to be a constant at constant pressure and temperature. After equating chemical potentials in both phases, we obtain

$$\mu_s^\ominus - \mu_m^\ominus + \int_0^{p_s} (V_s - V_m)dp = RT \ln a_m^{\text{sat}} \quad (5)$$

where  $\mu_s^\ominus$  and  $V_s$  are, respectively, the chemical potential and molar volume of the solid, and  $a_m^{\text{sat}}$  the activity of the solute at saturation in the solvent or mobile phase. (In situations where different allotropic forms of the solid can exist, there will be no difficulty at the transition temperature, where the chemical potentials and solubilities of the two forms will be identical. At other temperatures one form will be the stable allotrope and have the lower chemical potential, and this is the form to which this thermodynamic analysis strictly applies. However, it may be possible to study solubilities of metastable allotropes by the methods described in this paper, by determining the constant,  $C$ , defined below, from solubilities of the metastable allotrope.) Eqns. 4 and 5 are then added to obtain:

$$\mu_s^\ominus - \mu_{\text{st}}^\ominus + \int_0^{p_s} (V_s - V_m) dp + \int_0^{p_c} (V_m - V_{\text{st}}) dp = RT \ln (a_m^{\text{sat}} k' c_m^\ominus / r c_{\text{st}}^\ominus) \quad (6)$$

In the case of a supercritical fluid  $p_c = p_s$ , and the integral terms cancel, if it is assumed that the partial molar volume of the solute in the stationary phase,  $V_{\text{st}}$ , is equal to its molar volume,  $V_s$ , and eqn. 6 becomes:

$$\mu_s^\ominus - \mu_{\text{st}}^\ominus = RT \ln (a_m^{\text{sat}} k' c_m^\ominus / r c_{\text{st}}^\ominus) \quad (7)$$

For the case of a liquid, where  $p_c$  and  $p_s$  are different, eqn. 7 may also be obtained, but in this case it must be assumed that the partial molar volumes of the solute in both the stationary and mobile phases are equal to the molar volume (and that this is the case at all points in the column). The assumptions that must be made about partial molar volumes are not unreasonable in many cases, where the interaction between the solute and the phases are not strong as is often the case.

Eqn. 7 may be rearranged to give the following expression for the activity of the solute at saturation:

$$a_m^{\text{sat}} c_m^\ominus = (r c_{\text{st}}^\ominus \exp [(\mu_s^\ominus - \mu_{\text{st}}^\ominus) / RT]) (1/k') \quad (8)$$

The quantity  $\mu_{\text{st}}^\ominus$ , which is the chemical potential of the solute in the stationary phase at infinite dilution and standard pressure and at a particular temperature, will be a constant for a given solute and chromatographic column, provided that the interaction of the solute and stationary phase is not affected by the nature of the mobile phase. This will often not be the case, for example with cross-linked polymer phases used in SFC, which absorb the mobile phase and swell to an extent dependent upon pressure and change their solvating properties<sup>6,7</sup>. However, it is likely to be true for octadecylsilyl (ODS) bonded phases and  $\text{CO}_2$ , as it will be shown below that it is not necessary to take into account effects of the mobile phase on the stationary phase to quantitatively account for the dependence of retention on temperature. Adsorption of carbon dioxide on an ODS phase has been observed and this is maximised in the region of the critical point<sup>8</sup>. However, it does not follow that this affects the adsorption of solutes, and the effect is such that the environment of the ODS phase does not change as much with a drop in pressure as it would if this adsorption did not occur. In cases

where the above assumption can be made, the right-hand side of eqn. 8, apart from the factor  $(1/k')$  is therefore a constant for a particular system and temperature. Eqn. 8 can therefore be written as

$$a_m^{\text{sat}} c_m^{\ominus} = C/k' \quad (9)$$

where  $C$  is a constant for a particular solute, column and temperature.

If the assumption is now made that the activity coefficient of the solute in the mobile phase is constant (*i.e.* unity) from infinite dilution up to the solubility limit, the activity can be replaced by concentration (which for the saturated solution will be the solubility,  $S$ ) divided by the standard concentration, and eqn. 9 can be rewritten as

$$S = C/k' \quad (10)$$

This assumption will not always be valid in liquids, as will be seen from the experimental results below. For supercritical fluids, such as carbon dioxide, where interactions are not strong or specific, the activity coefficient can be calculated from equations of state with reasonable confidence and here it is known that the assumption is a good approximation, especially as supercritical solubilities are usually low.

Returning to the problem of pressure drop in SFC, equations have been obtained for the average capacity factor in a column with pressure drop<sup>9,10</sup>, and calculations have been carried out for a model system of the percentage difference of the true average and the value at the average of the inlet and outlet pressures<sup>10</sup>. These show that differences of up to a factor of two are obtained for a 30-bar drop 1 K above the critical temperature and near the critical pressures. The effect decreases with rise in temperature, with the peak effect rising to higher pressures. For the quantitative measurements described in the last section a short column and low flow-rates were used to reduce the pressure drop to around 2 bar and the critical region avoided.

The constant  $C$ , introduced in eqn. 9, is given by

$$C = r c_{\text{st}}^{\ominus} \exp [(\mu_s^{\ominus} - \mu_{\text{st}}^{\ominus})/RT] \quad (11)$$

The difference in standard chemical potentials in eqn. 11 corresponds to the standard Gibbs function change for the precipitation of the solid solute from solution at infinite dilution in the stationary phase. In common with other types of equilibria, it may be assumed, therefore, that the constant  $C$  is given approximately by

$$C = A \exp (B/T) \quad (12)$$

where  $A$  and  $B$  are constants over a limited temperature range for a particular column and solute. This equation allows the possibility of limited interpolation or extrapolation to obtain values of  $C$ , by plotting  $\ln C$  versus  $1/T$ .

PREDICTION OF SOLUBILITY AND RETENTION BASED ON THE SAME EQUATION OF STATE FOR A SUPERCRITICAL FLUID

*Prediction of solubilities*

Prediction of solubilities may be made on the basis of eqn. 5. This can be modified by assuming, firstly, that the solid molar volume does not change with pressure and, secondly, that as before, as the saturated solutions are dilute,  $a_m^{\text{sat}}$  can be replaced by the mole fraction  $y^{\text{sat}}$ . The choice of mole fraction, rather than the concentrations used earlier, is correct if it is consistent within the present calculation and implies different numerical values of the chemical potentials. Eqn. 5 becomes

$$\mu_s^{\ominus} - \mu_m^{\ominus} + p_s V_s = \int_0^{p_s} V_m dp + RT \ln y^{\text{sat}} \quad (13)$$

$V_m$  is a quantity which varies greatly from the solute molar volume (becoming large and negative in the critical region), but can be calculated from an appropriate equation of state. Expressions are given usually in published equations of state for the fugacity coefficient,  $\phi$  (in this case the fugacity coefficient at infinite dilution), which is related to the integral on the left side of eqn. 13. This equation can now be expressed as

$$\mu_s^{\ominus} - \mu_m^{\ominus} + p_s V_s = RT \ln (p_s \phi / p^{\ominus}) + RT \ln y^{\text{sat}} \quad (14)$$

In the absence of any supercritical fluid,  $p_s = p_v$ , the vapour pressure of the solute,  $y^{\text{sat}}$  is unity and as the pressure is low and  $\phi$  is also approximately unity, eqn. 14 becomes approximately

$$\mu_s^{\ominus} - \mu_m^{\ominus} = RT \ln (p_v / p^{\ominus}) \quad (15)$$

The solubility,  $S$ , in concentration terms, is related to  $y^{\text{sat}}$  by  $SV = y^{\text{sat}}$ , where  $V$  is the molar volume, approximately the molar volume of the pure supercritical fluid. Substitution of this relationship and eqn. 15 into eqn. 14 gives

$$\ln S = \ln (p_v / p_s) - \ln \phi - \ln V + p V_s / RT \quad (16)$$

This equation can then be used to calculate supercritical solubilities, provided the vapour pressure is known, using a suitable equation-of-state for predicting the fugacity coefficient. In the studies described here the Peng–Robinson equation-of-state is used<sup>11</sup>, which, in common with other possibilities, requires knowledge of an interaction parameter for each pair of components. These interaction parameters are empirical fine-tuning parameters for the bimolecular interactions to which predicted solubilities are very sensitive. Fig. 1 shows solubilities predicted for naphthalene based on a range of the interaction parameter,  $d$ , for naphthalene and  $\text{CO}_2$  at two temperatures, which illustrate this sensitivity along with the published experimental results<sup>12,13</sup>. In principle, the parameter  $d$  is a constant independent of temperature. In a comprehensive study, Haselow *et al.*<sup>14</sup> have shown that the use of temperature-

independent parameters often give poor predictions of solubility, and Fig. 1 also illustrates this. However, Yamato *et al.*<sup>15</sup> have shown that the use of a temperature-dependent parameter can fit some of the experimental data more accurately. The approach used here is therefore to obtain temperature-dependent interaction parameters,  $d$ , from published experimental solubility data where available and interpolate these graphically. All published solubility data have been treated by us in this way, where vapour pressures and parameters for the equation of state were available and some of the results have already been published<sup>16</sup>. Fig. 2 shows smoothed plots of the interaction parameters obtained from published solubilities<sup>12,13,17-20</sup> for four polynuclear aromatic compounds, which will be of use in the next section. For the two compounds fluorene and pyrene, the variation of  $d$  with temperature is inside the experimental error and constant values are shown.

Using values of  $d$  obtained in this way, good predictions of solubility can be made, which fit the experimental data well. In the interest of minimising the number of figures given, this can be appreciated from Fig. 1B, where it can be seen that using a value for  $d$  of about 0.09 will give good agreement.

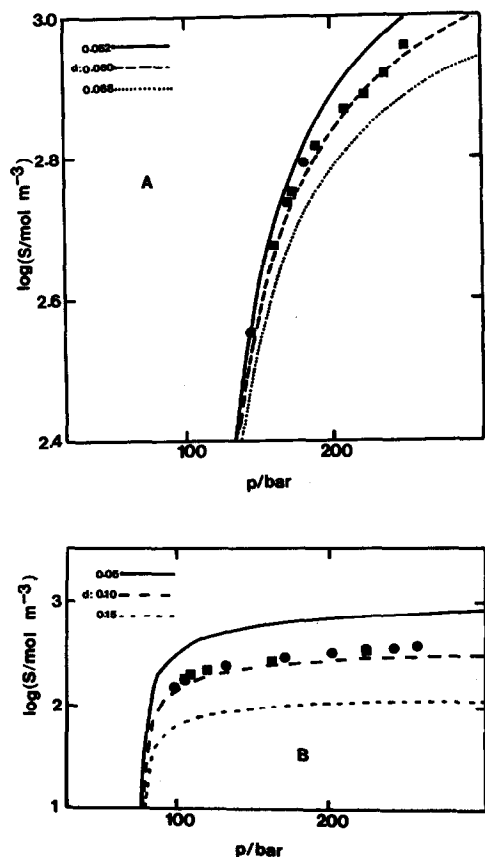


Fig. 1. Dependence of predicted values of the solubility,  $S$ , of naphthalene in  $\text{CO}_2$  as a function of pressure,  $p$ , on the Peng-Robinson interaction parameter,  $d$ . A is at  $55^\circ\text{C}$  and B at  $35^\circ\text{C}$ . Experimental results: ■ = McHugh and Paulaitis<sup>12</sup>; ● = Tsekhanskaya<sup>13</sup>.

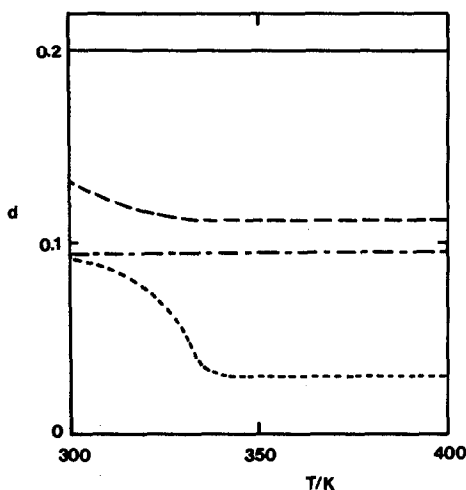


Fig. 2. Smoothed values of the Peng-Robinson parameter,  $d$ , obtained from experimental solubilities plotted as a function of temperature. — = Pyrene; --- = phenanthrene; - · - · - = fluorene; · · · · · = naphthalene.

#### *Prediction of the temperature dependence of retention in SFC*

At constant pressure,  $k'$  is observed to pass through a maximum with increasing temperature<sup>21</sup>. The qualitative explanation of this phenomenon is as follows. The rising portion of the curve is due to the decreasing density of the supercritical fluid, decreasing its solvating effect. The rising portion of the curve occurs when the increasing volatility of the solute outweighs this earlier effect. Quantitative analyses of this effect have been made<sup>22,23</sup>. The purpose here is to show that the same equation of state used to predict solubilities, described above can also give a good quantitative explanation of such results. Fig. 3 shows some experimental results obtained in our laboratory for the retention of four polynuclear hydrocarbons as a function of temperature<sup>24</sup>. A 25-cm ODS column was used with pure CO<sub>2</sub> as the mobile phase at an average pressure of 130 bar and a pressure drop along the column of 36 bar. Under the conditions used, the error caused by the pressure drop is not too important, although having studied the effect of pressure drop<sup>10</sup>, shorter columns and much lower pressure drops were used in subsequent experiments.

The equation used for the analysis of the experimental results can be obtained from eqn. 2. To obtain the appropriate chemical potentials, which will give the Gibbs function change for vaporisation from solution in the stationary phase, the activities are replaced, assuming dilute conditions, by  $c_{st}/c_{st}^{\ominus}$  and  $y = c_m V$ , respectively. The ratio  $a_{st}/a_m$  is therefore equal to (using eqn. 3)  $k'/c_{st}^{\ominus} V$ . Making also the assumptions, described earlier, that  $V_{st}$  is independent of pressure and equal to the molar volume,  $V_s$ , and that the integral involving  $V_m$  can be replaced by  $RT \ln(p_c \phi/p^{\ominus})$ , eqn. 2 can be rewritten as

$$\mu_m^{\ominus} - \mu_{st}^{\ominus} - V_s p_c = RT \ln(p_c \phi k'/p^{\ominus} c_{st}^{\ominus} V) \quad (17)$$



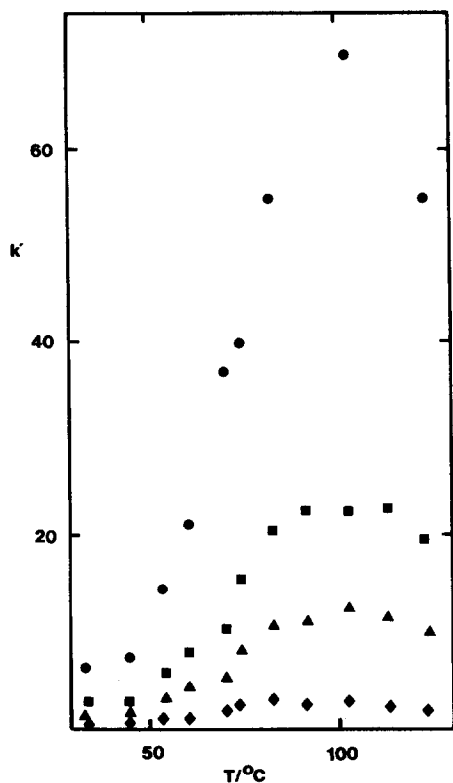


Fig. 3. Dependence of the capacity factor,  $k'$ , on temperature for an ODS column and  $\text{CO}_2$  as the mobile phase. ● = Pyrene; ■ = phenanthrene; ▲ = fluorene; ◆ = naphthalene.

Eqn. 17 can be rearranged to

$$\ln k' - \ln \phi - \ln V_{cst}^{\ominus} = D - (p_c V_s + \mu_{st}^{\ominus} - \mu_m^{\ominus})/RT \tag{18}$$

where

$$D = \ln r + \ln (p_c/p^{\ominus}) \tag{19}$$

is a constant at constant pressure. The terms  $\mu_{st}^{\ominus} - \mu_m^{\ominus}$  are equal to the standard Gibbs function change for solution of the solute from the vapour to the stationary phase, which can be expressed in terms of the entropy,  $\Delta S_s^{\ominus}$ , and enthalpy,  $\Delta H_s^{\ominus}$  components. Eqn. 18 becomes

$$\ln k' - \ln \phi - \ln V_{cst}^{\ominus} = D + \Delta S_s^{\ominus}/R - (p_c V_s + \Delta H_s^{\ominus})/RT \tag{20}$$

If it can be assumed that the enthalpy and entropy changes are not very sensitive to temperature, a graph of the left side of eqn. 20 against  $1/T$  should give an approximately straight line.

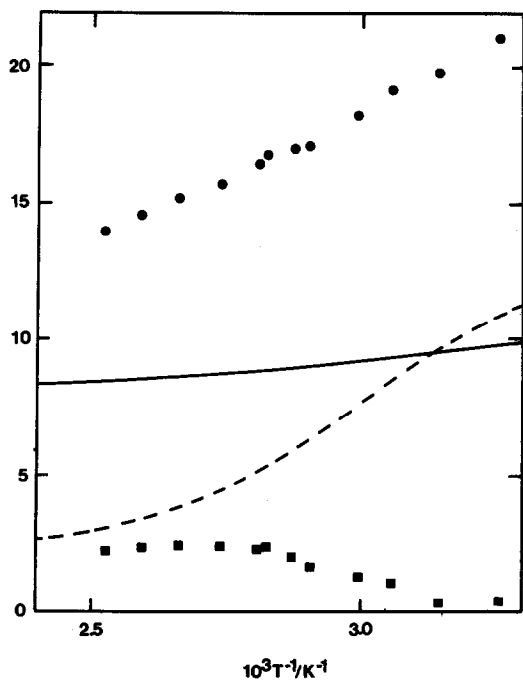


Fig. 4. Contributions to  $(\ln k' - \ln Vc_{st}^{\Theta} - \ln \phi)$  for fluorene as a function of reciprocal temperature. ■ =  $\ln k'$ ; — =  $-\ln Vc_{st}^{\Theta}$ ; --- =  $-\ln \phi$ ; ● =  $(\ln k' - \ln Vc_{st}^{\Theta} - \ln \phi)$ .

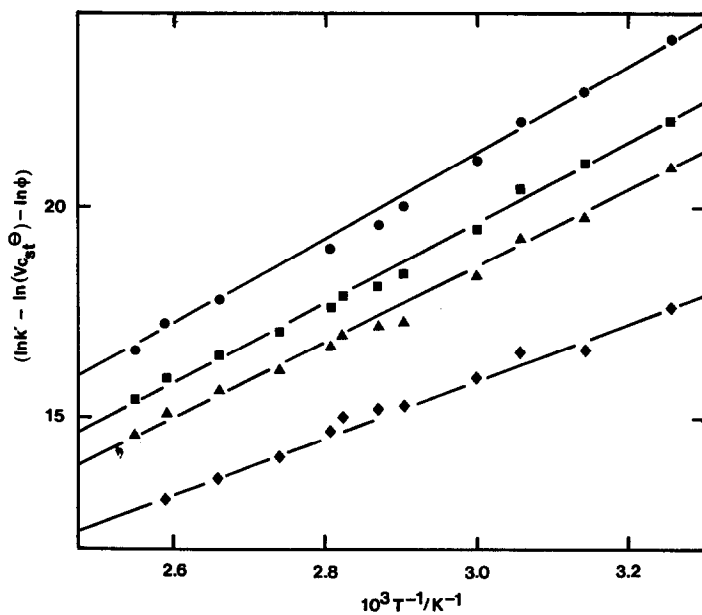


Fig. 5. Plots of  $(\ln k' - \ln Vc_{st}^{\Theta} - \ln \phi)$  versus reciprocal temperature. ● = Pyrene; ■ = phenanthrene; ▲ = fluorene; ◆ = naphthalene.

Fig. 4 shows the calculation of the left side of eqn. 20 for fluorene, with the curve in the experimental points becoming an approximately straight line as the terms in  $V$  and especially  $\phi$  are added. Fig. 5 shows the final curves for the four polynuclear hydrocarbons, from the slopes of which values for  $\Delta H_s^\ominus$  are obtained and given in Table I. These are compared in the table with enthalpies of vaporisation of the solid solutes<sup>25</sup>, and there is agreement within experimental error, indicating that the enthalpies of solution of the solid solutes in the stationary phase are small.

The success of this analysis, with data obtained from solubilities, indicates the validity of the assumptions made in the thermodynamic derivations for these particular systems and confirms the strong relationship between retention and solubility. In particular, it shows that for an ODS column the stationary phase does not appreciably change its solvation properties towards these solutes, either with temperature or with supercritical fluid density.

TABLE I

VALUES OF  $\Delta H_s^\ominus$ , THE ENTHALPIES OF SOLUTION FROM THE VAPOUR INTO THE ODS PHASE, OBTAINED FROM FIG. 5, COMPARED WITH THE ENTHALPIES OF VAPOURISATION OF THE SOLID,  $\Delta H_v^\ominus$  (REF. 25)

	$-\Delta H_s^\ominus/kJ\ mol^{-1}$	$\Delta H_v^\ominus/kJ\ mol^{-1}$
Naphthalene	$70 \pm 3$	70
Fluorene	$82 \pm 3$	83
Phenanthrene	$87 \pm 2$	87
Pyrene	$95 \pm 3$	94

#### DIRECT INVESTIGATION OF THE RELATIONSHIPS $S = 1/k'$ AND $C = A \exp(B/T)$ FOR SOME SYSTEMS

##### *The relationship $S = 1/k'$*

In this section direct experimental tests of the inverse relationship between the solubility and capacity factor for both SFC and HPLC are described. These results are representative of a more extensive study<sup>26</sup>, in which the same type of ODS column was used as before, but of shorter length (10 cm) to reduce the pressure drop. The polyaromatic hydrocarbons, naphthalene, fluorene, anthracene, pyrene and chrysene, were used as the solutes with the same column throughout for both types of mobile phase.  $CO_2$  was used as the mobile phase in the SFC measurements at pressures for which published solubility data for the solutes in  $CO_2$  are available. For the HPLC measurements mixtures of methanol and water were used as the mobile phase and solubilities of the solutes in the same methanol-water mixtures were also measured by UV absorption. The systems chosen constitute a severe test of the inverse relationship. Polyaromatic hydrocarbons tend to associate in a hostile polar environment, which could have a large effect on their activity coefficients, even at low concentrations. At the same time, the environment of the stationary phase covers a wide range from the non-polar pressurised  $CO_2$  fluid to a polar liquid the dielectric constant of which will vary markedly with composition.

As  $k'$  is related to retention volumes for the solute and mobile phase,  $V_R$  and  $V_M$ , respectively, by  $k' = (V_R - V_M)/V_M$ , a test of the relationship  $k' = C/S$  is therefore the linearity of plots of  $1/S$  against  $(V_R - V_M)$ . It is better to use these plots rather than plots of  $S$  versus  $1/(V_R - V_M)$ , because the estimated errors in  $(V_R - V_M)$  contain a constant element and their percentage errors increase as the values fall.

Some results for naphthalene are shown in Fig. 6. Because of the wide range of values, two plots are given with different scales to show the low and high values. (The alternative of a log-log plot is a less obvious test of linearity.) The lines drawn on both parts of the figure have the same slope and correspond to a value for  $S(V_R - V_M)/\text{mg}$  of 35. In spite of deviations due in part to experimental error, the figure is a remarkable display of linearity, in view of the fact that the data cover a range of 2.5 orders of magnitude, two different types of mobile phase or solvent, and a wide range of solvent polarity. The major deviations from the straight line may be explained as follows. The highest point arises from a very low supercritical fluid solubility which may be less

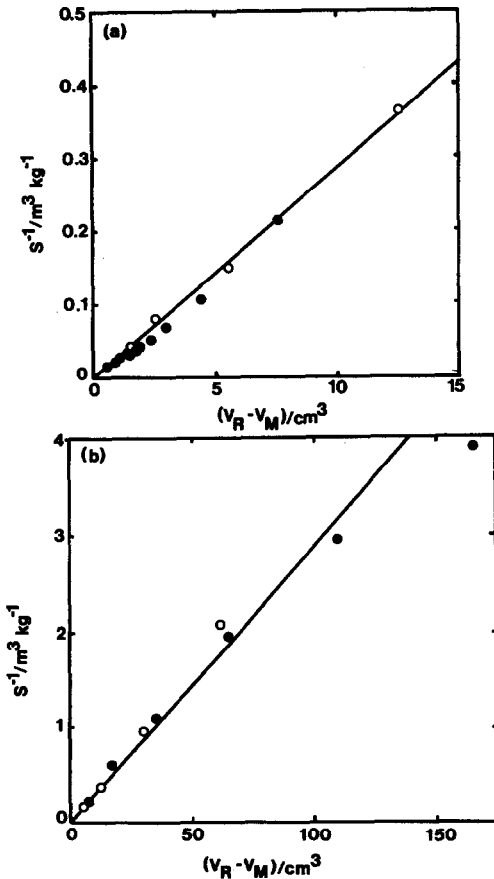


Fig. 6. The reciprocal solubility,  $1/S$ , plotted against  $V_R - V_M$  for naphthalene at 318.2 K. ○ = Liquid; ● = supercritical fluid. Lower and higher values are shown in (a) and (b), respectively and the lines drawn in the two parts are of the same slope equal to  $1/35$ .

accurate in percentage terms than the other values. The SFC points which lie below the curve in Fig. 6a are from low retention volumes which will be more erroneous. Thus, the assumptions listed in the introduction appear to be valid for these systems and, in particular, the assumption that the solvating effect of the stationary phase does not seem to be greatly affected by the nature of the mobile phase in the case of naphthalene and therefore probably in the case of the other solutes. Results at 308.2 K show similar linearity, although measurements at lower pressures were not made because of the errors introduced by the proximity of the critical point.

For the other solutes studied, the linear relationship was found to hold well for supercritical  $\text{CO}_2$ , but the plots for the methanol-water mixtures, which were sometimes curved, did not coincide with the supercritical fluid curves. An example is given for phenanthrene in Fig. 7. This can be explained as follows. In supercritical fluids, because calculations based on equations of state indicate that activity coefficients in supercritical fluids do not change markedly with concentration over the range up to the solubility limit, the inverse relationship of solubility and capacity factor holds well for all solutes. The deviations for the methanol-water mixtures are caused by molecular association (which sometimes increases with water content) reducing the activity coefficients. In conclusion, it appears that the relationship of eqn. 10 is valid in some situations, but not in others. It holds fairly well for naphthalene in both HPLC and SFC, but for the other solutes for SFC only.

*The relationship  $C = A \exp (B/T)$*

The validity of eqn. 12 is tested in Fig. 8 for phenanthrene by plotting the natural logarithm of the mean values of the product  $S(V_R - V_M) = CV_M$  at each temperature against  $1/T$ . The values deviate from the straight line by less than 5% of  $S(V_R - V_M)$ .

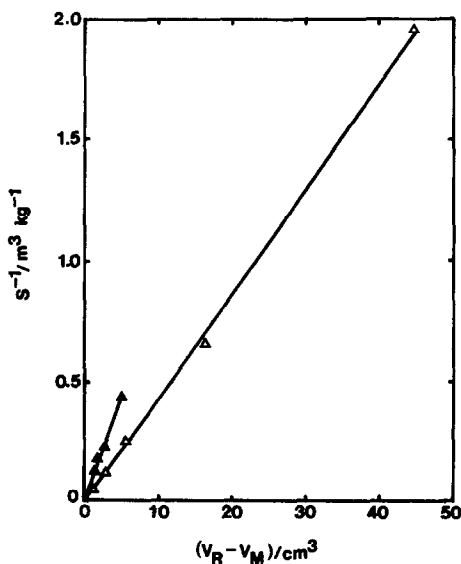


Fig. 7. The reciprocal solubility,  $1/S$ , plotted against  $V_R - V_M$  for phenanthrene at 318.2 K.  $\Delta$  = Liquid;  $\blacktriangle$  = supercritical fluid.

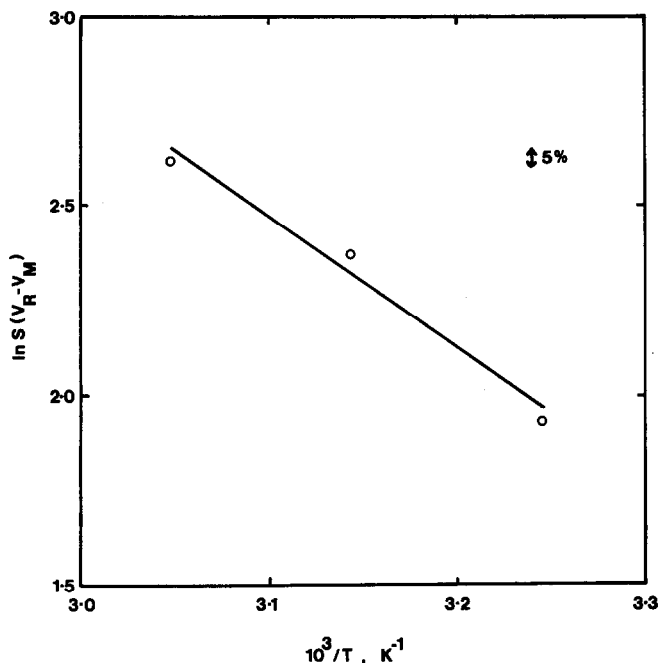


Fig. 8. Plot of  $\ln S(V_R - V_M)$  versus reciprocal temperature for phenanthrene.

The slope of the line corresponds to a standard enthalpy of solution (absorption) into the ODS stationary phase of  $23 \text{ kJ mol}^{-1}$ . This compares with enthalpy of fusion for phenanthrene of  $19 \text{ kJ mol}^{-1}$ . Although further tests of this relationship would be desirable, consistency with eqn. 12 is observed.

#### METHODS OF MEASURING SOLUBILITIES FROM RETENTION VALUES

##### *Solubilities in liquids especially liquid mixtures using HPLC*

The systems with liquid solvents, studied above, do not obey the inverse relationship well in all cases for perhaps predictable reasons. For this reason, solubilities in water, calculated from retention data, are described as ideal solubilities<sup>5</sup>. However, given the success with the unpromising naphthalene-water-methanol system, it is likely that there will be many systems of solutes and (particularly non-polar) solvents where it will be obeyed quite accurately. The relationship could therefore in many cases provide a method for generating rapidly a large body of solubility data, particularly for multicomponent solvent mixtures. The procedure would be to make by a relatively small number of direct solubility measurements with corresponding retention measurements at certain temperatures to establish linearity and obtain the constants  $C$  or  $A$  and  $B$ . A large number of retention measurements could then be made to generate solubility data.

*Solubilities in supercritical fluids at low pressures using SFC and vapour pressures*

If retention measurements are made in SFC which extend down to lower (subcritical) pressures, it may be possible to extrapolate  $k'$  to obtain a value,  $k'_0$ , corresponding to zero mobile phase pressure. The corresponding "solubility",  $S_0$ , will arise from the vapour pressure and will be equal to  $p_v/RT$ . Thus the constant  $C$  can be obtained from

$$C = k'_0 p_v/RT \quad (21)$$

The method of extrapolating  $k'$  is obtained by first writing eqn. 18 for the condition of zero mobile phase pressure, where since  $\phi$  and  $p_c$  are essentially unity and zero, respectively, and  $V = RT/p_v$ , it becomes

$$\ln k'_0 - \ln (RTc_{st}^0/p_v) = \ln r + \ln (p_v/p^0) - (\mu_{st}^0 - \mu_m^0)/RT \quad (22)$$

Subtraction of eqn. 22 from eqn. 18 and rearranging gives

$$\ln k' + p_c V_s/RT = \ln k'_0 + \ln \phi + \ln (p_c V/RT) \quad (23)$$

For extrapolation to low pressures the virial equation of state may be used to give an expression for  $\phi$ , which is

$$\ln \phi = \ln (RT/p_c V) + (2/V)B_{12} + (2/3V^2)C_{112} + \dots \quad (24)$$

where  $B_{12}$  and  $C_{112}$  are virial coefficients. At pressures below 5 MPa, the second virial coefficient alone is sufficient<sup>27</sup>, and after substituting a simplified eqn. 24 into eqn. 23 we obtain

$$\ln k' + p_c V_s/RT = \ln k'_0 + (2/V)B_{12} \quad (25)$$

This equation shows that  $k'_0$  can be obtained by extrapolating the left-hand side of eqn. 25 against  $1/V$ , from which the second mixed virial coefficient can also incidentally be obtained.

Retention measurements have been made to show the feasibility of the method, and results for 1-methylnaphthalene in CO<sub>2</sub> are reported here. The column used was an open stainless-steel tube, 0.5 m × 0.5 mm I.D. Solubility results are shown in Fig. 9 and compared to results obtained by freezing a known volume of saturated solution in liquid nitrogen, allowing the CO<sub>2</sub> to evaporate and measuring the amount of solute by gas chromatography. The solubilities, measured directly at the lowest pressures, where little solute was recovered, are accurate to only around 50% and the values obtained from retention appear to be superior.

*Generation of a larger body of supercritical solubility data from a small number of data at the same temperature*

If, in principle one solubility, or better a few solubility results, obtained by conventional methods, are available at one temperature, a value for the constant  $C$  can be obtained at that temperature by making retention measurements under corre-

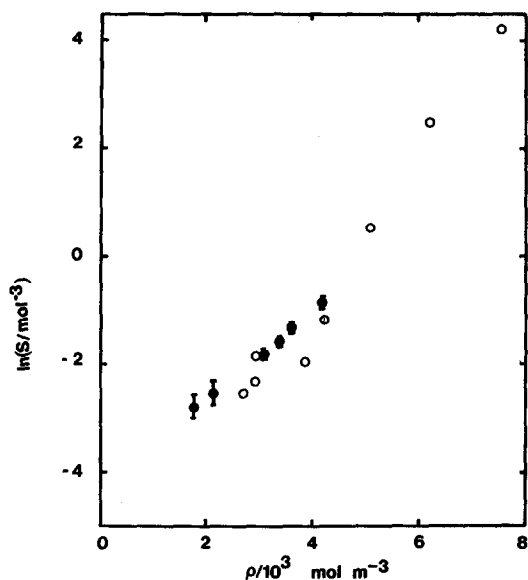


Fig. 9. Solubility,  $S$ , of 1-methylnaphthalene in  $\text{CO}_2$  versus density,  $\rho = 1/V$ . ● = Retention results; ○ = trapping results.

sponding conditions. This value can then be used to generate a larger body of data relatively rapidly, by making a large number of retention measurements. The supercritical data shown in Fig. 7 were used to determine  $C$  for phenanthrene in an ODS column at 318 K. In fact the second lowest point was not used as this gave a constant out of line from those obtained from the other three points. From the average value of  $C$  from the other three points and further retention measurements a large number of solubilities were obtained and shown in Fig. 10 in terms of mole fraction (the square solid points). Also shown are the conventionally measured values as open squares, which naturally fall on the same line except for the point which was not used in the calculation of  $C$ . (This is an indication that this published datum point could be in error.) The procedure described was also carried out at 308 and 328 K, in these cases by using all the published solubilities, and the results are also shown in Fig. 10.

#### *Measurement of supercritical solubilities at a temperature close to other temperatures where solubility data are available*

If conventionally measured solubility data are not available at the temperature of interest, but are at two or more close temperatures, interpolation of  $\ln C$  versus  $1/T$  may be used to obtain  $C$  at the required temperature. An example is given here, where the proportionality constant has been obtained for phenanthrene in  $\text{CO}_2$  at 323 K from the plot shown in Fig. 8. The results obtained by this method are given as the solid triangles in Fig. 10.

#### *Measurement of solubilities in modified supercritical fluids*

The use of modified supercritical fluids, such as by the addition of some



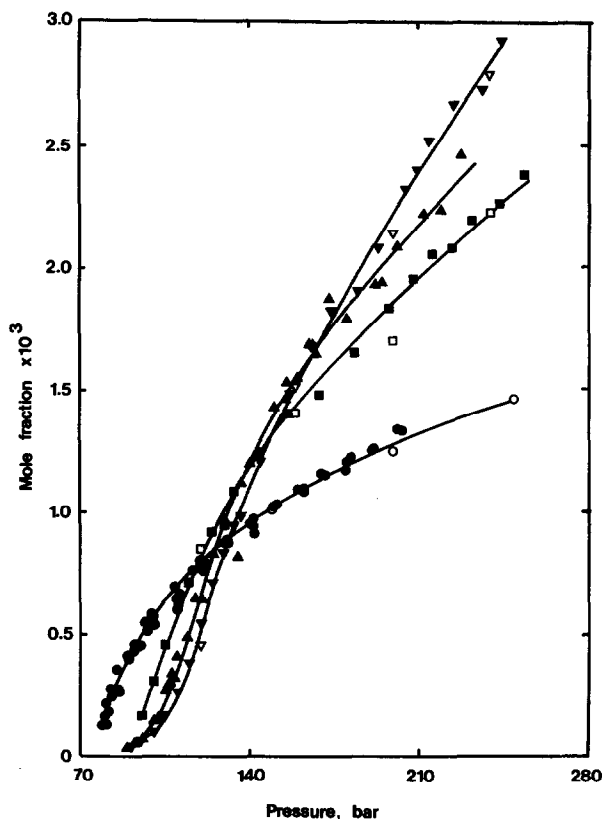


Fig. 10. Solubility of phenanthrene in supercritical carbon dioxide. Present work: ● = 308.2 K; ■ = 318.2 K; ▲ = 323.2 K; ▼ = 328.2 K. Dobbs *et al.*<sup>18</sup>: ○ = 308.2 K. Kurnik *et al.*<sup>19</sup>: □ = 318.2 K; ▽ = 328.2 K.

methanol to CO<sub>2</sub>, adds another dimension to the range of conditions to be covered, and relatively little published data are available. The use of chromatography could be of great advantage here as in many systems values of  $C$  obtained for the pure fluids would be applicable to the modified fluids. Of course, this would have to be tested for representative systems, including the effect of the modifier on the solvating properties of the stationary phase.

#### *Measurement of supercritical fluid solubilities from SFC, HPLC and liquid solubility measurements*

The most promising use of the relationship is perhaps the fact that supercritical fluid solubilities could in the right circumstances be obtained from SFC and HPLC retention measurements and the more easily measured liquid solubilities. No results are published for this method, although in principle the results obtained for naphthalene and given in Fig. 6 could be used to obtain supercritical solubilities. However, as so many data are available for the naphthalene-carbon dioxide system, this would not be worthwhile. It seems likely, though, that the method would work for

many systems, even for the polynuclear hydrocarbons, if the chromatography were carried out in normal- rather than reversed-phase mode (e.g. with an amino-bonded column and a non-polar solvent, such as hexane). It is possible, perhaps likely, that the relationship given in eqn. 10 would hold for both SFC and HPLC. Where the method could be used, it would be considerably easier and quicker than the conventional methods for supercritical fluid solubilities.

#### ACKNOWLEDGEMENTS

The authors would like to thank the Science and Engineering Research Council, British Gas and the Royal Society of Chemistry for financial support and Dr. T. Boddington for discussions.

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