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Quantitative correlation of the parameters log k'_w and $-S$ in the retention equation in reversed-phase high-performance liquid chromatographic and solvatochromic parameters

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ABSTRACT

Multi-variable regression analysis between log k'_w and $-S$ in the retention equation log $k' = $ log $k'_w - S\varphi$ and solvatochromic parameters was carried out with three kinds of mobile phase and the statistical significance strongly supported the following equations:

$$\log k'_w = p_1 + p_2 (V_w/100) + p_3\pi^* + p_4\beta_m + p_5\alpha_m$$
$$-S = q_1 + q_2 (V_w/100) + q_3\pi^* + q_4\beta_m + q_5\alpha_m$$

These equations indicate that the forces involved in the separation mechanism in reversed-phase liquid chromatography have a mutual nature.

INTRODUCTION

In high-performance liquid chromatography (HPLC), quantitative correlations between molecular structure parameters and retention values are important because they can (i) predict chromatographic retention behaviour, (ii) measure physico-chemical parameters and (iii) lead to an understanding of the retention mechanism. Various methods have been used to correlate quantitatively the logarithm of the capacity factor with the molecular structure parameters such as the molecular connectivity index [1,2], hydrophobic parameter [3,4], Van der Waals volume [5] and solvatochromic parameters [6] in reversed-phase (RP) HPLC. It is unfortunate that almost all of these investigations were carried out with isocratic elution, as it is very difficult to extrapolate the results to a wide range of mobile phase compositions.

We consider that it is better to correlate quantitatively the parameters log k'_w and $-S$ in the retention equation log $k' = $ log $k'_w - S\varphi$ in reversed-phase high-performance liquid chromatography with the molecular structure parameters of the solutes, which make it possible to predict the retention values for a fairly wide range of mobile phase compositions and to recommend separation modes in HPLC [7]. In this paper, we consider the quantitative correlation of log k'_w and $-S$ in the retention equation with solvatochromic parameters.

DERIVATION OF THE RELATIONSHIP

According to the solubility parameter concept [8], the relationship between solute retention and the composition of the mobile phase composition can be described by

$$\log k' = \log k'_w + A\varphi^2 - S\varphi \tag{1}$$

where $\log k'_w$ is the capacity factor obtained by extrapolation of retention data from binary eluents to 100% water, A and S are constants for a given solute–eluent combination and φ is the volume fraction of the organic modifier in the aqueous eluent. Snyder et al. [9] showed that over a volume fraction range of at most 0.1–0.9, eqn. 1 can be simplified as a good approximation as follows:

$$\log k' = \log k'_w - S\varphi \tag{2}$$

If the linearity prediced by eqn. 2 is actually observed for the series of solutes analysed with a given stationary phase, then one may assume that the constants $\log k'_w$ and $-S$ are functions of the solute molecular structure. Assuming linear free-energy relationships, the molecular properties of the solutes can be expressed as a linear combination of individual structure parameters. According to Park et al. [6], the linear free-energy relatonship of the solute can be expressed as

$$X = X_0 + mV_w/100 + s\pi^* + b\beta_m + a\alpha_m \tag{3}$$

where $mV_w/100$ is the cavity term, which measures the endoergic process of separating the solvent molecules to provide a suitably sized enclosure for the solute, $s\pi^*$ measures the exoergic effects of the solute–solvent dipole–dipole and dipole–induced dipole dielectric interactions, $b\beta_m$ and $a\alpha_m$ measure the exoergic effects of hydrogen bonding involving the solvent as an hydrogen bond donor (HBD) acid and solute as an hydrogen bond acceptor (HBA) base and the solvent as an HBA base and solute as an HBD acid, respectively. V_w can be estimated by simple additivity methods such as those of Bondi [10] or Abraham and McGowan [11], π^*, β_m and α_m are solvatochromic parameters that can be found in a paper by Kamlet et al. [12] or measured by UV–Visible, IR or NMR methods [13].

Thus, the constants $\log k'_w$ and $-S$ determined for a particular solute would be given by

$$\begin{aligned} \log k'_w &= p_1 + p_2V_w/100 + p_3\pi^* + p_4\beta_m + p_5\alpha_m \\ -S &= q_1 + q_2V_w/100 + q_3\pi^* + q_4\beta_m + q_5\alpha_m \end{aligned} \tag{4}$$

where p_i and q_i ($i = 1$–5) are regression coefficients, derived using conventional least-squares methods. Eqn. 4 shows that $\log k'_w$ and $-S$ in the retention equation can be quantitatively correlated with the solvatochromic parameters. On the other hand, if the cavity process is the unique factor in the separation mechanism in RP-HPLC, then eqn. 4 can be expressed as

$$\log k'_w = f_1 + f_2 V_w/100$$
$$-S = g_1 + g_2 V_w/100 \tag{5}$$

In this paper we intend to confirm the validity of eqn. 4 for RP-HPLC and to demonstrate that cavity process, dipole moment and hydrogen bonding interactions can be used in interpreting the separation mechanism by comparing the regression results of eqn. 4 with those of eqn. 5.

EXPERIMENTAL

The experimental results utilized in this work were taken from a paper by Schoenmakers et al. [14], which gives an exact description of the analytical conditions employed. In this paper we utilize the capacity factors for thirteen compounds measured in a chromatographic system with Nucleosil 10-RP 18 as stationary phase in a 30 cm × 4.6 mm I.D. and three kinds of binary mobile phases mixed from individually measured volumes of methanol, acetonitrile, tetrahydrofuran and water.

The $\log k'_w$ and $-S$ values for the thirteen solutes in the above chromatographic systems were calculated and taken from a paper by Braumann et al. [15].

PRACTICAL VERIFICATION OF THE RELATIONSHIPS

For compounds with single HBA sites that are not capable of self-association, ethe values of $V_w/100$ and the solvatochromic parameters used here were taken from a paper by Park et al. [6] and are given in Table I. Table II gives the experimental data for $\log k'_w$ and $-S$ for thirteen substituted aromatic compounds in RP-HPLC with methanol–water as the mobile phase, together with the regression analysis data of $\log k'_w$ and $-S$ according to eqn. 4.

Tables III and IV give the experimental data and regression analysis data for log

TABLE I

SOLVATOCHROMIC PARAMETERS USED IN CORRELATIONS [6]

Solute	$V_w/100$	π^*	β_m	α_m
Aniline	0.562	0.73	0.50	0.16
Acetophenone	0.69	0.90	0.49	0.006
Anisole	0.63	0.73	0.32	0
Benzaldehyde	0.606	0.92	0.44	0
Benzene	0.491	0.59	0.10	0
Benzonitrile	0.59	0.90	0.37	0
Diethyl phthalate	1.153	0.84	0.82	0
Ethylbenzene	0.687	0.53	0.12	0
Methyl benzoate	0.736	0.76	0.39	0
Nitrobenzene	0.631	1.01	0.30	0
p-Nitrophenol	0.676	1.15	0.32	0.93
Phenol	0.536	0.72	0.33	0.61
n-Propylbenzene	0.785	0.51	0.12	0

TABLE II

COMPARISON OF EXPERIMENTAL DATA FOR LOG k'_w AND $-S$ WITH VALUES CALCULATED FROM A CORRELATION EQUATION, WITH METHANOL–WATER AS MOBILE PHASE

The experimental data are from ref. 15.

Solute	Log k'_w			$-S$		
	Exp.	Calc.	Difference	Exp.	Calc.	Difference
Aniline	1.21	1.13	−0.08	−2.73	−2.63	0.10
Acetophenone	1.92	1.80	−0.12	−2.06	−2.09	−0.03
Anisole	2.15	2.13	−0.02	−2.66	−2.81	−0.15
Benzaldehyde	1.80	1.55	−0.25	−2.65	−2.41	0.24
Benzene	2.16	2.23	0.07	−2.63	−2.77	−0.14
Benzonitrile	1.77	1.72	−0.05	−2.63	−2.51	0.12
Diethyl phthalate	2.90	2.98	0.08	−3.70	−3.75	−0.05
Ethylbenzene	3.18	3.16	−0.02	−3.52	−3.53	−0.01
Methyl benzoate	2.28	2.41	0.13	−2.87	−3.07	−0.20
Nitrobenzene	2.03	2.17	0.14	−2.70	−2.82	−0.12
p-Nitrophenol	1.17	1.17	0	−2.79	−2.81	−0.02
Phenol	1.34	1.61	0.27	−2.35	−2.31	0.04
n-Propylbenzene	3.82	3.66	−0.16	−4.15	−3.93	0.22

k'_w and $-S$ for twelve and ten substituted aromatic compounds with acetonitrile–water and tetrahydrofuran–water as mobile phase, respectively.

Table V gives the coefficients p_i and q_i ($i = 1$–5) in eqn. 4 when three kinds of mobile phase were used. It can be seen that the regression coefficients in all instances

TABLE III

COMPARISON OF EXPERIMENTAL DATA FOR LOG k'_w AND $-S$ WITH VALUES CALCULATED FROM A CORRELATION EQUATION, WITH ACETONITRILE–WATER AS MOBILE PHASE

The experimental data are from ref. 15.

Solute	Log k'_w			$-S$		
	Exp.	Calc.	Difference	Exp.	Calc.	Difference
Acetophenone	1.42	1.50	0.08	−2.28	−2.40	−0.12
Anisole	1.86	1.76	−0.10	−2.62	−2.55	0.07
Benzaldehyde	1.36	1.34	−0.02	−2.22	−2.24	−0.02
Benzene	1.86	1.88	0.02	−2.57	−2.56	0.01
Benzonitrile	1.54	1.48	−0.06	−2.44	−2.34	0.10
Diethyl phthalate	2.30	2.26	−0.04	−3.22	−3.15	0.07
Ethylbenzene	2.64	2.54	−0.10	−3.37	−3.14	0.23
Methyl benzoate	1.82	1.95	0.13	−2.61	−2.74	−0.13
Nitrobenzene	1.80	1.82	0.02	−2.66	−2.66	0
p-Nitrophenol	1.49	1.47	−0.02	−2.81	−2.79	0.02
Phenol	1.06	1.09	0.03	−2.19	−2.22	−0.03
n-Propylbenzene	2.83	2.90	0.07	−3.27	−3.46	−0.19

TABLE IV

COMPARISON OF EXPERIMENTAL DATA FOR LOG k'_w AND $-S$ WITH VALUES CALCULATED FROM A CORRELATION EQUATION, WITH TETRAHYDROFURAN–WATER AS MOBILE PHASE

The experimental data are from ref. 15.

Solute	Log k'_w			$-S$		
	Exp.	Calc.	Difference	Exp.	Calc.	Difference
Aniline	1.21	1.40	0.19	−2.71	−2.86	−0.15
Acetophenone	1.27	1.14	−0.13	−2.26	−2.30	−0.04
Anisole	1.81	1.70	−0.11	−3.21	−3.01	0.20
Benzaldehyde	1.20	1.31	0.11	−2.62	−2.72	−0.10
Benzene	1.85	1.90	0.05	−3.08	−3.06	0.02
Benzonitrile	1.45	1.44	−0.01	−3.01	−2.87	0.14
Diethyl phthalate	1.80	1.78	−0.02	−3.52	−3.48	0.04
Ethylbenzene	2.33	2.35	0.02	−3.57	−3.68	−0.11
Nitrobenzene	1.80	1.67	−0.13	−3.36	−3.37	−0.01
Phenol	1.50	1.53	0.03	−3.19	−3.18	0.01

were higher than 0.95, and some even higher than 0.98 and 0.99, which strongly supports the relationships shown in eqn. 4.

The regression analysis data according to eqn. 5 are given in Table VI, and the correlation coefficients in all instances are much lower than those in Table V. Hence it can be concluded that forces involved in the separation mechanism in RP-HPLC have a mutual nature, but the cavity process may play the most important role.

For the quantitative correlation between log k'_w and solvatochromic parameters or the Van der Waals volume of a solute, the intercept values p_1 for different mobile phases increase in the order methanol–water < acetonitrile–water < tetrahydrofuran–water, which is the same as that reported by Carr et al. [6] when log k' was

TABLE V

PARAMETERS IN EQNS. 4 AND REGRESSION COEFFICIENTS (R) WHEN DIFFERENT KINDS OF MOBILE PHASE ARE USED

Mobile phases: 1 = methanol–water; 2 = acetonitrile–water; 3 = tetrahydrofuran–water.

Mobile phase	p_1	p_2	p_3	p_4	p_5	R
1	0.161	4.829	−0.1192	−0.5440	−3.417	0.983
2	0.3552	3.664	0.0115	−0.4987	−2.841	0.991
3	1.1036	2.428	−0.2731	0.1398	−2.307	0.953
	q_1	q_2	q_3	q_4	q_5	R
1	−1.029	−4.089	0.0859	0.1424	2.324	0.971
2	−1.0596	−3.257	−0.2228	0.0026	2.263	0.962
3	−0.8729	−3.858	−1.0555	−0.9422	3.325	0.962

TABLE VI

PARAMETERS IN EQNS. 5 AND CORRELATION COEFFICIENT (R) WHEN DIFFERENT KINDS OF MOBILE PHASE ARE USED

Mobile phases: 1 = methanol–water; 2 = acetonitrile–water; 3 = tetrahydrofuran–water.

Mobile phase	f_1	f_2	R
1	0.4040	2.5622	0.5434
2	0.7473	1.5847	0.5065
3	1.3286	0.4462	0.2290
	g_1	g_2	R
1	-1.3965	-2.1983	0.6331
2	-1.6726	-1.4845	0.6150
3	-2.5289	-0.7970	0.3540

correlated with solvatochromatic parameters at constant compositions the methanol–water and acetonitrile–water. According to its definition, k'_w is the capacity factor with pure water as the mobile phase and should have the same value when different organic modifiers are used, but in fact different log k'_w values are obtained on extrapolation. A possible explanation may lie in the sorption of organic modifiers in the stationary phase, and extrapolated log k'_w values contain contributions from cavity process and the sorbed organic modifier. The parameter p_2 (or f_2) has a positive sign, which means that the larger the size of the solute molecule the larger is the log k'_w value. We consider that this effect is caused mainly by the cavity process of water. The p_2 values decrease in the order methanol–water > acetonitrile–water > tetrahydrofuran–water, which is the same as their order of Hildebrand solubility parameters [16]. No clearly explicable pattern is seen for the coefficients p_3, p_4 and p_5, which may be caused by the different chemical properties of the stationary phase with sorption of different amounts of the organic modifiers.

For the quantitative correlation between $-S$ and solvatochromic parameters, the coefficients q_1–q_5 cannot be explained clearly, which may be due to the nature of the molecular interactions of the three different organic solvents. Methanol exhibits both hydrogen donor and acceptor abilities and will therefore easily be incorporated into the network of water molecules, whereas acetonitrile and tetrahydrofuran can serve only as hydrogen acceptors and will change the structure of mobile phase more drastically. Hence the solvatochromic parameters for three organic modifiers may be strongly influenced by the surroundings, which will exhibit different interaction behaviours between the solute and mobile phase. On the other hand, the sign of q_1 and q_2 (or g_1 and g_2) is opposite to that of p_1 and p_2 (or f_1 and f_2), which means that the larger the size of a solute molecule, the smaller is the $-S$ value. This effect may be caused mainly by the solute–mobile phase interactions. In order to understand further the retention mechanism in RP-HPLC, more investigations of the influence of the chemical nature of organic solvents on retention are necessary.

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