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Chromatographic quantification of hydrophobicity using micellar mobile phases

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Abstract

In micellar liquid chromatography (MLC), the hydrophobicity of a compound is the predominant effect on its retention and interaction with micelles; however, some contradictory results have been obtained concerning whether k or $\log k$ best correlates with the logarithm of partition coefficients ($\log P$) in the biphasic solvent system octanol–water. An empirical model which describes the relationship between retention in MLC and $\log P$ is presented. The retention data for series of neutral compounds eluted with different pure and mixed mobile phases and alkyl-bonded stationary phases were used to test the model. The results indicate that non-linear relationships between k or $\log k$ and $\log P$ are to be expected and only in particular circumstances can linear relationships be obtained. In contrast, in all the series studied, excellent correlations between the logarithm of the retention factor at zero micellar concentration, k_m , and $\log P$, were found (r^2 in the range 0.965–0.987 and F in the range 277–608). $\log k_m$ is proposed as the best chromatographic index for the quantification of the hydrophobicity of solutes using micellar mobile phases.

1. Introduction

The biological activity of many organic compounds has been attributed to the hydrophobic character of molecules. The quantification of the hydrophobicity of solutes is of great importance in quantitative structure–activity relationship (QSAR) studies, drug design and toxicology [1–3]. The hydrophobicity of drugs is most commonly characterized by their logarithm of the partition coefficients ($\log P$) in the biphasic solvent system octanol–water [4, 5]. The conventional “shake-flask” method to measure $\log P$ has several inconveniences. Many attempts have been made to establish a correlation between

$\log P$ and several reversed-phase liquid chromatographic (RPLC) retention data, assuming that the extent of chromatographic retention reflects the hydrophobicity of a solute. This approach is known as quantitative structure–retention relationships (QSRRs) [6].

The correlations between the chromatographic parameters of the compounds and their $\log P$ values are often expressed in logarithmic form. First, the $\log k$ values obtained for a given column and mobile phase composition were used [7,8]. However, the accuracy of predictions depends on the mobile phase composition. Next, the retention factor in a pure aqueous eluent (k_w), in which the only operative solvophobic effect is the hydrophobic effect, was used. However, k_w is difficult to obtain experimentally for

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most compounds and usually it must be obtained by extrapolation using linear [9], quadratic [10] or solvophobic [11] models. Finally, attempts have been made to find an alternative chromatographic parameter that was less dependent on the particular column and instrument used [12–15]. There are many discrepancies in the literature about whether $\log P$ or $\log k_w$ best predicts hydrophobicity. It has been suggested that $\log k_w$ may be a better descriptor than $\log P$ of the relevant partitioning process [16].

Micellar liquid chromatography (MLC) is a mode of conventional reversed-phase liquid chromatography which uses a surfactant solution (anionic, cationic or non-ionic) above the critical micellization concentration (cmc) as mobile phase. The retention of a compound in MLC depends on the type of interactions with the micelles and the surfactant-modified stationary phase [17].

The usefulness of MLC for the determination of hydrophobicity has been reported by several workers. Thus, linear relationships between $\log k$ values measured with different purely aqueous and mixed micellar mobile phases and $\log P$ have been found for different series of solutes [18–20]. On the other hand, Khaledi and Breyer [21] observed a curvature of $\log k$ vs. $\log P$ plots at higher $\log P$ values and a better linear relationship between k and $\log P$ was found. Recently, Marina and García [22] also reported a curvature of the $\log k$ vs. $\log P$ plots and indicated that the hydrophobicity range of the compounds is an important factor in the k or $\log k$ – $\log P$ correlations. The curvature was explained by the solubility limit theory [23].

In our opinion, reliable quantification of hydrophobicity by MLC still deserves more attention. Retention of a solute in MLC depends not only on the partitioning between water and the surfactant-modified stationary phase, but also between water and the micelle. This behaviour indicates some doubts about the capability of the retention factor to predict the hydrophobicity of solutes. In this paper, an empirical model which describes the dependence between retention in MLC and $\log P$ is proposed. It was found that $\log k_m$ is the best index to perform the chromatographic quantification of

the hydrophobicity of solutes using micellar mobile phases.

2. Experimental

Chromatographic data were collected from the literature. The solute–micelle binding constants (K_{AM}) and retention factors at zero micellar concentration (k_m) for 40 neutral compound–surfactant–stationary phase combinations reported by Foley [24] were used (series I, II, III and IV in this paper). The K_{AM} and k_m values for a set of aromatic compounds eluted with cetyltrimethylammonium bromide (CTAB) and sodium dodecyl sulfate (SDS) in the presence of 3% of propanol reported by Khaledi and Breyer [21] were also used (series V and VI in this paper). In addition, experimental capacity factors of series III and IV at different concentrations of CTAB and Brij 35 as mobile phases were used [18]. When no experimental k values were available (series I, II, V and VI), retention factors were calculated by using Eq. 1.

The $\log P$ values used were obtained from literature: anthracene 4.6, benzylamine 1.49, biphenyl 3.97, 1-bromonaphthalene 4.23, chlorobenzene 2.84, 1-methylnaphthalene 3.93, naphthalene 3.37, pyrene 4.55 and *p*-xylene 3.13 (from Ref. [12]); acetanilide 1.16, acetophenone 1.58, benzaldehyde 1.48, benzene 2.13, benzonitrile 1.56, benzyl alcohol 1.10, bromobenzene 2.99, methyl benzoate 2.12, methyl phenyl ether 2.11, nitrobenzene 1.85 and toluene 2.69 (from Ref. [18]); butyrophenone 2.65, hexaphenone 3.58, propiophenone 2.19 and valero-phenone 3.11 (from Ref. [25]).

Statgraphics 6.1 was used to perform the statistical analysis of the linear regressions between k , $\log k$, k_m , $\log k_m$, K_{AM} and $\log K_{AM}$ and $\log P$ data for each series.

3. Results and discussion

3.1. RPLC vs. MLC parameters

The use of a micellar solution instead of a conventional aqueous–organic mixture as mobile

phase in the quantification of hydrophobicity shows several advantages. First, the retention behaviour of compounds (apolar, polar or ionic) chromatographed with anionic, cationic and non-ionic surfactants has been accurately modelled. Thus, the retention of a non ionizable compound as a function of micellar concentrations can be deduced from

$$\frac{1}{k} = \frac{1}{k_m} + \frac{K_{AM}}{k_m} \cdot [M] \quad (1)$$

where k is the retention factor, $[M]$ is the total concentration of surfactant in the mobile phase minus the cmc, K_{AM} is the solute–micelle binding constant and k_m is the retention factor at zero micellar concentration, that is, the retention factor at a surfactant monomer concentration equal to the cmc. This parameter is very similar to k_w obtained in conventional RPLC. As k_w and k_m are independent of the composition of the mobile phase, they reflect polar-non-polar partitioning and are dependent on the solute's structure and polar functionalities; however, they are dependent on the type/manufacturer of the stationary phase. K_{AM} also has this feature with the advantage that is independent of the stationary phase.

According Eq. 1, the values of k_m and K_{AM} can be obtained from the intercept and slope, respectively, of the plot of $1/k$ vs. $[M]$. In contrast, the extrapolated k_w values obtained by using linear plots are significantly different for different organic modifiers and quadratic or ET-30 solvatochromic extrapolations should be performed [16].

Second, the presence of micelles in equilibrium with ionic surfactant monomers in the mobile phase produces silanophilic adsorption of surfactant monomers on the alkyl-bonded stationary phase, the stationary phase becoming more hydrophobic and reducing the concentration of residual silanol groups on the silica surface. In conventional RPLC, the residual activity of alkyl-bonded stationary phases can influence the retention of certain solutes, giving inadequate prediction of the hydrophobicity of those compounds.

Third, the stationary phase environment in MLC is independent of the micelle concentration

in the mobile phase (for most surfactants and stationary phases) and is similar to that of a purely aqueous eluent system. The use of aqueous–organic mobile phases alters the structure and composition of the stationary phase, but the use of a micellar eluent avoids this problem, conferring on the retention factors obtained in MLC a better predictive capability for the quantification of hydrophobicity than in RPLC.

There is also a limitation to the use of MLC for the quantification of hydrophobicity. When ionic surfactants are used as mobile phases, hydrophobic adsorption of monomers could occur, giving the stationary phase some ion-exchange capacity with charged solutes [17]. In some of these cases an adequate selection of the nature of surfactant and pH of the mobile phase could eliminate the electrostatic interactions.

3.2. MLC retention–log P relationships

In MLC, some contradictory results have been obtained concerning which k or $\log k$ best correlates with $\log P$. MLC is an example of the use of secondary chemical equilibria in liquid chromatography, where the retention is influenced by two competing equilibria of solute interactions with micelles in the mobile phase (controlled by K_{AM}) and their partitioning into the stationary phase (controlled by k_m). Both partitioning processes depend on the hydrophobicity, among the size and shape of the solute. As consequence, linear relationships between k_m and K_{AM} can be expected. Several workers have shown correlations between K_{AM} and $\log P$ [21, 26–28] and a correlation between k_m and $\log P$ for a set of sixteen aromatic compounds was also shown [21].

Let suppose that k_m and K_{AM} are correlated with the hydrophobicity of the solute:

$$\log k_m = A_0 + A_1 \log P \quad (2)$$

$$\log K_{AM} = B_0 + B_1 \log P \quad (3)$$

then Eq. 1 becomes

$$k = \frac{k_m}{1 + K_{AM}[M]} = \frac{10^{A_0 + A_1 \log P}}{1 + [M]10^{B_0 + B_1 \log P}} \quad (4)$$

and in the logarithmic form

$$\log k = A_0 + A_1 \log P - \log(1 + [M]10^{B_0 + B_1 \log P}) \quad (5)$$

As can be observed from Eqs. 4 and 5, a non-linear relationship between the retention of a compound (k or $\log k$) and the $\log P$ value for a constant micellar concentration should be expected. Two extreme situations can be considered. (a) For solutes with low hydrophobicity (low $\log P$ values) or for very low micellar concentrations in the mobile phase, the term $K_{AM}[M]$ could be negligible ($K_{AM}[M] \ll 1$), and Eq. (5) becomes $\log k \approx \log k_m = A_0 + A_1 \log P$, showing a linear relationship between $\log k$ and $\log P$. In contrast, Eq. 4 becomes $k \approx k_m = 10^{A_0 + A_1 \log P}$, showing a non-linear relationship between k and $\log P$. This behaviour has been shown experimentally [22]. (b) For highly hydrophobic solutes (high $\log P$ values) or for high micellar concentrations in the mobile phase, the term $K_{AM}[M]$ could be significantly higher than 1 and Eqs. 4 and 5 become

$$k = \frac{k_m}{K_{AM}[M]} = \frac{10^{A_0 + A_1 \log P}}{[M]10^{B_0 + B_1 \log P}} \quad (6)$$

$$\log k = A_0 - B_0 + (A_1 - B_1) \log P - \log[M] \quad (7)$$

Eq. 6 provides an apparent linear relationship between k and $\log P$. On the other hand, Eq. 7 describes a linear relationship between $\log k$ and $\log P$, but with a lower slope than in the former case. These observations have been reported in the literature [21,22]. On the other hand, Marina

and García [22] indicated that there is a value of $\log P$ on the curve of $\log k$ vs. $\log P$ where a "break" occurs, explaining why the $\log k$ – $\log P$ correlation improves when the most hydrophobic compounds are eliminated on the curve. According to Eq. 5, this "break" should occur when the term $K_{AM}[M] \approx 1$, and then $\log P$ for this point can be calculated as

$$\log P = -(\log[M] + B_0)/B_1 \quad (8)$$

As can be observed from Eq. 8, the linearity range of $\log k$ vs. $\log P$ plots increases when the micellar concentration in the mobile phase decreases.

In order to demonstrate the validity of the equations, some studies were performed using several series of neutral compounds. Tables 1–3 show the retention factors for a set of nine aromatic compounds eluted with a 0.1 M SDS mobile phase (at 25°C) and a C_{18} stationary phase (Table 1, series I); for a group of mono-substituted benzenes eluted with 0.1 M SDS (at 31°C), 0.016, 0.05 and 0.1 M CTAB (at 25°C) and 0.016 and 0.05 M Brij 35 (at 25°C) mobile phases and a C_{18} stationary phase (Table 2, series II, III and IV, respectively) and for a group of aromatic compounds eluted with a 0.12 M CTAB–3% 2-propanol mobile phase (at 25°C) and a C_8 stationary phase and with a 0.12 M SDS–3% 2-propanol mobile phase (at 25°C) and a C_{18} stationary phase (Table 3, series V and VI, respectively). The values of $\log P$, k_m and K_{AM} for each compound are also given.

Table 1

Log P , k_m , K_{AM} and retention factors calculated for a 0.1 M SDS mobile phase at 25°C and a C_{18} (Waters) stationary phase, for a set of aromatic compounds (series I)

Compound	Log P	k_m	K_{AM}	k
Anthracene	4.6	9280	5340	18.9
Benzene	2.13	27.0	25.0	8.2
Biphenyl	3.97	2140	1311	17.6
1-Bromonaphthalene	4.23	7860	4760	18.0
1-Methylnaphthalene	3.93	1870	1168	17.3
Naphthalene	3.37	325	239	14.2
Pyrene	4.55	17200	9070	20.6
Toluene	2.69	68.6	49.8	12.3
<i>p</i> -Xylene	3.13	225	140	16.2

Table 2

Log P , k_m , K_{AM} and retention factors for a set of monosubstituted benzenes obtained with C_{18} stationary phases eluted with SDS at 31°C (series II), CTAB at 25°C (series III) and Brij 35 at 25°C (series IV) mobile phases

Compound	Log P	SDS ^a			CTAB ^b					Brij35 ^c			
		k_m	K_{AM}	k^d	k_m	K_{AM}	k^e	k^f	k^g	k_m	K_{AM}	k^h	k^i
Acetanilide	1.16	12.5	12.8	5.7	–	–	–	–	–	–	–	–	–
Acetophenone	1.58	36.2	13.1	16.4	23.8	26.2	17.6	10.2	6.7	20.1	26.2	14.2	8.7
Benzaldehyde	1.48	17.0	4.7	11.9	23.3	24.4	16.6	10.9	6.7	14.8	18.1	11.5	7.8
Benzene	2.13	38.5	11.4	18.8	51.5	39.6	33.6	17.0	10.5	47.5	41.5	28.7	15.6
Benzonitrile	1.56	23.3	8.7	13.0	22.8	24.4	17.2	10.2	6.8	18.4	23.3	13.4	8.5
Benzyl alcohol	1.10	11.0	4.8	7.7	13.0	16.1	10.7	7.1	5.0	6.2	12.8	5.1	3.8
Benzylamine	1.49	24.4	8.5	13.7	–	–	–	–	–	–	–	–	–
Bromobenzene	2.99	–	–	–	340	228	81.7	26.9	14.4	439	353	67.6	23.8
Butyrophenone	2.65	105	20.8	36.1	–	–	–	–	–	–	–	–	–
Hexaphenone	3.58	305	34.5	73.2	–	–	–	–	–	–	–	–	–
Methyl benzoate	2.12	–	–	–	69.3	62.8	37.0	16.6	9.6	60.6	62.8	30.3	14.6
Methyl phenyl ether	2.11	–	–	–	63.1	54.7	36.2	16.6	9.9	57.8	57.3	30.4	15.1
Nitrobenzene	1.85	26.9	9.1	14.7	42.1	40.5	27.2	13.7	8.4	41.3	48.7	23.2	12.0
Propiophenone	2.19	61.6	16.9	24.2	–	–	–	–	–	–	–	–	–
Toluene	2.69	–	–	–	159	107	65.0	24.7	13.8	165	117	57.8	24.2
Valerophenone	3.11	171	25.0	51.9	–	–	–	–	–	–	–	–	–

^a C_{18} Rainin.

^b C_{18} Hypersil.

^c C_{18} Hypersil.

^d 0.1 M SDS.

^e 0.016 M CTAB.

^f 0.05 M CTAB.

^g 0.1 M CTAB.

^h 0.016 M Brij 35.

ⁱ 0.05 M Brij 35.

Different linear relationships were obtained by applying the least-squares method (LS), between the different MLC parameters, k and $\log k$ for a given mobile phase, k_m and $\log k_m$, K_{AM} and $\log K_{AM}$, and the $\log P$ values for all the groups of compounds reported. Table 4 shows the regression analysis of the data. An estimation of how well the data points fit a straight line is often made by examination of the correlation coefficients (r or r^2); however, this statistic is easily misinterpreted because non-linear data in character may give a relatively high r^2 value. In order to confirm how the regression explains the variability of the data, the residual variance to the variance modelled by regression ratio (F) can be used. Large F values ensure good agreement between data and the linear model. Attending to

these premises, some remarks can be made based on the data in Table 4.

(a) In relation to the linear relationship between k or $\log k$ and $\log P$, better correlations (larger r^2 and F values) from k – $\log P$ than from $\log k$ – $\log P$ data were observed in series I and III–VI. However, for series II, a better correlation between $\log k$ and $\log P$ was obtained. This confirms the contradictory behaviour of these parameters.

(b) In relation to the linear relationship between $\log k_m$ and $\log P$, excellent correlations (r^2 in the range 0.965–0.987 and F in the range 277–608) were found in all cases. These results are better than those found using k or $\log k$. This is important in two senses: first, it confirms the validity of Eq. 2, and second, it suggests the

Table 3

Log P , k_m , K_{AM} and retention factors calculated for a 0.12 M CTAB (series V) and 0.12 M SDS (series VI) surfactant concentration in the presence of 3% 2-propanol at 25°C for a set of aromatic compounds

Compound	Log P	CTAB ^a			SDS ^b		
		k_m	K_{AM}	k	k_m	K_{AM}	k
Acetophenone	1.58	27.6	18.0	9.2	25.1	20.3	7.7
Anthracene	4.45	1428	491	25.7	2500	409	53.9
Benzaldehyde	1.48	22.7	14.9	8.6	21.0	17.0	7.3
Benzene	2.13	51.0	26.0	13.1	61.7	23.6	17.0
Benzonitrile	1.56	43.5	26.3	11.1	19.7	16.2	7.0
Benzyl alcohol	1.10	14.6	11.3	6.5	7.9	9.2	3.9
Butyrophenone	2.65	161	61	20.7	147	63	18.4
Chlorobenzene	2.84	164	74	17.8	227	68	26.5
Naphthalene	3.37	417	180	20.0	909	238	33.2
Nitrobenzene	1.85	44.0	26.1	11.3	34.0	22.2	9.8
Propiophenone	2.19	66.7	31.7	14.8	62.9	36.6	12.4

^a C₈ Altex.

^b C₁₈ Altex.

superior capability of log k_m data than k or log k values to predict hydrophobicity. Also the sensitivity (slope) of log k_m –log P relationships is always larger than for log k –log P data, which is preferable in terms of future predictions of hydrophobicity. Finally, it is clear from Table 4 that the low F values found for k_m –log P data suggest a non-linear relationship between both variables.

(c) In relation to the linear relationship between log K_{AM} and log P , except in series II ($r^2 = 0.733$, $F = 28$), the correlations are good (r^2 in the range 0.948–0.975 and F in the range 146–354), although they are not as good as those corresponding to log k_m . In addition, the slopes of log k_m –log P straight lines are larger than those for log K_{AM} –log P . These results suggest that K_{AM} do not reflect the hydrophobicity of the compound as well as k_m for the series studied.

The empirical confirmation of Eqs. 2 and 3 allows the reliable modelling of the dependence between k or log k with respect to log P and micellar concentration by means of Eqs. 4 and 5. In order to obtain these models for each series, the fitting parameters of Eq. 2, A_0 and A_1 , and of Eq. 3, B_0 and B_1 , taken from Table 4, were used. Figs. 1–3 show the modelled log k vs.

log P (left) and k vs. log P (right) relationships, obtained according to Eqs. 4 and 5, for series I, III and IV at various micellar concentrations (solid lines), together with the log k –log P or k –log P points shown in Tables 1 and 2. In general, good agreement between the predicted and the experimental values was obtained. The same behaviour was observed for series II, V and VI (not shown).

As can be observed in Figs. 1–3 (left), the relationships between log k and log P are not linear (curves b–e), as predicted by Eq. 5. On the other hand, the relationships between log k_m and log P (curve a) are linear (note that for zero micellar concentration k becomes k_m according to Eq. 1 or 4). For solutes with low hydrophobicity and/or low micellar concentration, Eq. 5 predicts a linear relationship between log k and log P , which is demonstrated in Figs. 1–3. On the other hand, a change in the slope is observed for large log P values and/or high micellar concentration, in agreement with Eq. 7. The log P values at which the “break” occurs, obtained using Eq. 8, for the series in Fig. 1 were 2.22 for 0.05 M SDS, 1.94 for 0.1 M SDS and 1.78 for 0.15 M SDS. As can be observed, a decrease in the micellar concentration expands

Table 4

Statistical analysis of the linear regressions between chromatographic parameters and log *P* corresponding to data in Tables 1–3

Series	Stationary phase/ surfactant	Log <i>P</i> range	<i>n</i>	Dependent variable	Intercept ± <i>t</i> ₉₅	Slope ± <i>t</i> ₉₅	<i>s</i>	<i>r</i> ²	<i>F</i>
I	C ₁₈ / 0.1 M SDS	2.13–4.6	9	Log <i>k</i>	0.70 ± 0.18	0.13 ± 0.05	0.05	0.866	45
				<i>k</i>	1 ± 4	4.3 ± 1.2	1.22	0.910	71
				Log <i>k</i> _m	-1.2 ± 0.6	1.16 ± 0.16	0.16	0.978	308
				<i>k</i> _m	(-1.4 ± 1.5) · 10 ⁴	(5 ± 4) · 10 ³	4100	0.578	10
				Log <i>K</i> _{AM}	-1.1 ± 0.7	1.08 ± 0.19	0.16	0.973	250
				<i>K</i> _{AM}	(-7 ± 8) · 10 ³	(3 ± 2) · 10 ³	2300	0.515	7
II	C ₁₈ / 0.1 M SDS ^a	1.10–3.58	12	Log <i>k</i>	0.42 ± 0.13	0.42 ± 0.06	0.08	0.954	227
				<i>k</i>	-23 ± 9	24 ± 5	5.80	0.924	133
				Log <i>k</i> _m	0.47 ± 0.15	0.57 ± 0.07	0.09	0.965	277
				<i>k</i> _m	-120 ± 60	100 ± 30	36.5	0.834	55
				Log <i>K</i> _{AM}	0.5 ± 0.3	0.29 ± 0.12	0.14	0.733	28
				<i>K</i> _{AM}	-7 ± 7	10 ± 3	3.6	0.851	57
III	C ₁₈ / 0.1 M CTAB	1.10–2.99	10	Log <i>k</i>	0.44 ± 0.07	0.25 ± 0.03	0.03	0.974	293
				<i>k</i>	-1.4 ± 1.2	5.4 ± 0.6	0.45	0.982	430
				Log <i>k</i> _m	0.24 ± 0.15	0.74 ± 0.07	0.06	0.984	497
				<i>k</i> _m	-220 ± 240	150 ± 70	53	0.754	25
				Log <i>K</i> _{AM}	0.59 ± 0.09	0.6 ± 0.1	0.07	0.958	182
				<i>K</i> _{AM}	-130 ± 90	100 ± 40	33	0.750	25
IV	C ₁₈ / 0.05 M Brij 35	1.10–2.99	10	Log <i>k</i>	0.3 ± 0.2	0.41 ± 0.10	0.08	0.920	91
				<i>k</i>	-9 ± 3	11.6 ± 1.4	1.03	0.979	372
				Log <i>k</i> _m	-0.19 ± 0.18	0.93 ± 0.09	0.07	0.987	608
				<i>k</i> _m	-300 ± 200	200 ± 100	77	0.694	18
				Log <i>K</i> _{AM}	0.3 ± 0.3	0.72 ± 0.11	0.10	0.948	146
				<i>K</i> _{AM}	-210 ± 160	150 ± 80	62	0.668	16
V	C ₈ / 0.12 M CTAB ^b	1.10–4.45	11	Log <i>k</i>	0.68 ± 0.13	0.19 ± 0.05	0.08	0.853	58
				<i>k</i>	1 ± 3	6.1 ± 1.1	1.68	0.933	139
				Log <i>k</i> _m	0.54 ± 0.13	0.60 ± 0.05	0.08	0.982	500
				<i>k</i> _m	-600 ± 300	350 ± 150	213	0.744	29
				Log <i>K</i> _{AM}	0.48 ± 0.15	0.50 ± 0.06	0.08	0.975	354
				<i>K</i> _{AM}	-210 ± 120	130 ± 50	70	0.791	34
VI	C ₁₈ / 0.12 M SDS ^b	1.10–4.45	11	Log <i>k</i>	0.3 ± 0.2	0.37 ± 0.08	0.12	0.904	95
				<i>k</i>	-16 ± 4	14.8 ± 1.9	2.80	0.968	301
				Log <i>k</i> _m	0.14 ± 0.18	0.77 ± 0.08	0.10	0.983	534
				<i>k</i> _m	-1000 ± 600	600 ± 300	384	0.747	29
				Log <i>K</i> _{AM}	0.43 ± 0.18	0.51 ± 0.07	0.10	0.965	248
				<i>K</i> _{AM}	-190 ± 90	120 ± 40	53	0.841	48

Temperature 25°C and pure micellar mobile phases, except where indicated.

^a Temperature 31°C.^b Mobile phase containing 3% 2-propanol.

the range of linearity (Figs. 1–3, curves b–e). In fact, it has been reported that, in many cases, the log *k*–log *P* correlations improves when surfactant concentration decreases [21,22].

On the other hand, as predicted by Eq. 4, the *k*_m (or *k*)–log *P* relationships are not linear (Figs. 1–3, right). The shape of the *k*–log *P* curves is also influenced by the micellar concentration. In most cases an apparent linear

relationship between *k* and log *P*, especially for large log *P* values, was found, in agreement with Eq. 6. For solutes with low log *P* values the degree of curvature is always strong.

The deviations between the predicted curve and some experimental points can reveal some degree of inadequacy of the model. However, inaccurate measures of the experimental chromatographic parameters or log *P* values could

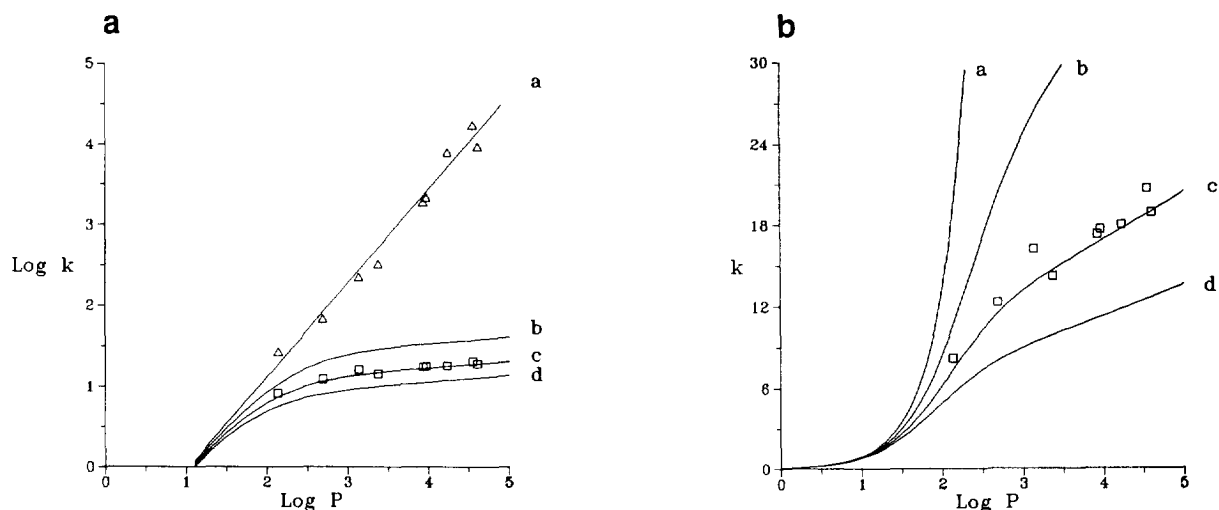


Fig. 1. $\log k$ - $\log P$ (a) and k - $\log P$ (b) relationships predicted by Eqs. 4 and 5 (solid lines) and experimental values (symbols) from series I at several micellar concentrations: (a, Δ) 0; (b) 0.05; (c, \square) 0.1; (d) 0.15 M.

also explain those irregularities. On the other hand, the general agreement between the model and the experimental points confirms the predictive ability of Eqs. 4 and 5 and the validity of Eqs. 2 and 3.

4. Conclusions

The results presented in this paper demonstrate, for the series of compounds studied, that (1) the use of the retention factors of compounds

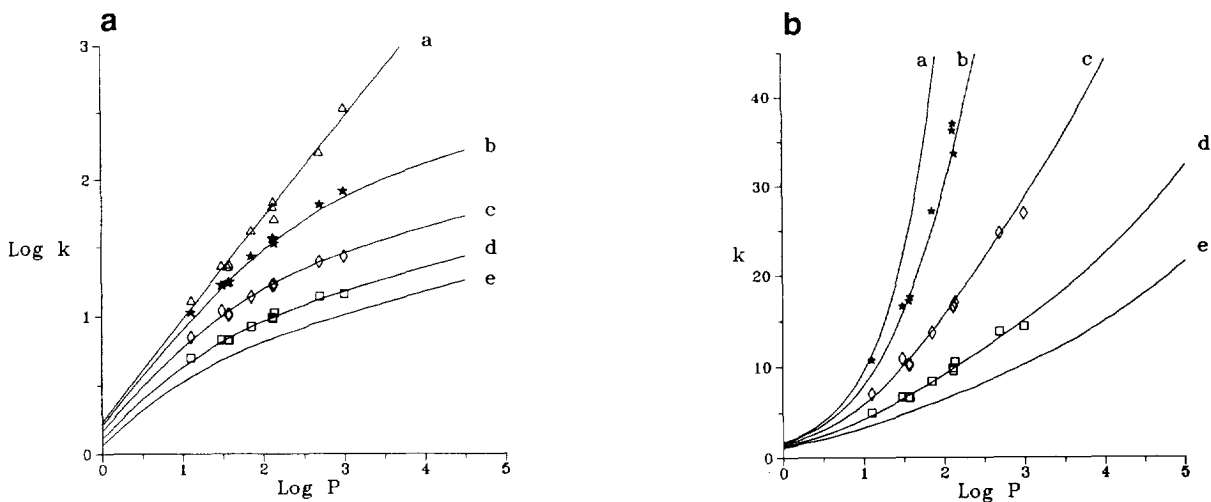


Fig. 2. $\log k$ - $\log P$ (a) and k - $\log P$ (b) relationships predicted by Eqs. 4 and 5 (solid lines) and experimental values (symbols) from series III at several micellar concentrations: (a, Δ) 0; (b, \star) 0.016; (c, \diamond) 0.05; (d, \square) 0.1; (e) 0.15 M.

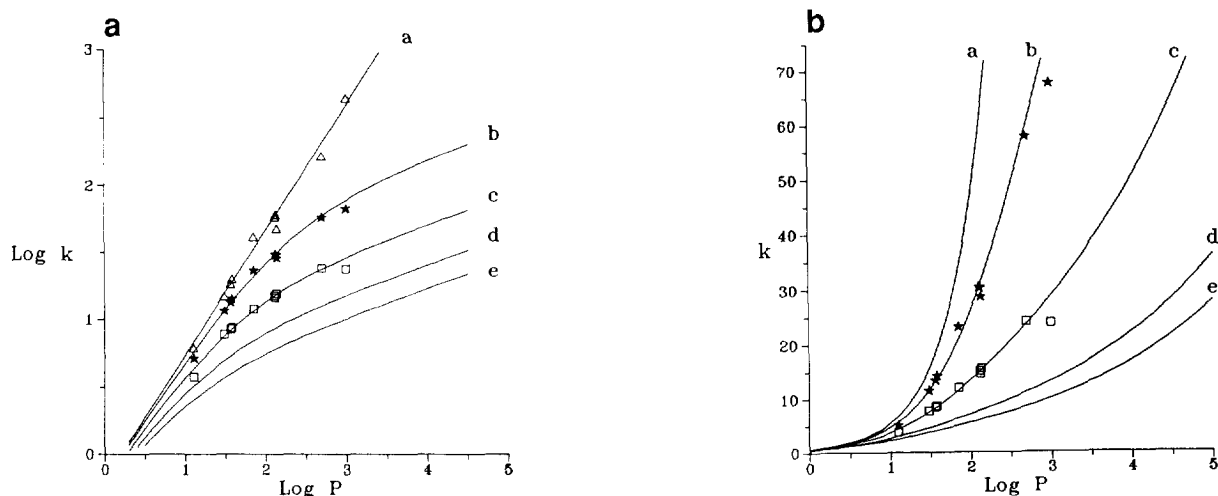


Fig. 3. Log k –log P (a) and k –log P (b) relationships predicted by Eqs. 4 and 5 (solid lines) and experimental values (symbols) from series IV at several micellar concentrations: (a, Δ) 0; (b, \star) 0.016; (c, \square) 0.05; (d) 0.1; (e) 0.15 M.

obtained in a given mobile phase is, in general, not adequate as a hydrophobicity index. Only in singular cases can good linear correlations ($\log k$ or k vs. $\log P$) be obtained. (2) The $\log k_m$ value is the best parameter to predict the hydrophobicity of a solute using micellar mobile phases, showing a high correlation (high r^2 and F ratio) and high slope (high sensitivity) with $\log P$ values. (3) Eqs. 4 and 5 gave an adequate description of the relationship between retention of solutes in MLC with pure and mixed micellar mobile phases and $\log P$. The relationship between k or $\log k$ and $\log P$ can be modelled by determining $\log k_m$ and $\log K_{AM}$ of the compounds and their fitting parameter with the corresponding $\log P$ values. Such a model permits the prediction of $\log P$ values from k or $\log k$ data, and also the estimation of the retention of congeneric compounds from their $\log P$ values. (4) For most compounds, the k_w and k_m parameters should be equivalent for the prediction of P . However, the modification of the alkyl-bonded stationary phases by surfactant monomers increases their hydrophobicity and reduces the concentration of residual silanol groups on the silica surface. As consequence, for certain solutes the k_m values would be better

than k_w for the prediction of hydrophobicity. In contrast, for charged solutes eluted with an ionic surfactant, electrostatic interactions will occur. In this case hydrophobicity predictions using k_m would fail. However, an adequate selection of the nature of surfactant and pH of the mobile phase could eliminate this problem.

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