

# Effects of molecular structure on the $\log k'_w$ index and linear $S$ – $\log k'_w$ correlation in reversed-phase high-performance liquid chromatography

Nong Chen\*, Yukui Zhang and Peichang Lu

*National Chromatographic Research and Analysis Center, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, 116011 Dalian (China)*

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## ABSTRACT

The  $\log k'_w$  index in the retention equation  $\log k' = \log k'_w - S\phi$  in reversed-phase high-performance liquid chromatography was systematically studied as a function of molecular structure parameters. The  $\log k'_w$  index or the "hydrophobic index", which was observed to be nearly constant for a specific solute on the particular column system, was quantitatively correlated with the solvatochromic parameters of the solutes. The coefficients in the correlation of the  $\log k'_w$  index in methanol–water and acetonitrile–water mixtures with solvatochromic parameters of the solutes were systematically investigated and were found to be consistent with the results of using solvatochromic comparison method. A linear relationship between  $S$  and  $\log k'_w$  was obtained only when two or three of the solute parameters are constant and solute volume varies. The linear relationship between  $S$  and  $\log k'_w$  for structurally related compounds were systematically described. The parameters of the correlation equations referring to various reversed-phase columns with different carbon loadings were compared.

## INTRODUCTION

The popularity of reversed-phase high-performance liquid chromatography (RP-HPLC) can be attributed to the development of chemically stable, microparticulate bonded phases [1–4]. The most prevalent type of RP-HPLC column packing is prepared by reacting uniform silica gel particles with an alkylchlorosilane; the reaction with trimethylchlorosilane (TMCS) was followed to eliminate the residual silanols. The molecular organization of highly densely bonded phases resembles that of biomembranes and may be used as a model system to study quantitative structure–retention relationships (QSRR). There have been many studies on increasing the bonding density [2–4], as originally described by Szabo *et al.* [2] using dimethylamino leaving

groups. The steric constraints made further increases in high bonding densities extremely difficult, but this steric hindrance was reduced by Golding *et al.* [3] through the use of dihydrochlorosilane [3].

Despite the enormous popularity of RP-HPLC, there is a lack of understanding of the solute retention mechanism. Such an understanding ultimately requires a sufficiently detailed description of the relationships between retention and various mobile and stationary phase variables. As the rigorous theoretical study of retention mechanisms is very complicated, it is more practical to approximate the retention behaviour of a solute by using empirical relationships. In RP-HPLC, there is ample evidence that the chemical bonded phase (CBP) structure depends also on the nature of the organic modifier [4]. The organic component of the mobile phase is sorbed by the CBP and alters its properties. These alterations are not significant in methanol–water and acetonitrile–water mixtures.

\* Corresponding author.

In RP-HPLC, the mobile phase effects can be separated from stationary phase effects by using the linear relationship between the retention values and the composition of the mobile phase. The linear approximation of the relationship between the logarithm of the capacity factors ( $\log k'$ ) and the composition of the mobile phase ( $\varphi$ ) has found considerable applications [5–8], and can be described by

$$\log k' = \log k'_w - S\varphi \quad (1)$$

where  $k'$  is the capacity factor,  $\varphi$  is the volume fraction of strong solvent in binary mobile phase,  $k'_w$  is the extrapolated value of the capacity factor in pure water and  $S$  is the negative of the slope of the plot. Eqn. 1 was derived from the hydrophobic interaction model using the thermodynamic method combined with empirical relationships [7].

The slope of the  $\log k'$  vs  $\varphi$  plot is determined by the mobile phase effects, whereas the intercepts of the linear plots are determined mainly by the properties of the stationary phases and solvent water [7,8]. Both parameters are functions of solute molecular structural parameters [7].

The solute distribution in RP-HPLC appears to approach that of partition between two bulk liquid phases, and therefore the capacity factor in RP-HPLC has been used to describe quantitatively the partition coefficient measured in the *n*-octanol–water system ( $\log P$ ). The capacity factor in RP-HPLC has been extensively used as a hydrophobic parameter [9–23]. The retention parameter  $\log k'$  over a certain concentration range of the mobile phase has been correlated with the classical *n*-octanol–water partition coefficient  $\log P$  but, in view of the fact that  $\log k'$  values vary with the volume fraction of the strong solvent, in some instances, different conclusions can be reached owing to a cross-over of peaks at different compositions of the mobile phase.

Many attempts have been made to use the extrapolated  $k'$  value ( $\log k'_w$ ) as a hydrophobic index [9–19]. It has been found that  $\log k'_w$  has some advantage over the isocratic  $k'$  [20]. The  $\log k'_w$  value plays an important role in understanding the hydrophobic interactions of the solute and stationary phase. The  $\log k'_w$  index or the “hydrophobic index” is an intrinsic property of the solute on a particular column. The extrapolated  $\log k'_w$  of a specific solute for pure water as the eluent should be constant for a given stationary phase, independent of

the organic modifier used in mixtures with water, but the reported parameter  $\log k'_w$  obtained by extrapolation of eqn. 1 depends on the nature of the organic modifier present in the aqueous mobile phase. Much effort has been directed at making liquid chromatographic systems mimic the conventional *n*-octanol–water system [20–23].

$\log k'_w$  is a function of molecular structure parameters. There have been few studies to explore the effects of molecular structure parameters on  $\log k'_w$  [20–23]. Many studies have shown that there was a better relationship between  $\log k'_w$  and  $\log P$  for structurally related compounds [9–23]. Other studies have found that  $\log k'_w$  has the property of additivity [20–23], as expressed by

$$\tau_i = \log k'_{w(j)} - \log k'_{w(i)} \quad (2)$$

where  $j$  and  $i$  differ in a substituent, but non-additivity has been found for multi-substituted intra- and intermolecular hydrogen-bonding solutes.

In several other studies,  $\log k'_w$  has been found empirically to be linearly correlated with  $S$  (eqn. 1) [24–26], but there is a lack of understanding of the quantitative relationship between  $\log k'_w$  and solute parameters. Therefore systematic studies on the relationship between  $\log k'_w$  and structural parameters need to be established.

In previous papers,  $S$  or the “hydrophilic index” has been observed to be nearly constant for a specific solute even when column systems with different  $C_{18}$  packing materials are used [7,8]. The solvatochromic parameters are widely used molecular structural parameters for characterizing the size, the dipolarity/polarizability interactions and hydrogen bonding interactions of the solute in an aqueous mobile phase [27–32]. The  $S$  index has been quantitatively correlated with the solvatochromic parameters of the solutes [8].

In this work, the quantitative correlation of the  $\log k'_w$  index with the solvatochromic parameters of the solutes was studied and the coefficients in the correlation of  $\log k'_w$  in methanol–water and acetonitrile–water mixtures with the solvatochromic parameters were investigated through the use of the solvatochromic comparison method. The linear relationships between  $S$  and  $\log k'_w$  are also systematically described for structurally related compounds.

## EXPERIMENTAL

The experimental results utilized in this paper were taken from papers by Hammers *et al.* [13], Hafkenschied and Tomlinson [33], Hanai and Hubert [34,35], Harnisch *et al.* [36] and Petrovic and Lomic [37,38], which gave an exact description of the chromatographic conditions employed. All data were processed with a BASIC program on AST-286 micro-computer.

## RESULTS AND DISCUSSION

Log  $k'_w$  mainly describes the difference in free-energy change between the solute and a weak solvent and between the solute and a hydrocarbonaceous ligand, as is shown by the following equation [7]:

$$\log k'_w = \log \phi + (\Delta G_{A,C}^0 - \Delta G_{A,L}^0)/RT \quad (3)$$

where  $\Delta G_{A,C}^0$  and  $\Delta G_{A,L}^0$  are the non-electrostatic solute-weak solvent and solute-ligand free-energy change, respectively,  $R$  is the gas constant,  $T$  is the absolute column temperature and  $\phi$  is the phase ratio.

The non-electrostatic free-energy change consists of the Van der Waals interactions [ $\Delta G^0(\text{van})$ ] and hydrogen-bonding interactions [ $\Delta G^0(\text{H})$ ]. These interactions can be characterized by the solvatochromic parameters. The molecular solute Van der Waals volume is measured by the solvatochromic parameter  $V_2$ , the solute dipolarity/polarizability is measured by the solvatochromic parameter,  $\pi_2$  and the solvatochromic parameters  $\alpha_2$  and  $\beta_2$  measure the solute hydrogen-bond donor (HBD) acidity and hydrogen-bond acceptor (HBA) basicity, respectively [27–32]. Accordingly, the distribution or partition between a pair of solvents takes the form

$$SP = SP_0 + mV_2/100 + d\pi_2 + b\beta_2 + a\alpha_2 \quad (4)$$

where  $SP$  denotes solvent-dependent properties,  $V_2$ ,  $\pi_2$ ,  $\beta_2$  and  $\alpha_2$  characterize the solutes, and the  $m$ ,  $d$ ,  $b$  and  $a$  coefficients characterize the solvent water and the quasi-liquid-like stationary phase.

As the solvent complementary to solute HBA basicity is solvent HBD acidity, for the energetically homogeneously distributed bonded phases the property of the bonded phase that complements the solute's ability to accept a hydrogen bond ( $\beta$ ) is the

ligand's ability to donate a hydrogen bond ( $\alpha$ ). The chemical property of water or the quasi-liquid-like bonded phase that complements the solute molar volume is its cohesive energy taken as  $\delta^2$ , the square of the Hildebrand solubility parameter.

In RP-HPLC, log  $k'_w$ , which mainly characterizes the partitioning between water and the quasi-liquid-like bonded phase, can be quantitatively correlated with the solvatochromic parameters. Therefore, according to the solvatochromic comparison method, we have the following equation:

$$\log k'_w = SP_0 + mV_2/100 + d\pi_2 + b\beta_2 + a\alpha_2 \quad (5)$$

where

$$m = f(\delta_C^2 - \delta_L^2) \quad (6)$$

$$d = g(\pi_L - \pi_C) \quad (7)$$

$$b = h(\alpha_L - \alpha_C) \quad (8)$$

$$a = l(\beta_L - \beta_C) \quad (9)$$

where  $\delta_C$  and  $\delta_L$  are the solubility parameters for water and hydrocarbonaceous ligands, respectively,  $\pi_L$ ,  $\beta_L$  and  $\alpha_L$  are solvatochromic parameters for ligands,  $\pi_C$ ,  $\beta_C$  and  $\alpha_C$  are solvatochromic parameters for water and  $f$ ,  $g$ ,  $h$  and  $l$  are constants. In eqn. 5, the magnitude of the coefficient  $m$  denotes the difference in solubility parameters of water and hydrocarbonaceous ligands and  $d$  denotes the difference in dipolarity/polarizability parameters between ligands and water, the coefficient  $b$  shows the difference in hydrogen donor ability of the bonded ligands and water and  $a$  shows the difference in hydrogen acceptor ability of the ligands and water. The solvatochromic and solubility parameters for  $C_{18}$  bonded ligand and water are given in Table I.

TABLE I  
SOLUBILITY AND THE SOLVATOCHROMIC PARAMETERS FOR  $C_{18}$  BONDED PHASE AND WATER

Solubility and solvatochromic parameters taken from refs. 20 and 27.

Parameter	$C_{18}$	Water
$\pi$	0.01	1.09
$\beta$	0.00	0.18
$\alpha$	0.00	1.17
$\delta$ (cal/ml) <sup>1/2</sup>	8.00	23.4

TABLE II

VALUES OF SOLVATOCHROMIC PARAMETERS AND COMPARISON OF THE EXPERIMENTAL LOG  $k'_w$  VALUES WITH CALCULATED VALUES FOR VARIOUS AROMATICSColumn, LiChrosorb RP-C<sub>18</sub>; eluent, methanol-water. Log  $k'_w$  values taken from ref. 13 and solvatochromic parameters from ref. 27.

Compound	$V_2/100$	$\pi_2$	$\beta_2$	$\alpha_2$	Log $k'_w$ (exp.)	Log $k'_w$ (calc.) <sup>a</sup>	$\Delta$
Benzene	0.491	0.59	0.10	0	2.11	2.25	0.14
Toluene	0.592	0.55	0.11	0	2.74	2.82	0.08
1,2-Dimethylbenzene	0.668	0.51	0.12	0	3.19	3.23	0.04
1,3-Dimethylbenzene	0.668	0.51	0.12	0	3.30	3.23	-0.07
1,4-Dimethylbenzene	0.668	0.51	0.12	0	3.29	3.23	-0.06
1,3,5-Trimethylbenzene	0.769	0.47	0.13	0	3.90	3.79	-0.11
1,2,3,4-Tetramethylbenzene	0.867	0.43	0.15	0	4.20	4.30	0.10
1,2,3,5-Tetramethylbenzene	0.867	0.43	0.15	0	4.26	4.30	0.04
Pentamethylbenzene	0.965	0.39	0.17	0	4.70	4.81	0.11
Hexamethylbenzene	1.063	0.35	0.19	0	5.30	5.31	0.01
Ethylbenzene	0.668	0.53	0.12	0	3.27	3.22	-0.05
<i>n</i> -Propylbenzene	0.769	0.51	0.12	0	3.97	3.81	-0.16
<i>n</i> -Butylbenzene	0.867	0.49	0.12	0	4.57	4.37	-0.20
Naphthalene	0.753	0.70	0.15	0	3.48	3.51	0.03
Fluorene	0.960	1.18	0.22	0	4.26	4.20	-0.06
Phenanthrene	1.015	0.80	0.20	0	4.54	4.78	0.24
Anthracene	1.015	0.80	0.20	0	4.73	4.78	0.05
Pyrene	1.156	0.90	0.25	0	5.10	5.35	0.25
Biphenyl	0.92	1.18	0.20	0	4.17	4.05	-0.12
Bibenzyl	1.116	1.10	0.22	0	4.92	5.13	0.21
Fluorobenzene	0.520	0.62	0.07	0	2.28	2.51	0.23
Chlorobenzene	0.581	0.71	0.07	0	2.80	2.81	0.01
Bromobenzene	0.624	0.79	0.06	0	2.90	3.05	0.15
1,2-Dichlorobenzene	0.671	0.80	0.03	0	3.36	3.41	0.05
1,3-Dichlorobenzene	0.671	0.75	0.03	0	3.49	3.44	-0.05
1,4-Dichlorobenzene	0.671	0.70	0.03	0	3.43	3.47	0.04
1,2,3-Trichlorobenzene	0.761	0.85	0	0	3.95	4.01	0.06
1,2,4-Trichlorobenzene	0.761	0.75	0	0	4.03	4.06	0.03
1,3,5-Trichlorobenzene	0.761	0.70	0	0	4.26	4.09	-0.17
1,2,3,4-Tetrachlorobenzene	0.851	0.80	0	0	4.53	4.55	0.02
1,2,3,5-Tetrachlorobenzene	0.851	0.80	0	0	4.66	4.55	-0.11
1,2,4,5-Tetrachlorobenzene	0.851	0.70	0	0	4.65	4.60	-0.05
Pentachlorobenzene	0.941	0.75	0	0	5.25	5.08	-0.17
Hexachlorobenzene	1.031	0.70	0	0	5.90	5.62	-0.28
2-Chloroaniline	0.652	0.83	0.40	0.25	1.89	1.81	-0.08
3-Chloroaniline	0.652	0.78	0.40	0.31	1.90	1.91	0.01
4-Chloroaniline	0.653	0.73	0.40	0.31	1.92	1.94	0.02
3-Chlorophenol	0.626	0.77	0.23	0.69	2.29	2.23	-0.06
4-Chlorophenol	0.626	0.72	0.23	0.67	2.27	2.26	-0.01
Aniline	0.562	0.73	0.50	0.26	1.05	1.09	0.04
Phenol	0.536	0.72	0.33	0.61	1.27	1.42	0.15
Benzyl alcohol	0.634	0.99	0.52	0.39	1.39	1.25	-0.14
Benzaldehyde	0.606	0.92	0.44	0	1.74	1.55	-0.19
Benzonitrile	0.590	0.90	0.37	0	1.83	1.72	-0.11
Nitrobenzene	0.631	1.01	0.30	0	1.91	2.14	0.23
Acetophenone	0.690	0.90	0.49	0.04	2.02	1.85	-0.17
Anisole	0.639	0.73	0.32	0	2.23	2.26	0.03
Methyl benzoate	0.736	0.75	0.39	0	2.44	2.55	0.11
N,N-Dimethylaniline	0.752	0.90	0.43	0	2.57	2.43	-0.14

<sup>a</sup> Log  $k'_w = (0.113 \pm 0.12) + (5.69 \pm 0.13)V_2/100 - (0.51 \pm 0.11)\pi_2 - (3.50 \pm 0.15)\beta_2 - (0.37 \pm 0.12)\alpha_2$ ;  $n = 49$ ;  $R = 0.995$ ; S.D. = 0.133.

The log  $k'_w$  values reported by Hammers *et al.* [13] for 49 solutes whose solvatochromic parameters are known are given in Table II together with values of  $V_2/100$ ,  $\pi_2$ ,  $\beta_2$  and  $\alpha_2$ .

The correlation of log  $k'_w$  index and the solvatochromic parameters for 49 solutes in methanol–water mixtures was also established; the correlation according to eqn. 5 is as follows:

$$\log k'_w = (0.113 \pm 0.12) + (5.69 \pm 0.13) V_2/100 - (0.51 \pm 0.11)\pi_2 - (3.50 \pm 0.15)\beta_2 - (0.37 \pm 0.12)\alpha_2$$

$$n = 49; R = 0.995; \text{S.D.} = 0.133 \quad (10)$$

In this and all regression equations that follow,  $n$  is the number of data points in the regression,  $R$  is the regression coefficient and S.D. is the standard deviation. It is seen that the goodness of the statistical fit of the data to eqn. 10 is excellent. The calculated log  $k'_w$  values for 49 compounds according to eqn. 10 are listed in Table II. For comparison, we also listed the correlation of the  $S$  index with the solvatochromic parameters for these 49 solutes, as shown in the equation

$$S = (1.09 \pm 0.14) + (4.55 \pm 0.15) V_2/100 - (0.252 \pm 0.13)\pi_2 - (2.50 \pm 0.17)\beta_2 + (0.0948 \pm 0.15)\alpha_2$$

$$n = 49; R = 0.987; \text{S.D.} = 0.156 \quad (11)$$

It can be seen in eqns. 10 and 11 that the chief factors that control log  $k'_w$  and  $S$  are solute size and hydrogen bond basicity, less important factors are the polarizability/dipolarity and hydrogen bond acidity of the solute and the contributions of  $\alpha$  to log  $k'_w$  and  $S$  is not very significant. This reveals that the predominant mechanism of retention in RP-HPLC is the hydrophobic expulsion of the solute from the aqueous mobile phase, and therefore log  $k'_w$  is often referred to as the “hydrophobic index”, indicating the hydrophobicity of the solute, and  $S$  is often referred to as the “hydrophilic index”,  $-S$  revealing the hydrophilicity of the solute. The coefficients  $m$ ,  $d$ ,  $b$  and  $a$  in eqn. 10 have the expected signs. As the value of the solubility parameter for water is greater than for a  $C_{18}$  phase (see Table I), and the dipolarity of water ( $\pi_C = 1.09$ ) is higher than that of  $C_{18}$  ligands ( $\pi_L = 0.01$ ),  $m$  has a positive and  $d$  a negative sign. As  $C_{18}$  ( $\beta_L = 0$ ) is less basic than water ( $\beta_C = 0.18$ ), then  $a$  is negative, whereas as water is a stronger HB acid ( $\alpha_C = 1.17$ ) than  $C_{18}$  ( $\alpha_L = 0.00$ ),  $b$  is negative.

The correlation of log  $k'_w$  and the solvatochromic parameters for 27 solutes was also elucidated (see Table III). The following equations were obtained by least-square regression for log  $k'_w$  and  $S$ :

$$\log k'_w = (0.60 \pm 0.10) + (5.14 \pm 0.11) V_2/100 - (0.95 \pm 0.12)\pi_2 - (3.52 \pm 0.19)\beta_2 - (0.068 \pm 0.09)\alpha_2$$

$$n = 27; R = 0.997; \text{S.D.} = 0.10 \quad (12)$$

$$S = (1.55 \pm 0.11) + (4.13 \pm 0.12) V_2/100 - (0.52 \pm 0.14)\pi_2 - (2.36 \pm 0.21)\beta_2 + (0.25 \pm 0.10)\alpha_2$$

$$n = 27; R = 0.993; \text{S.D.} = 0.12 \quad (13)$$

The calculated log  $k'_w$  values for 27 compounds are also given in Table III.

Table IV shows the results of another example for seventeen compounds in methanol–water mixtures.

Table V gives the experimental log  $k'_w$  values and the calculated values for 32 solutes in acetonitrile–water mixtures based on the relationship between log  $k'_w$  and the solvatochromic parameters. The resulting regression equations for log  $k'_w$  and  $S$  are

$$\log k'_w = (1.12 \pm 0.12) + (3.08 \pm 0.17) V_2/100 - (0.82 \pm 0.09)\pi_2 - (3.02 \pm 0.36)\beta_2 - (1.52 \pm 0.53)\alpha_2$$

$$n = 32; R = 0.987; \text{S.D.} = 0.13 \quad (14)$$

$$S = (1.88 \pm 0.12) + (1.79 \pm 0.17) V_2/100 - (0.47 \pm 0.07)\pi_2 - (1.55 \pm 0.35)\beta_2 - (2.06 \pm 0.51)\alpha_2$$

$$n = 32; R = 0.975; \text{S.D.} = 0.13 \quad (15)$$

On comparing the pairs of eqns. 10 and 11, 12 and 13, and 14 and 15, it can be seen that the signs of the coefficients in eqns. 10, 12 and 14 are almost the same as those in eqns. 11, 13 and 15, except for the terms whose coefficients are not very significant, which implies that the magnitude of log  $k'_w$  increases with increase in the size of the solute, whereas  $-S$  decreases with increasing solute size; increasing hydrogen bonding interaction results in a large decrease in log  $k'_w$  and a large increase in  $-S$  when other conditions remain the same, which are widely consistent with the practical observations that when other factors are equal, more polar or strong hydrogen bonding interactions will decrease the  $k'$  values, whereas increasing the size of the solute leads to an increase in  $k'$ . Therefore, when two or three solute parameters are equal, there is a general trend that as the solute becomes increasingly hydrophobic, log

TABLE III

VALUES OF SOLVATOCHROMIC PARAMETERS AND COMPARISON OF EXPERIMENTAL  $\log k'_w$  VALUES WITH CALCULATED VALUES FOR VARIOUS COMPOUNDS

Column, Hypersil-ODS; eluent, methanol-water; phosphate buffer was used when applied to ionizable compounds.  $\log k'_w$  values taken from ref. 33 and solvatochromic parameters from ref. 27.

Compound	$V_2/100$	$\pi_2$	$\beta_2$	$\alpha_2$	$\log k'_w$ (exp.)	$\log k'_w$ (calc.) <sup>a</sup>	$\Delta$
4-Nitrophenol	0.676	1.15	0.32	0.82	1.77	1.81	0.04
4-Nitroaniline	0.702	1.25	0.48	0.42	1.30	1.31	0.01
Benzene	0.491	0.59	0.10	0	2.05	2.22	0.17
Toluene	0.592	0.55	0.11	0	2.59	2.74	0.15
Chlorobenzene	0.581	0.71	0.07	0	2.72	2.67	-0.05
Nitrobenzene	0.631	1.01	0.30	0	1.93	1.84	-0.09
Phenol	0.536	0.72	0.33	0.61	1.35	1.48	0.13
Aniline	0.562	0.73	0.50	0.26	0.98	1.03	0.05
Benzoic acid	0.650	0.74	0.40	0.59	1.86	1.80	-0.06
<i>p</i> -Xylene	0.668	0.51	0.12	0	3.18	3.14	-0.04
4-Chlorotoluene	0.679	0.67	0.08	0	3.32	3.18	-0.14
4-Nitrotoluene	0.729	0.97	0.31	0	2.46	2.35	-0.11
<i>p</i> -Cresol	0.634	0.68	0.34	0.58	1.90	1.99	0.09
<i>p</i> -Toluidine	0.660	0.69	0.51	0	1.53	1.55	0.02
<i>p</i> -Toluic acid	0.748	0.70	0.41	0.59	2.40	2.31	-0.09
1,4-Dichlorobenzene	0.671	0.70	0.03	0	3.33	3.29	-0.04
4-Nitrochlorobenzene	0.721	1.01	0.26	0	2.42	2.44	0.02
4-Chlorophenol	0.626	0.72	0.23	0.67	2.22	2.29	0.07
4-Chloroaniline	0.653	0.73	0.40	0.31	1.82	1.84	0.02
4-Chlorobenzoic acid	0.740	0.74	0.36	0.63	2.63	2.40	-0.23
1,3,5-Trimethylbenzene	0.769	0.47	0.13	0	3.75	3.66	-0.09
1,2,4,5-Tetramethylbenzene	0.867	0.43	0.15	0	4.12	4.13	0.01
Naphthalene	0.753	0.70	0.15	0	3.28	3.29	0.01
Phenanthrene	1.015	0.80	0.20	0	4.30	4.36	0.06
Anthracene	1.015	0.80	0.20	0	4.45	4.36	-0.09
Pyrene	1.156	0.90	0.25	0	4.69	4.82	0.13
Perylene	1.415	1.0	0.30	0	5.82	5.88	0.06

<sup>a</sup>  $\log k'_w = (0.603 \pm 0.10) + (5.14 \pm 0.11)V_2/100 - (0.945 + 0.12)\pi_2 - (3.517 \pm 0.19)\beta_2 - (0.068 \pm 0.09)\alpha_2$ ;  $n = 27$ ;  $R = 0.997$ ; S.D. = 0.104.

$k'_w$  and  $S$  will become increasingly positive and, in contrast, as the solute becomes more hydrophilic and more polar,  $\log k'_w$  and  $S$  will decrease.

Hence it can be concluded that for a given RP-HPLC column system, it is possible to obtain a linear relationship between  $S$  and  $\log k'_w$  if two or three structural parameters ( $\pi_2$ ,  $\beta_2$ ,  $\alpha_2$ ) are equal or close and  $V_2$  varies. These compounds are often called structurally related. Homologues and non-polar and structurally related polar compounds belong to solutes of this kind. For non-polar compounds such as polynuclear aromatic hydrocarbons

(PAHs), the solvatochromic parameters  $\pi_2$ ,  $\beta_2$  and  $\alpha_2$  are almost identical, and therefore, from eqn. 5, it can be seen that linear relationships between  $\log k'_w$  and  $S$  and the Van der Waals volume of the solute can be obtained, which results in a linear  $S$ - $\log k'_w$  correlation for PAHs. The dependence of  $S$  on  $\log k'_w$  for PAHs in methanol-water eluent is demonstrated in Fig. 1.

Table VI shows the experimental  $\log k'_w$  values and values calculated from the Van der Waals volume for some PAHs in methanol-water mixtures.

For homologous series, it is strictly observed that

TABLE IV

EXPERIMENTAL  $\log k'_w$  VALUES AND CALCULATED VALUES FOR SEVENTEEN SOLUTES IN METHANOL-WATER MIXTURES

Column, LiChrosorb  $C_{18}$  with a surface coverage of 0.255 mmol/g; eluent, methanol-water (methanol from 10 to 60%, v/v).  $\log k'_w$  values taken from refs. 37 and 38 and solvatochromic parameters from ref. 27.

Compound	$V_2/100$	$\pi_2$	$\beta_2$	$\alpha_2$	$\log k'_w$ (exp.)	$\log k'_w$ (calc.) <sup>a</sup>	$\Delta$
Acetophenone	0.690	0.90	0.49	0.04	1.43	1.55	0.12
<i>p</i> -Cresol	0.634	0.68	0.34	0.58	1.40	1.52	0.12
Benzyl alcohol	0.634	0.99	0.52	0.39	0.95	0.85	-0.10
Phenol	0.536	0.72	0.33	0.61	0.86	0.82	-0.04
Aniline	0.562	0.73	0.50	0.26	0.80	0.64	-0.16
Benzene	0.491	0.59	0.10	0	1.48	1.54	0.06
Toluene	0.592	0.55	0.11	0	2.15	2.25	0.10
Ethylbenzene	0.668	0.53	0.12	0	2.87	2.77	-0.10
<i>n</i> -Propylbenzene	0.769	0.51	0.12	0	3.54	3.50	-0.04
<i>n</i> -Butylbenzene	0.867	0.49	0.12	0	4.20	4.20	0
Pentane	0.553	-0.08	0	0	2.72	2.73	0.01
Hexane	0.648	-0.04	0	0	3.40	3.38	-0.02
Heptane	0.745	-0.02	0	0	4.08	4.05	-0.03
Octane	0.842	0.01	0	0	4.74	4.72	-0.02
1-Butanol	0.499	0.40	0.45	0.33	0.57	0.55	-0.02
1-Pentanol	0.593	0.40	0.45	0.33	1.19	1.21	0.02
1-Hexanol	0.690	0.40	0.45	0.33	1.80	1.90	0.10

<sup>a</sup>  $\log k'_w = (-1.23 \pm 0.16) + (7.07 \pm 0.23)V_2/100 - (0.70 \pm 0.10)\pi_2 - (2.95 \pm 0.20)\beta_2 - (0.44 \pm 0.15)\alpha_2$ ;  $n = 17$ ;  $R = 0.998$ ; S.D. = 0.09.

their solvatochromic parameters  $\pi_2$ ,  $\beta_2$  and  $\alpha_2$  are equal and only  $V_2$  varies, and  $V_2$  can be written as a linear function of the number of methylene groups [8]. Therefore, linear dependences of  $\log k'_w$  on  $n_c$  for homologues are found, which leads to an excellent linear  $S$ - $\log k'_w$  correlation (see Fig. 2).

For homologues, the insertion of a methylene group into a compound gives a constant change in  $\log k'_w$ , as can be seen from Tables VII and VIII. The average contribution of a methylene group to  $\log k'_w$  is almost constant. The average contribution of a methylene group to  $\log k'_w$  for alkylbenzenes is defined by

$$\Delta \log k'_w (\text{CH}_2) = [\log k'_w (n\text{-alkylbenzene}) - \log k'_w (\text{benzene})]/n_c \quad (16)$$

The calculated  $\log k'_w$  values obtained by using the linear relationships between  $\log k'_w$  and  $n_c$  are also given in Tables VII and VIII.

For structurally related polar compounds whose solvatochromic parameters  $\pi_2$ ,  $\beta_2$  and  $\alpha_2$  are almost the same, a linear  $S$ - $\log k'_w$  correlation (LSLC) can be derived and LSLC analysis can be suggested as a measure of the structural similarity of compounds. Fig. 3 illustrates the linear  $S$ - $\log k'_w$  correlations for chloro-substituted benzenes in methanol-water mixtures. For these compounds, the solvatochromic parameters  $\pi_2$ ,  $\beta_2$  and  $\alpha_2$  are almost identical (see Table II). Details of LSLC analysis will be discussed elsewhere.

Table IX gives the coefficients  $m$ ,  $d$ ,  $b$  and  $a$  on four different  $C_{18}$  packings with surface coverages ranging from 0.255 to 0.699 mmol/g. These coefficients are approximately equal on the four columns, showing the characteristic constants of water and the  $C_{18}$  used, whereas the  $SP_0$  values increase with increasing surface coverage of the  $C_{18}$  bonded phases, which resulted in a simplified linear  $\log k'_w$ -

TABLE V

VALUES OF SOLVATOCHROMIC PARAMETERS AND COMPARISON OF THE EXPERIMENTAL  $\log k'_w$  VALUES WITH CALCULATED VALUES FOR VARIOUS AROMATICS

Column, Develosil-ODS; eluent, acetonitrile-water (acetonitrile from 60 to 95%, v/v).  $\log k'_w$  values taken from ref. 34 and solvatochromic parameters from ref. 27.

Compound	$V_2/100$	$\pi_2$	$\beta_2$	$\alpha_2$	$\log k'_w$ (exp.)	$\log k'_w$ (calc.) <sup>a</sup>	$\Delta$
Benzene	0.491	0.59	0.10	0	1.83	1.85	0.02
Naphthalene	0.753	0.70	0.15	0	2.34	2.42	-0.12
Biphenyl	0.92	1.18	0.20	0	2.71	2.39	-0.32
Fluorene	0.960	1.18	0.22	0	2.78	2.45	-0.33
Phenanthrene	1.015	0.80	0.20	0	2.87	2.99	0.12
Anthracene	1.015	0.80	0.20	0	2.76	2.99	0.23
Pyrene	1.156	0.90	0.25	0	2.94	3.19	0.15
Toluene	0.592	0.55	0.11	0	2.13	2.16	0.03
Ethylbenzene	0.668	0.53	0.12	0	2.43	2.38	-0.05
<i>n</i> -Propylbenzene	0.769	0.51	0.12	0	2.77	2.71	-0.06
Isopropylbenzene	0.769	0.51	0.12	0	2.69	2.71	0.02
<i>n</i> -Butylbenzene	0.867	0.49	0.12	0	3.11	3.03	-0.08
Chlorobenzene	0.581	0.71	0.07	0	2.12	2.12	0.00
1,2-Dichlorobenzene	0.671	0.80	0.03	0	2.35	2.44	0.09
1,3-Dichlorobenzene	0.671	0.75	0.03	0	2.48	2.48	0.00
1,4-Dichlorobenzene	0.671	0.70	0.03	0	2.45	2.53	0.08
1,2,4-Trichlorobenzene	0.761	0.75	0	0	2.76	2.85	0.09
1,3,5-Trichlorobenzene	0.761	0.70	0	0	2.93	2.89	-0.04
1,2,3,4-Tetrachlorobenzene	0.851	0.80	0	0	2.98	3.09	0.11
1,2,3,5-Tetrachlorobenzene	0.851	0.80	0	0	3.14	3.09	-0.05
1,2,4,5-Tetrachlorobenzene	0.851	0.70	0	0	3.12	3.17	0.05
Pentachlorobenzene	0.941	0.75	0	0	3.42	3.40	-0.02
Hexachlorobenzene	1.031	0.70	0	0	3.75	3.73	-0.02
Bromobenzene	0.624	0.79	0.06	0	2.18	2.22	0.04
Iodobenzene	0.671	0.81	0.05	0	2.34	2.35	0.01
Butyl alcohol	0.499	0.40	0.45	0.33	0.46	0.47	0.01
Pentyl alcohol	0.593	0.40	0.45	0.33	0.76	0.76	0.00
Hexyl alcohol	0.690	0.40	0.45	0.33	1.07	1.06	-0.01
<i>n</i> -Pentane	0.553	-0.08	0	0	2.81	2.89	0.07
<i>n</i> -Hexane	0.648	-0.04	0	0	3.18	3.15	-0.03
<i>n</i> -Heptane	0.745	-0.02	0	0	3.55	3.43	-0.12
<i>n</i> -Octane	0.842	0.01	0	0	3.91	3.71	-0.20

<sup>a</sup>  $\log k'_w = (1.12 \pm 0.12) + (3.08 \pm 0.17)V_2/100 - (0.82 \pm 0.09)\pi_2 - (3.02 \pm 0.36)\beta_2 - (1.52 \pm 0.53)\alpha_2$ ;  $n = 32$ ;  $R = 0.987$ ; S.D. = 0.13.

TABLE VI

COMPARISON OF EXPERIMENTAL  $\log k'_w$  VALUES [ $\log k'_w$  (exp.)] WITH THOSE CALCULATED [ $\log k'_w$  (calc.)] FROM THE SOLVATOCHROMIC PARAMETERS FOR SOME PAH COMPOUNDS

Column, YWG-C<sub>18</sub>; eluent, methanol-water (methanol from 60 to 90%, v/v). For experimental conditions, see ref. 7.

Compound	$V_2/100$	$\log k'_w$ (exp.)	$\log k'_w$ (calc.) <sup>a</sup>	$\Delta$
Benzene	0.49	2.05	2.06	0.01
Naphthalene	0.75	3.03	3.06	0.03
Biphenyl	0.92	3.70	3.72	0.02
Phenanthrene	1.01	4.04	4.07	0.03
Anthracene	1.01	4.17	4.07	-0.10
Chrysene	1.25	5.06	4.99	-0.07
<i>p</i> -Terphenyl	1.38	5.40	5.49	0.09

<sup>a</sup>  $\log k'_w = (0.17 \pm 0.10) + (3.85 \pm 0.10)V_2/100$ ;  $n = 7$ ;  $R = 0.998$ ; S.D. = 0.03.



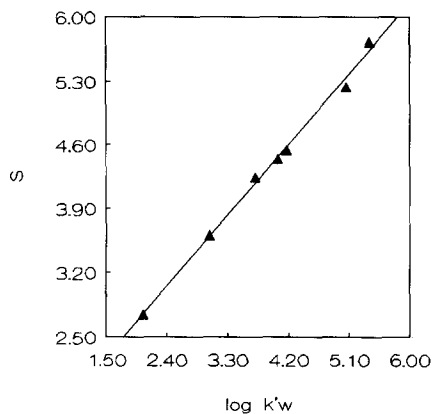


Fig. 1. Linear relationship between  $S$  and  $\log k'_w$  for some PAHs in methanol-water on YWG-C<sub>18</sub>. Conditions as in Table VI.

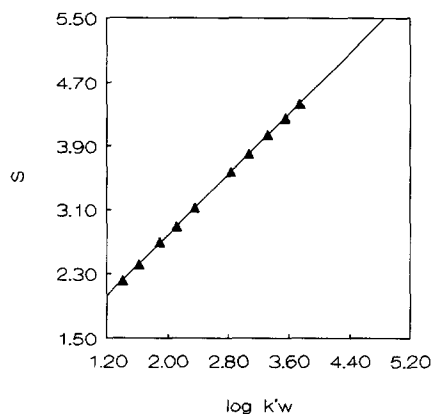


Fig. 2. Linear relationship between  $S$  and  $\log k'_w$  for alkylbenzenes in acetonitrile-water mixtures. Conditions as in Table VIII.

TABLE VII

EXPERIMENTAL  $\log k'_w$  VALUES [ $\log k'_w$  (exp.)],  $\Delta \log k'_w(\text{CH}_2)$  AND CALCULATED VALUES [ $\log k'_w$  (calc.)] FOR  $n$ -ALKYLBENZENES IN METHANOL-WATER SYSTEM

Column, SIL-X-5-C<sub>18</sub>; eluent, methanol-water (methanol from 60 to 95%, v/v).  $\log k'_w$  values taken from ref. 36.

Compound	$n_c$	$\log k'_w$ (exp.)	$\Delta \log k'_w(\text{CH}_2)$	$\log k'_w$ (calc.) <sup>a</sup>	$\Delta$
Benzene	0	2.39	—	2.39	0
Toluene	1	3.03	0.64	2.98	-0.05
Ethylbenzene	2	3.54	0.58	3.58	0.04
Propylbenzene	3	4.17	0.59	4.17	0
Butylbenzene	4	4.76	0.59	4.77	0.01
Hexylbenzene	6	5.95	0.59	5.96	0.01
Octylbenzene	8	7.15	0.60	7.15	0
Decylbenzene	10	8.36	0.60	8.34	-0.02

<sup>a</sup>  $\log k'_w = (2.39 \pm 0.02) + (0.60 \pm 0.003)n_c$ ;  $n = 8$ ;  $R = 0.9999$ ; S.D. = 0.004.

TABLE VIII

EXPERIMENTAL  $\log k'_w$  VALUES [ $\log k'_w$  (exp.)],  $\Delta \log k'_w(\text{CH}_2)$  AND CALCULATED VALUES [ $\log k'_w$  (calc.)] FOR  $n$ -ALKYLBENZENES IN ACETONITRILE-WATER SYSTEM

Column, YMC-phenyl; eluent, acetonitrile-water (acetonitrile from 50 to 80%, v/v).  $\log k'_w$  values recalculated from ref. 35.

Compound	$n_c$	$\log k'_w$ (exp.)	$\Delta \log k'_w(\text{CH}_2)$	$\log k'_w$ (calc.) <sup>a</sup>	$\Delta$
Benzene	0	1.41	—	1.41	0.00
Toluene	1	1.62	0.21	1.64	0.02
Ethylbenzene	2	1.89	0.24	1.88	-0.01
Propylbenzene	3	2.11	0.23	2.12	0.01
Butylbenzene	4	2.36	0.24	2.35	-0.01
Hexylbenzene	6	2.83	0.24	2.83	0.00
Heptylbenzene	7	3.07	0.24	3.06	-0.01
Octylbenzene	8	3.32	0.24	3.30	-0.02
Nonylbenzene	9	3.55	0.24	3.54	-0.01
Decylbenzene	10	3.74	0.23	3.77	0.03

<sup>a</sup>  $\log k'_w = (1.41 \pm 0.01) + (0.237 \pm 0.002)n_c$ ;  $n = 10$ ;  $R = 0.9999$ ; S.D. = 0.003.

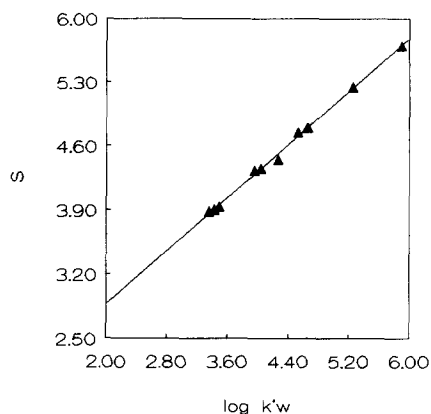


Fig. 3. Linear relationship between  $S$  and  $\log k'_w$  for chlorosubstituted benzenes in methanol-water mixtures. Conditions as in Table II.

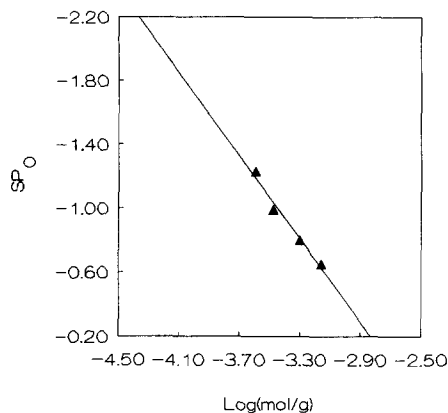


Fig. 4. Linear relationship between  $SP_0$  and the logarithm of the surface coverage of  $C_{18}$  packings. For details, see Table IX.

$\log k'_w$  relationship for column pairs in RP-HPLC. As the phase ratio can be written as the ratio of the volume of the bonded ligands to that of the mobile phase [37,38], a linear relationship between  $SP_0$  and the logarithm of the surface coverage can be obtained (see Fig. 4).

In conclusion,  $\log k'_w$  in the retention equation  $\log k' = \log k'_w - S\phi$  in RP-HPLC can be calculated by using the solvatochromic parameters. The coefficients in the correlation of  $\log k'_w$  with the sol-

vatochromic parameters of the solutes are determined mainly by the properties of water and the quasi-liquid-like chemical bonded phases.

When two or three of the solute parameters are constant and  $V_2$  varies, a linear relationship between  $S$  and  $\log k'_w$  was obtained. The parameter  $SP_0$  in the correlation equation referring to the various reversed-phase columns with different carbon loadings was linearly correlated with the logarithm of the surface coverage.

TABLE IX

COEFFICIENTS OF  $SP_0$ ,  $m$ ,  $d$ ,  $b$  AND  $a$  ON DIFFERENT COLUMNS PACKED WITH VARIOUS  $C_{18}$  PACKING MATERIALS WITH SURFACE COVERAGES RANGING FROM 0.255 TO 0.690 mmol/g

$\log k'_w$  values for regression taken from refs. 37 and 38. The compounds used for the regression were acetophenone, *p*-cresol, benzyl alcohol, phenol, aniline, benzene, toluene, ethylbenzene, *n*-propylbenzene, *n*-butylbenzene, pentane, hexane, heptane, octane, 1-butanol, 1-pentanol and 1-hexanol.

$C_{18}$ coverage (mmol/g)	$SP_0$	$m$	$d$	$b$	$a$	$R$	$n$
0.255	-1.23 $\pm 0.16$	7.07 $\pm 0.23$	-0.70 $\pm 0.10$	-2.95 $\pm 0.20$	-0.44 $\pm 0.15$	0.998	17
0.335	-0.99 $\pm 0.16$	6.97 $\pm 0.23$	-0.74 $\pm 0.10$	-2.92 $\pm 0.20$	-0.51 $\pm 0.15$	0.998	17
0.499	-0.80 $\pm 0.16$	6.93 $\pm 0.22$	-0.64 $\pm 0.10$	-2.96 $\pm 0.20$	-0.53 $\pm 0.15$	0.998	17
0.690	-0.65 $\pm 0.16$	6.95 $\pm 0.23$	-0.63 $\pm 0.10$	-2.94 $\pm 0.20$	-0.54 $\pm 0.15$	0.998	17

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