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Journal of Chromatography A, 955 (2002) 19–34

JOURNAL OF  
CHROMATOGRAPHY A

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## Prediction of the retention in reversed-phase liquid chromatography using solute–mobile phase–stationary phase polarity parameters

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Received 14 January 2002; received in revised form 25 February 2002; accepted 25 February 2002

### Abstract

A previously reported algorithm, based on the equation:  $\log k = (\log k)_0 + p(P_m^N - P_s^N)$ , that relates the retention in reversed-phase liquid chromatography with solute ( $p$ ), mobile phase ( $P_m^N$ ) and stationary phase ( $P_s^N$ ) relative polarity parameters, is improved. The retention data reported by several authors for different sets of compounds, eluted with acetonitrile–water and methanol–water mixtures, are used to test the algorithm and elaborate a database of  $p$  values. The methodology is successfully applied to predict the retention using  $P_m^N$  values calculated as  $P_m^N = 1.00 - (2.13\varphi)/(1 + 1.42\varphi)$  for acetonitrile–water and  $P_m^N = 1.00 - (1.33\varphi)/(1 + 0.47\varphi)$  for methanol–water,  $\varphi$  being the organic solvent volumetric fraction. The polarity parameters are demonstrated to be useful to transfer retention data between solvent systems and between columns. Accordingly, the retention in a solvent system is predicted by characterising the working column with a small training set of compounds having diverse polarities, and using the  $p$  values known for another solvent system or column. The  $p$  polarity parameter is found to be a good descriptor of the retention, allowing the prediction of the expected elution order and peak overlaps. © 2002 Elsevier Science B.V. All rights reserved.

**Keywords:** Retention prediction; Polarity measurements

### 1. Introduction

In reversed-phase liquid chromatography (RPLC), the retention behaviour is usually described using an equation where the retention factor,  $k$ , is exponentially related to the volume fraction of organic solvent in the mobile phase,  $\varphi$  [1]:

$$\log k = c_0 + c_1 \varphi \quad (1)$$

This equation yields systematic deviations in the prediction of the retention when a wide range of compositions is considered [2]. In such a case, a quadratic relationship should be used to improve the accuracy [3]:

$$\log k = c_0 + c_1 \varphi + c_2 \varphi^2 \quad (2)$$

Acceptable predictions can be achieved in a wider composition range by using measurements of the solvent polarity, instead of the volume fraction. Johnson et al. [4] proposed the Dimroth-Reichardt polarity parameter,  $E_T(30)$  [5], as a descriptor of the

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mobile phase. When this parameter is normalised ( $E_T^N$ ), the retention can be described as:

$$\log k = q' + p' E_T^N \quad (3)$$

which includes two descriptors for each solute,  $q'$  and  $p'$ , besides the mobile phase descriptor,  $E_T^N$ . The solute descriptors were found to be correlated, which gave rise to a new model [6,7]:

$$\log k = (\log k)_0' + p'(E_{T_m}^N - E_{T_s}^N) \quad (4)$$

containing four descriptors related to the solute ( $p'$ ), mobile phase ( $E_{T_m}^N$ ) and column ( $(\log k)_0'$  and  $E_{T_s}^N$ ). Although a good correlation exists between  $\log k$  and  $E_{T_m}^N$ , Eq. (4) is limited to the same linearity range as Eq. (3), which for the most common solvent systems is approximately 20–100% methanol and 0–80% acetonitrile [7]. To overcome this limitation, new normalised polarity parameters, related to  $E_T(30)$ , were proposed for both mobile phase ( $P_m^N$ ) and stationary phase ( $P_s^N$ ), which extend Eq. (4) to the whole range of mobile phase compositions (0–100%):

$$\log k = (\log k)_0 + p(P_m^N - P_s^N) \quad (5)$$

The value  $P_m^N = 1$  was assigned to pure water for both methanol–water and acetonitrile–water systems, and  $P_s^N = 0$  to the working stationary phase, a Merck LiChrospher 100 RP-18 (100×5 mm) column [7], which was taken as reference. Since the polarity of C<sub>18</sub> stationary phases is very low,  $P_s^N$  is expected to be close to zero, slightly positive and negative for stationary phases more and less polar than the reference, respectively.

The description of the retention given by Eq. (5) is based on relative polarity measurements. The  $p$  values depend mainly on the solute polarity, but also on the nature of the mobile and stationary phases. Similarly, the larger contribution to  $P_m^N$  is the mobile phase composition, and  $(\log k)_0$  and  $P_s^N$  are constants that depend mainly on the working column. Since in RPLC the mobile phase is more polar than the stationary phase,  $P_m^N$  is always greater than  $P_s^N$ . For the reference column,  $P_m^N$  ranges between 0.138 and 1, and 0.113 and 1, using acetonitrile–water and methanol–water mobile phases, respectively. The  $P_m^N$  values can be calculated from the mobile phase volume fractions as [7]:

$$P_m^N = 1.00 - \frac{2.13\varphi}{1 + 1.42\varphi} \quad (6)$$

for acetonitrile–water, and

$$P_m^N = 1.00 - \frac{1.33\varphi}{1 + 0.47\varphi} \quad (7)$$

for methanol–water.

The intercept in Eq. (5),  $(\log k)_0$ , is the retention of any solute eluted with a hypothetical mobile phase showing the same polarity as the stationary phase ( $P_m^N = P_s^N$ ). In such a situation, the polarity of the solute would not influence its retention.

The parameters in Eq. (5) are obtained following a procedure where the retention factors in all available experimental mobile phases are first fitted for each solute, according to:

$$\log k = q + p P_m^N \quad (8)$$

This yields independent values of the slope,  $p$ , and intercept,  $q$ , for each solute. A linear correlation is then established between  $q$  and  $p$ , for all solutes, to obtain the parameters  $(\log k)_0$  and  $P_s^N$  that characterise the column for the applied solvent system:

$$q = (\log k)_0 - p P_s^N \quad (9)$$

Observe that substitution of Eq. (9) in Eq. (8) leads to Eq. (5), which permits the prediction of  $\log k$  using the known values of  $(\log k)_0$ ,  $P_s^N$  and  $p$ .

In a previous work [7], more accurate  $p$  values were calculated from:

$$p = \frac{\log k - (\log k)_0}{P_m^N - P_s^N} \quad (10)$$

using the available  $\log k - P_m^N$  data, together with the column parameters,  $(\log k)_0$  and  $P_s^N$ , obtained previously from Eqs. (8) and (9). For a given solute, Eq. (10) yields an estimation of  $p$  for each mobile phase composition. The mean value of these estimations was taken as final polarity measurement of the considered solute. In this work, the refining procedure of  $p$  values is improved, and the feasibility of transferring the retention data of solutes between different solvent systems and columns is examined.

## 2. Data treatment

The procedure described above to obtain solute and column parameters was improved in an iterative process, which permitted a direct relationship between the retention and column parameters. The calculation starts as explained previously, by performing an independent linear least-squares fitting of all available  $\log k - P_m^N$  data to Eq. (8) for each solute, in order to obtain first estimates of the  $p$  values. Next, initial values of  $(\log k)_0$  and  $P_s^N$  are calculated through Eq. (9). At this point, owing to the insufficient correlation between  $q$  and  $p$ , the algorithm is modified. Eq. (5) is fitted considering the  $p$  values and  $\log k$  data for all solutes and available mobile phases simultaneously, through the minimisation of the sum of squared residuals (SSR) between the predicted and experimental  $\log k$ . In this way, more reliable  $(\log k)_0$  and  $P_s^N$  estimations are obtained. The  $p$  values are further improved using Eq. (10), which finishes an iteration. In the following iteration, these values are used to recalculate  $(\log k)_0$  and  $P_s^N$  using again Eq. (5). During the process, SSR is gradually reduced up to reach a minimum. The values of the polarity parameters reached in the minimum are accepted as the optimal.

## 3. Literature data

An initial set of 167 compounds of diverse polarity, chromatographed with acetonitrile–water and methanol–water mobile phases, and published by Smith and Burr in several reports [8–13], was used to develop and validate the proposed procedure. These data were previously analysed by one of the authors through the solvation equation proposed by Abraham [14]. The experimental mobile phases were seven acetonitrile–water mixtures, with the following volume fractions of organic solvent (30, 40, 50, 60, 70, 80 and 90%) and six methanol–water mixtures (40, 50, 60, 70, 80 and 90%). A Spherisorb ODS-2 (100×5 mm) column was used for both systems.

From the set of 167 compounds, those having an insufficient number of  $\log k$  data (less than three mobile phases) were discarded. In some cases, the lack of data was due to the low polarity of the

compounds, which yielded prohibitive retention times with the mobile phases of lower elution strength. From the remaining compounds, only those for which  $\log k$  data were available in both acetonitrile–water and methanol–water systems were taken; altogether, the data for 152 compounds (Table 1a,b). The data set analysed included mainly alkylbenzenes, phenols, anilines, phenones, halobenzenes, nitrobenzenes, and aromatic amides, aldehydes, esters, ethers and nitriles.

Three sets of data reported by Hanai and Hubert for mobile phases of acetonitrile–water [15–17] were also studied. These data corresponded to 77 compounds (including aliphatic and polyaromatic hydrocarbons, alkylbenzenes, aliphatic alcohols, phenols and halobenzenes) chromatographed in an ERC-1000 ODS (150×6 mm) column (Table 2) [15], nine benzene derivatives in a Develosil ODS-5 (150×4.6 mm) column [16], and 18 phenol derivatives in a Unisil Q C<sub>18</sub> (150×4.1 mm) column [17]. Acetonitrile volume fractions were: 50, 60, 70, 80 and 90% for the first set; 60, 70, 80, 85, 90 and 95% for the second; and 40, 50, 60, 70, 80 and 90% for the third one. Other data were taken from the report of Bosch et al. [7] for a group of 31 benzene and phenol derivatives, chromatographed with acetonitrile–water and methanol–water systems (30, 40, 50, 60, 70, 80 and 90% in both cases) in a Merck LiChrospher 100 RP-18 (100×5 mm) column, and from Kaibara et al. [18] for a group of 38 compounds (including alkylbenzenes, polyaromatic hydrocarbons, phenols, nitrobenzenes, anilines, halobenzenes and aromatic acids) chromatographed with methanol–water (45, 50, 60, 65, 70, 75 and 80%) in a Nucleosil C<sub>18</sub> (150×4.6 mm) column (Table 2).

Since Eq. (5) applies to neutral compounds, all test solutes were uncharged at the working pH. An extension of Eq. (5) to partially ionised solutes has been recently published [19,20].

## 4. Results and discussion

### 4.1. Refining of polarity parameters

Eq. (5) describes the retention as a function of polarity parameters that measure the contributions of solute ( $p$ ), mobile phase ( $P_m^N$ ) and column ( $(\log k)_0$

Table 1a

Polarity parameters for compounds eluted with acetonitrile–water and methanol–water mixtures calculated using the data of Smith and Burr [8–13]

Compound	$p(\text{MeCN})$	$p(\text{MeOH})$	Compound	$p(\text{MeCN})$	$p(\text{MeOH})$	Compound	$p(\text{MeCN})$	$p(\text{MeOH})$
Acetophenone	3.14	3.35	3-Bromotoluene	5.11	5.37	Dimethylphthalate	3.18	3.11
2-Aminophenol	2.02	1.96	4-Bromotoluene	5.10	5.35	<i>N</i> -Ethylaniline	3.93	3.76
3-Aminophenol	1.41	1.40	Butylbenzene	6.13	6.32	Ethylbenzene	4.99	5.13
4-Aminophenol	1.17	1.10	<i>s</i> -Butylbenzene	5.99	6.11	Ethyl benzoate	4.23	4.34
Aniline	2.51	2.48	<i>t</i> -Butylbenzene	5.79	5.93	Ethyl phenylacetate	3.91	4.00
Benzaldehyde	3.11	3.11	4- <i>t</i> -Butylphenol	3.89	4.23	Ethyl 3-phenylpropionate	4.40	4.57
Benzamide	1.69	2.10	Butyrophenone	4.19	4.36	Heptanophenone	5.78	6.06
Benzene	3.85	4.07	Chlorobenzene	4.38	4.61	Hexanophenone	5.24	5.46
Benzonitrile	3.09	3.15	2-Chlorophenol	2.90	3.01	2-Hydroxyacetophenone	3.44	3.59
Benzyl acetate	3.60	3.73	3-Chlorophenol	3.06	3.30	3-Hydroxyacetophenone	2.16	2.36
Benzyl alcohol	2.42	2.63	4-Chlorophenol	3.00	3.26	4-Hydroxyacetophenone	1.93	1.99
Benzyl bromide	4.41	4.42	2-Chlorotoluene	4.97	5.19	2-Hydroxybenzaldehyde	3.43	3.11
Benzyl 2-bromoacetate	3.90	4.00	3-Chlorotoluene	4.95	5.22	3-Hydroxybenzaldehyde	2.03	2.20
Benzyl chloride	4.13	4.26	4-Chlorotoluene	4.94	5.15	4-Hydroxybenzaldehyde	1.73	1.57
Benzyl cyanide	3.20	2.96	$\alpha$ -4-Dibromoacetophenone	4.30	4.33	2-Hydroxybenzamide	2.01	2.06
Biphenyl	5.45	5.72	1,2-Dihydroxybenzene	1.79	1.98	4-Hydroxybenzamide	0.77	1.03
2-Bromoaniline	3.60	3.52	1,3-Dihydroxybenzene	1.36	1.52	2-Hydroxybenzonitrile	1.97	1.82
3-Bromoaniline	3.42	3.30	1,4-Dihydroxybenzene	1.17	1.32	3-Hydroxybenzonitrile	2.36	2.32
Bromobenzene	4.55	4.79	<i>N,N</i> -Dimethylbenzamide	2.37	2.64	4-Hydroxybenzonitrile	2.12	1.96
2-Bromo-4-methylphenol	3.50	3.71	1,2-Dimethylbenzene	4.83	5.07	Isobutylbenzene	6.12	6.27
1-Bromo-2-nitrobenzene	3.90	3.92	1,3-Dimethylbenzene	4.94	5.16	Isopropylbenzene	5.46	5.56
2-Bromophenol	3.01	3.18	1,4-Dimethylbenzene	4.95	5.19	Methoxybenzene	3.86	3.92
3-Bromophenol	3.16	3.46	2,6-Dimethyl-4-nitrophenol	2.66	2.49	2-Methoxyphenol	2.67	2.68
4-Bromophenol	3.14	3.45	2,4-Dimethylphenol	3.20	3.48	3-Methoxyphenol	2.45	2.52
2-Bromotoluene	5.11	5.37	2,5-Dimethylphenol	3.34	3.56	4-Methoxyphenol	2.26	2.34

and  $P_s^N$ ). However, the evaluation of the column parameters needs an intermediate correlation (Eq. 9), which is carried out independently for the  $q$ – $p$  data obtained from Eq. (8) for each solute. As commented, the results can be improved by refining the initial parameters that this direct fitting originates. The process usually converges after two to five iterations.

The refining procedure was applied to the  $\log k$  values of 152 compounds reported by Smith and Burr, using acetonitrile–water and methanol–water mobile phases. The retention data were fitted to Eqs. (8) and (9) to obtain a first estimate of solute and column parameters,  $p$ ,  $(\log k)_0$  and  $P_s^N$  (without applying the refining algorithm). These parameters were next processed according to the procedure outlined in the data treatment section. Finally, the retention factors were predicted with Eq. (5) for the available experimental mobile phases, using both the unrefined and refined parameters.

Fig. 1a,b shows the correlation plots and some

statistics for the calculated versus experimental  $\log k$  for the 152 compounds, chromatographed with acetonitrile–water mixtures, using the unrefined and refined parameters, respectively. Fig. 1d,e depicts the results for methanol–water mixtures. As indicated, retention data from seven and six mobile phases were used for acetonitrile and methanol, respectively. However, the data for some compounds could not be measured in all mobile phases, due to the strong retention. For this reason, 883 and 745 experimental data were plotted, for acetonitrile and methanol, respectively.

The  $(\log k)_0$  and  $P_s^N$  parameters that characterised the column were  $(-1.040, -0.033)$  for acetonitrile–water mixtures, and  $(-1.243, -0.075)$  for methanol–water, respectively. The values obtained for the polarity parameter,  $p$ , for each solute and organic solvent, are given in Table 1a,b. The  $p$  values were usually larger for methanol than for acetonitrile. This means that a given change in solvent polarity, as measured by  $P_m^N$ , produces a change in retention in

Table 1b

Polarity parameters for compounds eluted with acetonitrile–water and methanol–water mixtures calculated using the data of Smith and Burr [8–13]

Compound	$p(\text{MeCN})$	$p(\text{MeOH})$	Compound	$p(\text{MeCN})$	$p(\text{MeOH})$	Compound	$p(\text{MeCN})$	$p(\text{MeOH})$
2-Methylacetophenone	3.74	3.80	3-Methylphenol	2.82	2.98	2-Phenylethyl chloride	4.59	4.74
3-Methylacetophenone	3.72	3.82	4-Methylphenol	2.84	3.01	5-Phenyl-1-pentanol	3.71	4.38
4-Methylacetophenone	3.69	3.81	Methyl phenylacetate	3.55	3.61	2-Phenylphenol	3.90	4.18
2-Methylaniline	2.96	2.88	Methyl 4-phenylbutyrate	4.40	4.64	3-Phenylphenol	3.75	4.20
3-Methylaniline	2.95	2.88	Methyl phenylethyl ether	3.94	4.07	4-Phenylphenol	3.75	4.20
4-Methylaniline	2.96	2.90	Methyl 3-phenylpropionate	3.99	4.17	1-Phenyl-1-propanol	3.10	3.44
2-Methylanisole	4.55	4.63	2-Nitroaniline	3.07	3.07	1-Phenyl-2-propanol	2.90	3.34
3-Methylanisole	4.35	4.45	3-Nitroaniline	2.85	2.71	2-Phenyl-1-propanol	2.91	3.32
2-Methylbenzaldehyde	3.62	3.68	Nitrobenzene	3.37	3.63	2-Phenyl-2-propanol	2.92	3.30
3-Methylbenzaldehyde	3.65	3.68	3-Nitrobenzyl alcohol	2.50	2.64	3-Phenyl-1-propanol	2.92	3.39
4-Methylbenzaldehyde	3.58	3.63	4-Nitrobenzyl alcohol	2.40	2.56	1-Phenyl-1-propene	5.19	5.37
2-Methylbenzamide	2.00	2.22	4-Nitrophenacyl bromide	3.49	3.47	3-Phenyl-1-propene	5.04	5.20
3-Methylbenzamide	2.12	2.48	3-Nitrophenol	2.62	2.60	3-Phenyl-1-propionamide	2.09	2.60
4-Methylbenzamide	2.17	2.47	2-Nitrotoluene	3.88	3.98	3-Phenyl-1-propionitrile	3.38	3.18
<i>N</i> -Methylbenzamide	1.89	2.23	3-Nitrotoluene	4.01	4.14	3-Phenyl-1-propyl bromide	5.38	5.61
Methyl benzoate	3.59	3.89	4-Nitrotoluene	3.95	4.08	3-Phenyl-1-propyl chloride	5.17	5.36
2-Methylbenzotrile	3.59	3.61	Phenacyl bromide	3.66	3.52	2-Phenyltoluene	5.87	6.21
3-Methylbenzotrile	3.67	3.65	Phenol	2.36	2.56	3-Phenyltoluene	5.94	6.30
4-Methylbenzotrile	3.62	3.62	Phenylacetaldehyde	3.10	3.01	4-Phenyltoluene	6.00	6.34
Methyl 2-hydroxybenzoate	3.89	4.21	Phenylacetamide	1.78	2.20	Propiophenone	3.70	3.88
Methyl 3-hydroxybenzoate	2.48	2.75	4-Phenyl-1-butanol	3.34	3.78	Propylbenzene	5.56	5.71
Methyl 4-hydroxybenzoate	2.39	2.58	1-Phenyl-2-butanone	3.73	3.70	<i>n</i> -Propyl 4-hydroxybenzoate	3.17	3.69
Methyl 2-methylbenzoate	4.10	4.33	4-Phenyl-2-butanone	3.62	3.67	Thymol	4.20	4.49
Methyl 3-methylbenzoate	4.13	4.39	4-Phenyl-1-butyronitrile	3.82	3.74	Toluene	4.44	4.66
Methyl 4-methylbenzoate	4.12	4.39	2-Phenylethanol	2.61	3.01	Valerophenone	4.70	4.90
2-Methylphenol	2.89	3.07	2-Phenylethyl bromide	4.78	4.95			

methanol–water larger than in acetonitrile–water mobile phases. The refined  $p$  values of the 152 compounds were in the range 0.77–6.13 for acetonitrile and 1.03–6.34 for methanol, and showed the following distribution: 20.1% ( $p \leq 2.5$ ), 27.9% ( $2.5 < p \leq 3.5$ ), 31.8% ( $3.5 < p \leq 4.5$ ), and 20.1% ( $p > 4.5$ ) for acetonitrile, and 15.6% ( $p \leq 2.5$ ), 28.6% ( $2.5 < p \leq 3.5$ ), 33.1% ( $3.5 < p \leq 4.5$ ), and 22.7% ( $p > 4.5$ ) for methanol.

The improvement in the predictions achieved with the refined parameters is remarkable (Fig. 1), especially for methanol. The predictions with the proposed algorithm were also compared with those obtained using the classical polynomial models (Eqs. (1) and (2)), and the model that relates the retention with  $P_m^N$  (Eq. (8)) (Fig. 2). It should be noted that for the 152 compounds, the total number of parameters that should be evaluated was 304 ( $152 \times 2$ ) for Eqs. (1) and (8), 456 ( $152 \times 3$ ) for Eq. (2), and 154 ( $152 + 2$ , one for each solute plus two additional

parameters for the column) for Eq. (5). For the latter equation, once the column is characterised, each solute can be defined with a single experiment.

Eq. (8) is similar to Eq. (1), but makes use of  $P_m^N$  as factor instead of  $\varphi$ . In spite of the fact that Eq. (8) is simpler than the quadratic model (Eq. 2), the quality of the predictions is comparable. However, the experimental work is reduced with Eq. (8), since it requires one mobile phase less to perform the fittings. Eq. (8) can be considered as a particular case of Eq. (5), where the parameter of the column,  $q$ , has a specific value for each solute. Owing to the higher degrees of freedom, Eq. (8) gives better predictions than Eq. (5). Finally, the predictions with Eq. (5) were similar to those with Eq. (1), which includes practically twice the number of parameters.

#### 4.2. Predictions with a small training set

The use of such a high number of experimental

Table 2

Polarity parameters for compounds eluted with acetonitrile–water and methanol–water mixtures calculated using the data of Hanai and Hubert [15], Bosch et al. [7] and Kaibara et al. [18]

Compound	$p_{HH1}$	$\hat{p}_{SB}^a$	Compound	$p_{HH1}$	$\hat{p}_{SB}^a$	Compound	$p_{HH1}$	$\hat{p}_{SB}^a$
Hanai and Hubert: acetonitrile ( $\log k_o = -1.379$ , $P_s^N = -0.121$ )								
Benz[ <i>a</i> ]anthracene	6.81	7.02	3,5-Dichlorophenol	4.25	3.84	Pentachlorobenzene	6.75	6.95
Benzene <sup>b</sup>	4.34	3.95	2,3-Dimethylphenol	3.79	3.27	Pentachlorophenol	5.40	5.27
Bromobenzene <sup>b</sup>	4.87	4.61	2,5-Dimethylphenol <sup>b</sup>	3.82	3.31	<i>n</i> -Pentane	5.94	5.94
3-Bromophenol <sup>b</sup>	3.70	3.15	2,6-Dimethylphenol	3.93	3.44	Pentan-1-ol	3.44	2.83
4-Bromophenol <sup>b</sup>	3.63	3.07	3,4-Dimethylphenol	3.63	3.07	Phenanthrene	5.77	5.73
Butan-1-ol	3.04	2.34	3,5-Dimethylphenol	3.70	3.16	Phenol <sup>b</sup>	3.08	2.38
<i>n</i> -Butylbenzene <sup>b</sup>	6.03	6.05	2,4-Dinitrophenol	3.44	2.84	<i>n</i> -Propylbenzene <sup>b</sup>	5.58	5.49
Chlorobenzene <sup>b</sup>	4.74	4.45	2,5-Dinitrophenol	3.55	2.97	1,2,3,4-Tetrachlorobenzene	6.13	6.18
2-Chloro-5-methylphenol	3.82	3.31	2,6-Dinitrophenol	3.56	2.98	1,2,3,5-Tetrachlorobenzene	6.31	6.40
4-Chloro-2-methylphenol	3.98	3.51	Dodecan-1-ol	6.73	6.92	1,2,4,5-Tetrachlorobenzene	6.26	6.33
4-Chloro-3-methylphenol	3.88	3.38	Ethylbenzene <sup>b</sup>	5.13	4.94	2,3,4,5-Tetrachlorophenol	4.93	4.68
2-Chlorophenol <sup>b</sup>	3.48	2.89	2-Ethylphenol	3.74	3.20	2,3,5,6-Tetrachlorophenol	4.97	4.74
3-Chlorophenol <sup>b</sup>	3.59	3.02	4-Ethylphenol	3.73	3.20	2,3,5,6-Tetramethylphenol	4.56	4.22
4-Chlorophenol <sup>b</sup>	3.53	2.94	<i>n</i> -Heptane	6.93	7.17	Toluene <sup>b</sup>	4.76	4.47
Chrysene	6.60	6.75	Heptan-1-ol	4.33	3.94	1,2,4-Trichlorobenzene	5.74	5.69
Decan-1-ol	5.71	5.65	Hexachlorobenzene	7.21	7.51	1,3,5-Trichlorobenzene	6.00	6.01
2,4-Dibromophenol	4.26	3.85	<i>n</i> -Hexane	6.40	6.51	2,3,4-Trichlorophenol	4.36	3.97
2,6-Dibromophenol	4.22	3.80	Hexan-1-ol	3.88	3.37	2,3,5-Trichlorophenol	4.12	3.68
1,2-Dichlorobenzene	5.12	4.91	<i>n</i> -Hexylbenzene	6.95	7.19	2,3,6-Trichlorophenol	4.39	4.01
1,3-Dichlorobenzene	5.29	5.13	Iodobenzene	5.09	4.88	2,4,5-Trichlorophenol	4.48	4.13
1,4-Dichlorobenzene	5.20	5.01	2-Methylphenol <sup>b</sup>	3.50	2.90	2,4,6-Trichlorophenol	4.57	4.24
2,3-Dichlorophenol	3.88	3.38	4-Methylphenol <sup>b</sup>	3.38	2.76	3,4,5-Trichlorophenol	4.56	4.23
2,4-Dichlorophenol	4.02	3.55	Naphthalene	5.04	4.82	2,3,5-Trimethylphenol	4.13	3.68
2,5-Dichlorophenol	3.98	3.51	4-Nitrophenol	3.08	2.39	2,3,6-Trimethylphenol	4.24	3.83
2,6-Dichlorophenol	3.95	3.46	<i>n</i> -Octane	7.43	7.79	2,4,6-Trimethylphenol	4.28	3.88
3,4-Dichlorophenol	4.00	3.52	Octan-1-ol	4.78	4.49			
Compound	$p_{BR}$	$\hat{p}_{SB}^a$	Compound	$p_{BR}$	$\hat{p}_{SB}^a$	Compound	$p_{BR}$	$\hat{p}_{SB}^a$
Bosch et al.: acetonitrile ( $\log k_o = -0.676$ , $P_s^N = -0.051$ )								
Anthracene	5.50	6.12	4-Chlorophenol <sup>b</sup>	2.80	2.95	Nitrobenzene <sup>b</sup>	3.21	3.43
Benzene <sup>b</sup>	3.58	3.86	Chrysene	6.53	7.33	3-Nitrophenol <sup>b</sup>	2.49	2.58
Biphenyl <sup>b</sup>	4.83	5.34	2,4-Dichlorophenol	3.30	3.53	4-Nitrophenol	2.40	2.48
Bromobenzene <sup>b</sup>	4.21	4.60	2,6-Dichlorophenol	3.17	3.39	Pentachlorophenol	4.76	5.25
3-Bromophenol <sup>b</sup>	2.97	3.14	3,5-Dichlorophenol	3.55	3.83	Phenol <sup>b</sup>	2.35	2.42
4-Bromophenol <sup>b</sup>	2.92	3.09	1,4-Dimethylbenzene <sup>b</sup>	4.57	5.03	Propylbenzene <sup>b</sup>	5.01	5.54
Butylbenzene <sup>b</sup>	5.54	6.16	2,4-Dimethylphenol <sup>b</sup>	3.06	3.26	Pyrene	6.03	6.74
Chlorobenzene <sup>b</sup>	4.06	4.43	2,4-Dinitrophenol	2.63	2.75	Toluene <sup>b</sup>	4.06	4.42
4-Chloro-3-methylphenol	3.13	3.34	Ethylbenzene <sup>b</sup>	4.49	4.94	2,4,6-Trichlorophenol	3.87	4.21
2-Chlorophenol	2.73	2.87	2-Methylphenol <sup>b</sup>	2.73	2.86			
3-Chlorophenol	2.86	3.02	Naphthalene	4.43	4.86			
Bosch et al.: methanol ( $\log k_o = 0.638$ , $P_s^N = -0.039$ )								
Anthracene	6.47	6.81	4-Chlorophenol <sup>b</sup>	3.12	3.33	Nitrobenzene <sup>b</sup>	3.27	3.48
Benzene <sup>b</sup>	3.59	3.83	Chrysene	8.06	8.46	3-Nitrophenol <sup>b</sup>	2.68	2.87
Biphenyl <sup>b</sup>	5.51	5.81	2,4-Dichlorophenol	3.84	4.08	4-Nitrophenol	2.61	2.81
Bromobenzene <sup>b</sup>	4.45	4.71	2,6-Dichlorophenol	3.36	3.58	Pentachlorophenol	6.16	6.48
3-Bromophenol <sup>b</sup>	3.27	3.49	3,5-Dichlorophenol	4.26	4.51	Phenol <sup>b</sup>	2.37	2.56
4-Bromophenol <sup>b</sup>	3.26	3.48	1,4-Dimethylbenzene <sup>b</sup>	4.95	5.23	Propylbenzene <sup>b</sup>	5.47	5.77
Butylbenzene <sup>b</sup>	6.09	6.42	2,4-Dimethylphenol <sup>b</sup>	3.33	3.55	Pyrene	7.18	7.54
Chlorobenzene <sup>b</sup>	4.34	4.60	2,4-Dinitrophenol	2.70	2.89	Toluene <sup>b</sup>	4.22	4.47
4-Chloro-3-methylphenol	3.59	3.82	Ethylbenzene <sup>b</sup>	4.76	5.04	2,4,6-Trichlorophenol	4.55	4.82
2-Chlorophenol	2.86	3.06	2-Methylphenol <sup>b</sup>	2.87	3.07			
3-Chlorophenol	3.15	3.36	Naphthalene	4.85	5.12			

Table 2. Continued

Compound	$p_{\text{KHN}}$	$\hat{p}_{\text{SB}}^{\text{a}}$	Compound	$p_{\text{KHN}}$	$\hat{p}_{\text{SB}}^{\text{a}}$	Compound	$p_{\text{KHN}}$	$\hat{p}_{\text{SB}}^{\text{a}}$
Kaibara et al.: methanol ( $\log k)_0 = -0.190$ , $P_s^N = 0.057$								
2-Aminobiphenyl	3.30	3.97	1-Chloro-4-nitrobenzene	3.09	3.79	3-Methylphenol <sup>b</sup>	2.08	2.91
Aniline <sup>b</sup>	1.56	2.45	4-Chlorophenol <sup>b</sup>	2.37	3.16	4-Methylphenol <sup>b</sup>	2.02	2.86
Anthracene	5.88	6.22	4-Chlorotoluene <sup>b</sup>	4.40	4.93	Naphthalene	4.34	4.88
Benzene <sup>b</sup>	3.10	3.80	4-Fluoroaniline	1.63	2.51	1-Naphthoic acid	2.79	1.96
Benzoic acid	1.92	2.77	Fluorobenzene	3.04	3.75	2-Naphthol	2.57	3.33
Biphenyl <sup>b</sup>	5.12	5.56	(4-Fluorophenyl)acetic acid	1.88	2.73	1-Naphthylamine	2.54	3.31
4-Bromoaniline	2.32	3.12	4-Iodoaniline	2.60	3.36	4-Nitroaniline	1.30	2.22
Bromobenzene <sup>b</sup>	3.93	4.52	Iodobenzene	4.25	4.80	Nitrobenzene <sup>b</sup>	2.61	3.37
4-Bromobenzoic acid	2.90	3.62	4-Iodophenol	2.82	3.55	4-Nitrophenol	1.86	2.71
4-Bromophenol <sup>b</sup>	2.55	3.32	3-Methylaniline <sup>b</sup>	1.95	2.79	4-Nitrotoluene <sup>b</sup>	3.15	3.84
4-Chloroaniline	2.14	2.96	4-Methylaniline <sup>b</sup>	1.96	2.80	Phenol <sup>b</sup>	1.64	2.52
Chlorobenzene <sup>b</sup>	3.72	4.34	3-Methylbenzoic acid	2.38	3.17	Toluene <sup>b</sup>	3.72	4.34
4-Chlorobenzoic acid	2.72	3.46	4-Methylbenzoic acid	2.37	3.16			

<sup>a</sup>  $\hat{p}_{\text{SB}}$  are predicted polarity parameters referred to the column used by Smith and Burr.

<sup>b</sup> Compounds used to establish the correlations between  $p$  values (see Fig. 5).

data, as the retention values for the set of 152 compounds of diverse polarity, obtained with three to six or seven mobile phases, guarantees accurate parameters to characterise both column and compounds. However, in practice, a description of similar quality using a smaller number of experiments is desirable. According to this requirement, the possibility of using a smaller training set was studied. The selected set should include solutes of diverse polarity to guarantee a correct characterisation.

Different sets of 10 compounds were randomly selected, each of them with the same distribution of polarities ( $p$  values) as that found in the set of 152 compounds: two compounds with  $p \leq 2.5$ , three with  $2.5 < p \leq 3.5$ , three with  $3.5 < p \leq 4.5$ , and two with  $p > 4.5$ . In this way, 300 sets of compounds were checked, giving rise to 300 pairs of column parameters,  $(\log k)_0$  and  $P_s^N$ . Those sets exceeding  $[\bar{x} - 2.5s, \bar{x} + 2.5s]$  were discarded, where  $\bar{x}$  and  $s$  are the mean and standard deviation of the 300 values of  $(\log k)_0$  (or  $P_s^N$ ). The outlier rejection was repeated to obtain a self-coherent population. The mean values and associated standard deviations of the column parameters of the remaining sets of compounds were  $(\log k)_0 = -1.056 \pm 0.091$  and  $P_s^N = -0.037 \pm 0.025$  (282 valid sets) for acetonitrile–water, and  $(\log k)_0 = -1.26 \pm 0.15$  and  $P_s^N = -0.081 \pm 0.041$  (256 valid sets) for methanol–water. These values should be compared with those obtained for the full population of 152 compounds:  $(\log k)_0 = -1.040$  and  $P_s^N = -0.033$  for acetonitrile–

water, and  $(\log k)_0 = -1.258$  and  $P_s^N = -0.078$  for methanol–water.

Fig. 1c,f shows the quality of the predictions for the 152 compounds eluted with acetonitrile–water and methanol–water mixtures, respectively. The  $\log k$  data were predicted using Eq. (5), the  $p$  values listed in Table 1a,b and the column parameters obtained using one of the 300 sets of 10 compounds, randomly selected among the valid sets, which will be called the reference set. The compounds in this set, ordered according to their polarity parameter,  $p$  (acetonitrile–water, methanol–water) were: benzamide (1.69, 2.10), phenylacetamide (1.78, 2.20), 3-methylaniline (2.95, 2.88), 2-bromophenol (3.01, 3.18), 2-bromo-4-methylphenol (3.50, 3.71), benzyl 2-bromoacetate (3.90, 4.00), butyrophenone (4.19, 4.36), thymol (4.20, 4.49), 1,4-dimethylbenzene (4.95, 5.19), and butylbenzene (6.13, 6.32). The column parameters obtained with these compounds were:  $(\log k)_0 = -1.011$  and  $P_s^N = -0.030$  for acetonitrile–water and  $(\log k)_0 = -1.173$  and  $P_s^N = -0.057$  for methanol–water. As observed (see Fig. 1b,c,e,f), the predictions achieved using a small training set are similar to those using the full set of 152 compounds to characterise the column.

#### 4.3. Transference of retention data between solvent systems

Another study was performed to check whether the retention in a new solvent system can be

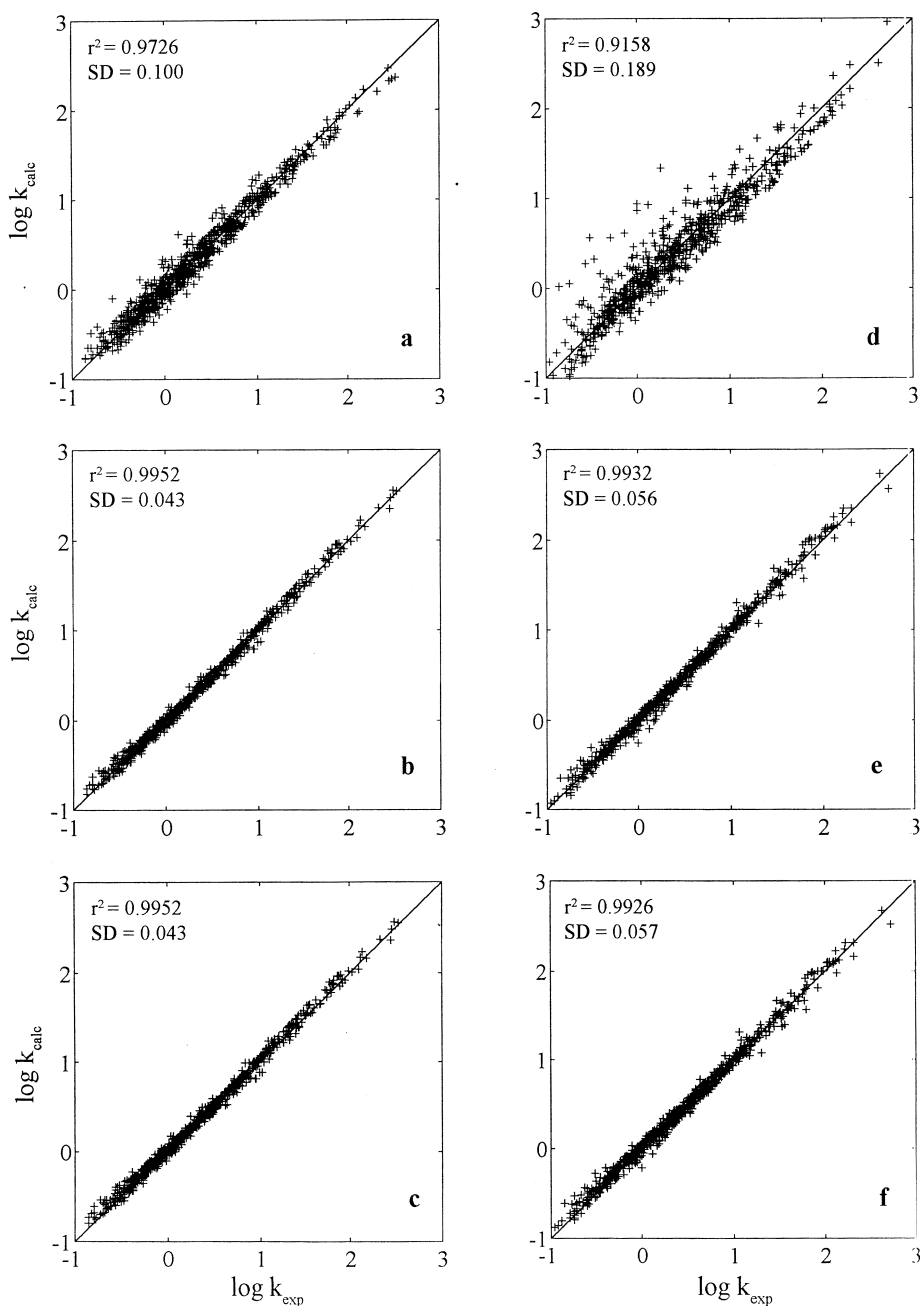


Fig. 1. Prediction of retention factors according to Eq. (5), for a set of 152 compounds eluted with: (a–c) acetonitrile–water ( $n=883$  points), and (d–f) methanol–water ( $n=745$ ) mixtures. The polarity parameters,  $p$ ,  $(\log k)_0$  and  $P_s^N$ , were used unrefined in (a,d), and refined in (b,c,e,f). The column polarity parameters were obtained using the data from the 152 compounds (a,b,d,e), or from a small set of 10 compounds of diverse polarity (c,f).



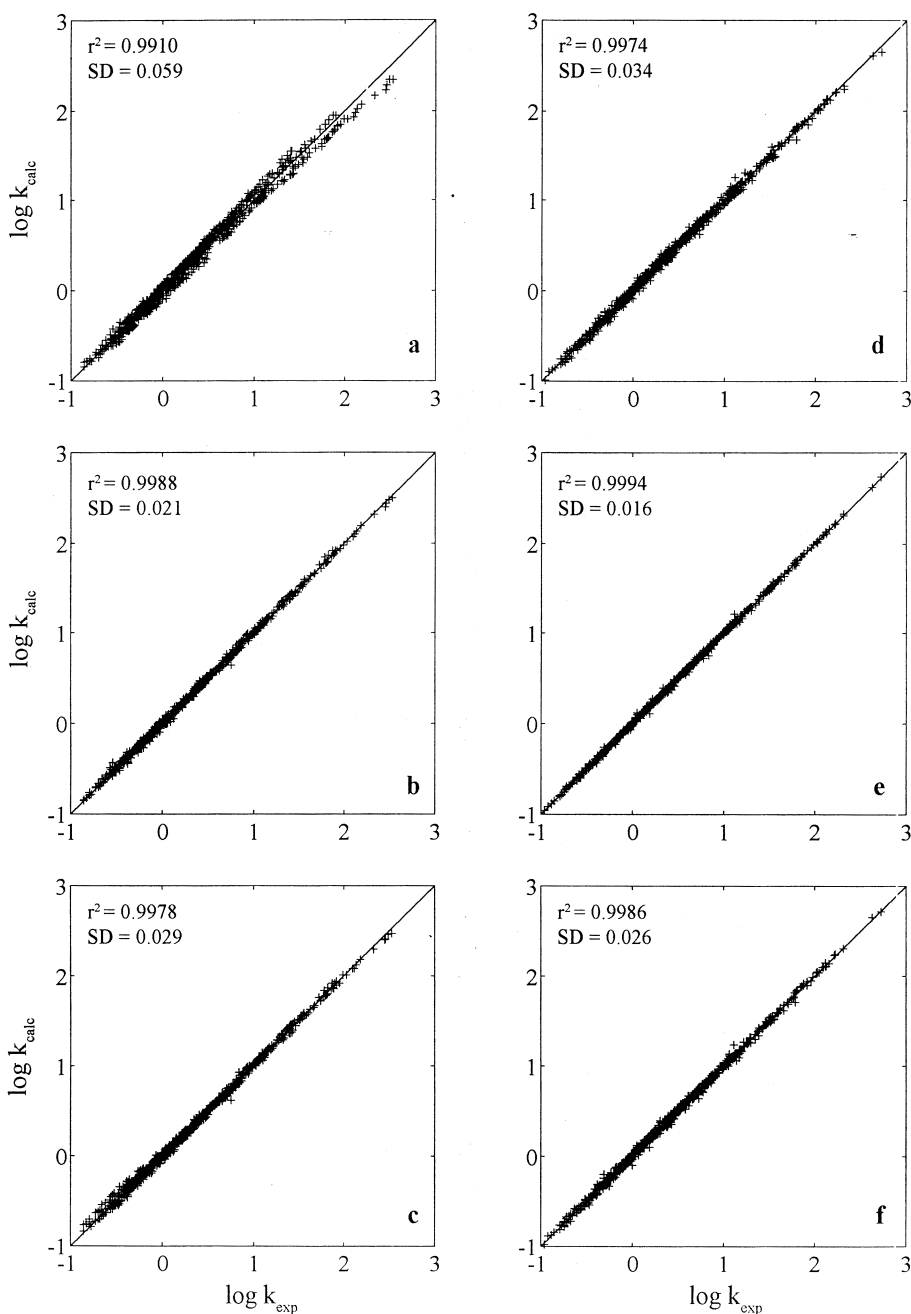


Fig. 2. Comparison of several retention models used in the prediction of the retention of 152 compounds, eluted with: (a–c) acetonitrile–water ( $n=883$ ), and (d–f) methanol–water ( $n=745$ ) mixtures: (a,d) Eq. (1), (b,e) Eq. (2), and (c,f) Eq. (8).

predicted using known  $p$  values in another solvent system. For this purpose, the parameters  $(\log k)_0$ ,  $P_s^N$  and  $p$  should be evaluated for a small set of

compounds (the reference set), in the new solvent system. The  $p$  values in both systems are then correlated for this set, which allows transferring the

$p$  values of any other compound to the new solvent. Finally, the retention is predicted with Eq. (5) using these  $p$  values and the column parameters obtained with the reference set.

This procedure was applied using the 10 compounds selected in the previous section as the reference set, and the  $p$  values of the 152 compounds given in Table 1a,b. The prediction quality was assessed by plotting predicted versus experimental  $\log k$  for all available mobile phases. Fig. 3 shows the performance of the transference when acetonitrile (Fig. 3a) or methanol (Fig. 3c) are used as the new solvent system. As commented, the  $p$  values are systematically larger in methanol than in acetonitrile (see Table 1a,b). When the 152 compounds were

considered, the correlation between the  $p$  values in both solvents was:  $p_{\text{methanol}} = (0.079 \pm 0.045) + (1.021 \pm 0.012) p_{\text{acetonitrile}}$ . The slope is almost the unity, which indicates the possibility of transforming the  $p$  values by the simple addition of a constant. According to this, the mean of the differences between the  $p$  values in acetonitrile and methanol was obtained for the 152 compounds, being 0.16.

These observations suggest that the  $p$  polarity parameter consists of two additive contributions, one depending on the nature of the solute (the true polarity) and the other depending on its environment (i.e., the solvent in this case), which changes the apparent polarity. The transformation of  $p$  values between two solvent systems for compounds chro-

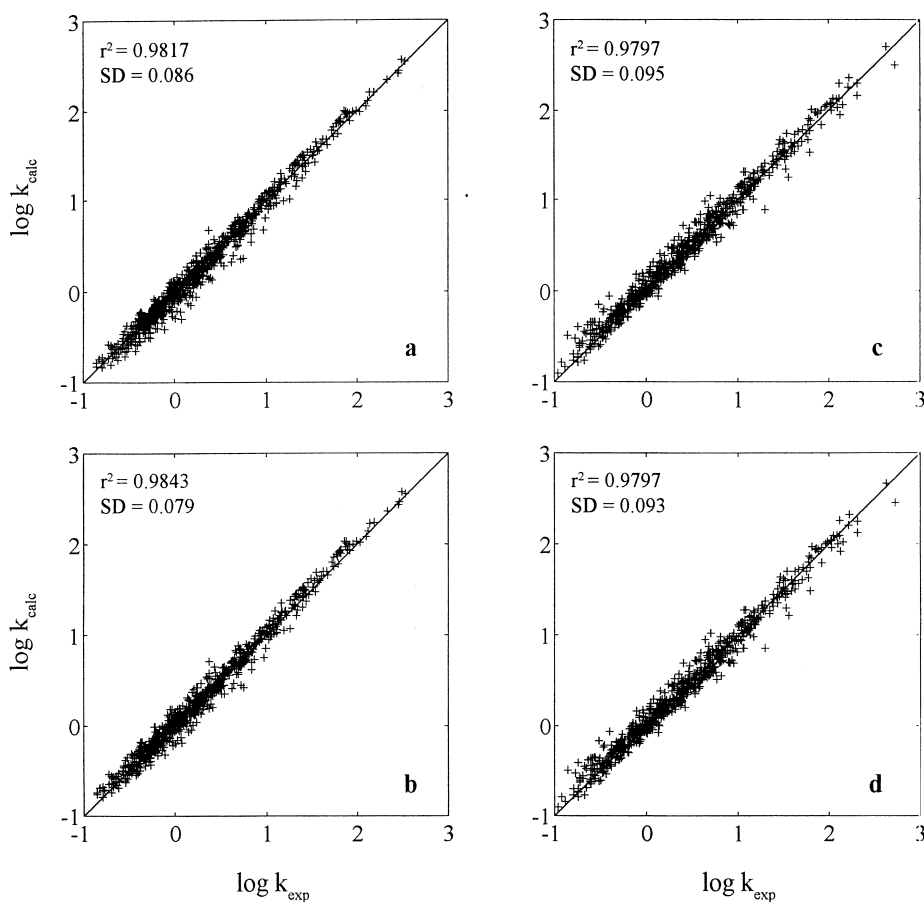


Fig. 3. Transference of retention data from: methanol to acetonitrile (a,b) ( $n=883$ ), and acetonitrile to methanol (c,d) ( $n=745$ ) mobile phases. In (a,c), the transference was made using  $p_{\text{MeOH}} = 0.079 + 1.021 p_{\text{MeCN}}$ . In (b,d), a constant factor of 0.16 was applied to correct the  $p$  values between solvent systems.

matographed in the same column can be roughly made by adding or subtracting a constant. In the example shown, any  $p$  value in methanol can be considered 0.16  $p$  units larger than in acetonitrile. This constant was used to transfer the retention data from one solvent to the other, following the procedure explained above. Fig. 3b,d illustrates the corresponding  $\log k$  correlation plots. As observed, these diagrams are similar to those achieved using the correlation equation indicated above (Fig. 3a,c).

According to these results, the retention in a solvent system can be predicted by characterising the working column with a small training set of compounds having diverse polarities and using the  $p$  values known for another solvent system.

#### 4.4. Transference of retention data between columns

The feasibility of transferring retention data obtained in a given column, to another column filled with a different stationary phase, was next considered. For this study,  $\log k$  data measured with mobile phases of acetonitrile–water of several compounds reported by Hanai and Hubert [15–17], which were also in the list of Smith and Burr, were used. The selected compounds were 18 benzene and phenol derivatives (HH1 series), nine benzene derivatives (HH2 series), and 18 phenol derivatives (HH3 series). Each of these series was chromatographed in a different  $C_{18}$  column: ERC-1000 ODS (150×6 mm), Develosil ODS-5 (150×4.6 mm), and Unisil Q  $C_{18}$  (150×4.1 mm), respectively. The Smith and Burr data (SB) were obtained with a Spherisorb ODS-2 (100×5 mm) column.

Fig. 4a–c shows that the retention in the HH1, HH2 and HH3 series can be predicted with similar errors to those achieved for the SB data (Fig. 1b), using the column and solute parameters obtained inside each series. These plots are useful to evaluate the performance of the transference procedure, which is explained below. The column parameters,  $(\log k)_0$  and  $P_s^N$ , were: (−1.717, −0.197) for HH1, (−1.276, −0.076) for HH2, and (−0.261, −0.082) for HH3, which should be compared with the parameters for SB (−1.040 and −0.033). The  $P_s^N$  values indicate that the columns used by Hanai and Hubert, are slightly less polar than that used by Smith and Burr.

The polarity ranges ( $p$  values) for the HH1, HH2 and HH3 series were 3.31–5.74, 4.52–6.55 and 0.78–3.75, respectively. It should be noted that only a few compounds were found in all the three series, and that the  $p$  values depend on the column. The mean of the differences between the  $p$  values in these series and the corresponding values for SB was  $0.49 \pm 0.38$  (HH1),  $0.50 \pm 0.14$  (HH2), and  $-0.37 \pm 0.15$  (HH3). As an example, for benzene and *n*-butylbenzene,  $p=4.35$  and 5.74 (HH1), 4.52 and 6.55 (HH2), and 3.85 and 6.13 (SB), and for phenol and 3-bromophenol,  $p=3.31$  and 3.82 (HH1), 1.90 and 2.85 (HH3), and 2.36 and 3.16 (SB). The  $p$  values and the retention were similar for HH1 and HH2, and different from HH3. The  $p$  values were usually smaller for SB with respect to HH1 and HH2, but greater than for HH3. However, the retention was always longer for SB, since it also depends on  $(\log k)_0$  and  $P_s^N$ .

The performance of the transference of retention data between columns was checked using the Hanai and Hubert series, and the  $p$  values calculated with the data reported by Smith and Burr, for the shared compounds. These values were adapted to the new columns (those of the HH1, HH2 and HH3 series) by establishing a correlation similar to that made between acetonitrile–water and methanol–water mixtures, in the previous section. The correlation equations were:  $p_{HH1} = 1.754 + 0.657p_{SB}$ ,  $p_{HH2} = 1.263 + 0.847p_{SB}$ , and  $p_{HH3} = -0.664 + 1.106p_{SB}$ . Fig. 4d–f shows the quality of the predicted  $\log k$  for the columns used by Hanai and Hubert, taking the known  $p$  values for Smith and Burr, and the established correlations. Regarding Fig. 4a–c, the predictions are satisfactory.

As a final test about the possibility of transferring the data from one column to another, the data reported by Hanai and Hubert (for 77 compounds) [15] and Bosch et al. (31 compounds) [7] in acetonitrile–water, and Kaibara et al. (38 compounds) [18] and Bosch et al. (31 compounds) [7] in methanol–water, were used to obtain solute and column polarity parameters. These series contained retention data from compounds found in the list of Smith and Burr, and from other new compounds. The common compounds with those found in the list of Smith and Burr were selected in order to correlate the  $p$  values between both lists (Fig. 5). The correlation functions

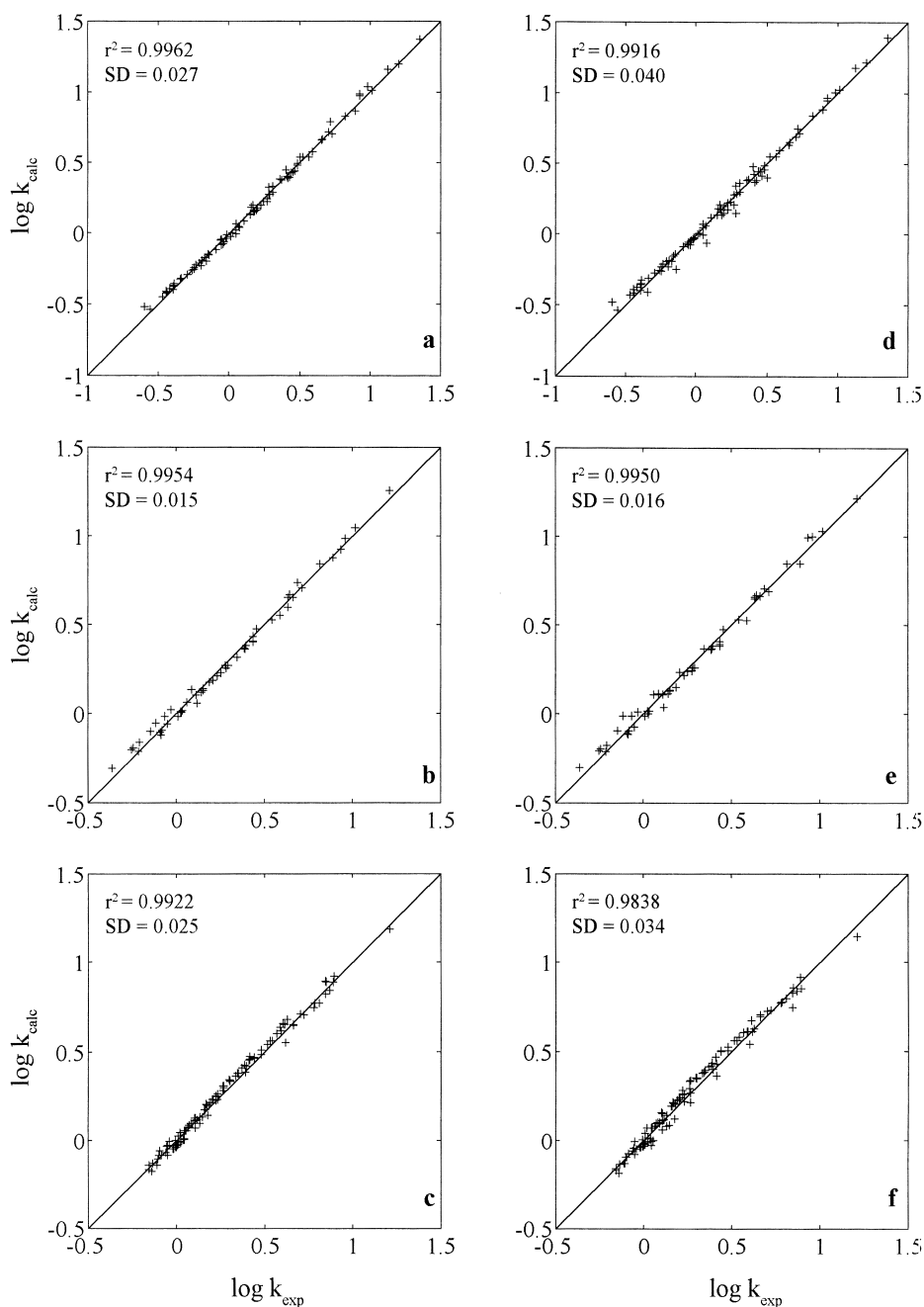


Fig. 4. Transference of retention data between columns: (a,d) HH1 ( $n=89$ ), (b,e) HH2 ( $n=54$ ), and (c,f) HH3 ( $n=108$ ). The correlation plots illustrate the quality of the predictions using the solute polarity parameters obtained inside each series (a–c), or predicted from the Smith and Burr data using the following correlations: (d)  $p_{\text{HH1}} = 1.754 + 0.657p_{\text{SB}}$ ,  $p_{\text{HH2}} = 1.263 + 0.847p_{\text{SB}}$ , and  $p_{\text{HH3}} = -0.664 + 1.106p_{\text{SB}}$ .

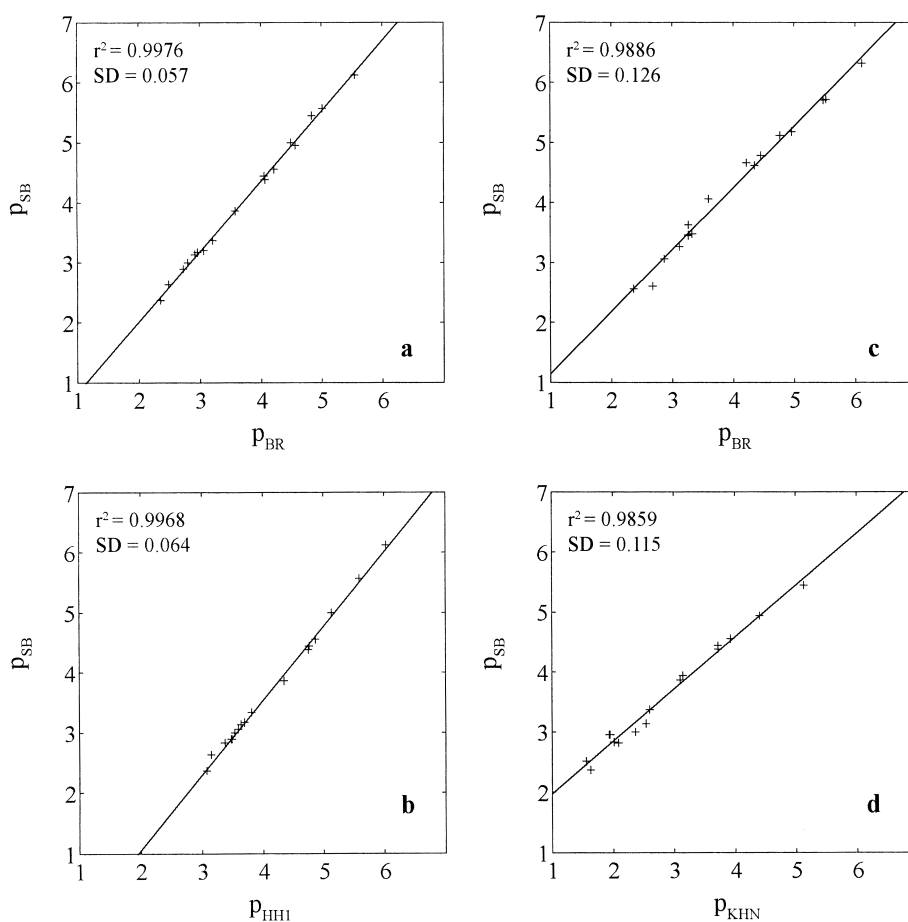


Fig. 5. Correlations between the solute polarity parameters obtained by Smith and Burr (SB) and the data reported by: (a) Bosch et al. (BR) and (b) Hanai and Hubert (HH1) in acetonitrile–water ( $n=17$ ), and (c) Bosch et al. ( $n=17$ ) and (d) Kaibara et al. (KHN) ( $n=16$ ), in methanol–water.

were used to calculate the  $p$  values expected for the new compounds if they were chromatographed using the column of Smith and Burr. The solute polarity parameters obtained in this study are given in Table 2 and extend the database in Table 1a,b.

The reliability of the transference of  $p$  data was checked by comparing the values in acetonitrile–water mixtures referred to Smith and Burr, calculated for compounds found in the lists of Hanai and Hubert, and Bosch et al., but not included in the list of Smith and Burr. The predicted  $p$  values were the following: 4-nitrophenol (2.39, 2.48), 2,4-dinitrophenol (2.84, 2.75), 2,6-dichlorophenol (3.46, 3.39), 2,4-dichlorophenol (3.55, 3.53), 3,5-dichlorophenol (3.84, 3.83), 2,4,6-trichlorophenol (4.24, 4.21), and

chrysene (6.75, 7.33), using the data of Hanai and Hubert and Bosch et al., respectively. As observed, the predictions performed using two different columns as starting point are similar, except for the most hydrophobic compound, which is found in the upper limit of the polarity domain.

#### 4.5. The $p$ polarity parameter as a retention descriptor

For each column and solvent system, the  $p$  parameter is mainly a measurement of the solute polarity, and can be useful as a descriptor of the retention behaviour in aqueous–organic RPLC. Ideally, two compounds with the same  $p$  value must have the

same retention behaviour in the same column. This is shown in Table 3, which lists retention data of compounds from the Smith and Burr series that have similar  $p$  values. As predicted by the model, solutes with similar  $p$  values present close  $k$  values in different mobile phases. The solute polarity parameter allows thus the prediction, within certain limits, of the relative location of the peaks in a chromatogram.

This means that this parameter will establish an approximate elution order and the possible overlaps or peak crossings.

In order to illustrate the descriptive capability of  $p$ , a set of 12 phenones were selected from the list of 152 compounds of Smith and Burr, chromatographed with acetonitrile–water and methanol–water mobile phases. The identity of the peaks depicted in Fig. 6,

Table 3

The polarity parameter as a descriptor of the elution behaviour in mobile phases of acetonitrile–water

Compound	$p$	Retention factor/mobile phase composition (% v/v)						
		30	40	50	60	70	80	90
<i>N,N</i> -Dimethylbenzamide	2.37		1.12	0.81	0.60	0.46	0.35	
3-Hydroxybenzotrile	2.36	2.50	1.47	0.87	0.58	0.38	0.33	
3-Methoxyphenol	2.41	2.73	1.62	0.97	0.64	0.42	0.32	
Methyl 4-hydroxybenzoate	2.39	2.44	1.48	0.88	0.61	0.40	0.33	
4-Nitrobenzyl alcohol	2.40			0.80	0.60	0.46	0.35	
Phenol	2.36	2.54	1.47	0.99	0.63	0.44	0.35	0.20
2-Chlorophenol	2.90	4.69	2.75	1.43	0.89	0.56	0.44	
2-Methylphenol	2.89	5.26	2.55	1.41	0.89	0.58	0.41	
1-Phenyl-2-propanol	2.90	4.61	2.23	1.41	0.92	0.64	0.43	
2-Phenyl-1-propanol	2.91	4.96	2.35	1.45	0.94	0.63	0.42	
2-Phenyl-2-propanol	2.92	4.73	2.29	1.48	0.97	0.66	0.42	
3-Phenyl-1-propanol	2.90	5.18	2.37	1.42	0.91	0.62	0.41	
Benzyl acetate	3.60		5.95	2.87	1.64	0.99	0.57	
2-Bromoaniline	3.60			2.41	1.57	0.97	0.70	
Methyl benzoate	3.59	10.72	5.19	2.81	1.63	1.03	0.73	0.38
4-Phenyl-2-butanone	3.62	13.05	5.05	3.16	1.66	1.01	0.58	
2-Tolualdehyde	3.62	10.73	5.43	2.89	1.70	1.11	0.58	
2-Toluonitrile	3.59	11.43	5.08	2.67	1.58	0.98	0.65	
4-Toluonitrile	3.62	12.21	5.33	2.77	1.61	0.99	0.65	
Benzene	3.85	12.52	6.57	3.42	2.04	1.27	0.87	0.45
Benzyl 2-bromoacetate	3.90		9.91			1.23	0.64	
1-Bromo-2-nitrobenzene	3.90			3.30	2.13	1.10	0.81	
4- <i>t</i> -Butylphenol	3.89			3.51	2.04	1.15	0.77	
<i>N</i> -Ethylaniline	3.93			3.03	2.08	1.18	0.87	
Ethyl phenylacetate	3.91			3.30	2.18	1.11	0.82	
Methoxybenzene	3.86	13.43	6.85	3.43	1.98	1.17	0.81	
Methyl 2-hydroxybenzoate	3.89	14.59	7.29	3.41	2.00	1.18	0.82	
Benzyl bromide	4.41	34.10	13.08	5.69	2.84	1.67	1.11	0.62
Chlorobenzene	4.38	28.58	12.32	5.51	3.01	1.77	1.13	0.57
Ethyl 3-phenylpropionate	4.40		13.39	6.18	3.12	1.69	0.89	
3-Methylanisole	4.35	26.81	11.94	5.84	2.84	1.58	1.04	
Methyl 4-phenylbutyrate	4.40	38.09	13.35	5.63	2.79	1.64	1.01	
Toluene	4.44	30.63	11.95	6.29	3.02	1.86	1.23	0.58
2-Chlorotoluene	4.97	64.45	21.19	9.16	4.73	2.56	1.50	
3-Chlorotoluene	4.95	65.48	21.29	9.13	4.68	2.51	1.45	
4-Chlorotoluene	4.94	65.56	21.45	9.07	4.64	2.48	1.44	
1,3-Dimethylbenzene	4.94	63.40	20.43	8.99	4.54	2.52	1.47	
Ethylbenzene	4.99	59.53	22.38	9.46	4.66	2.67	1.58	

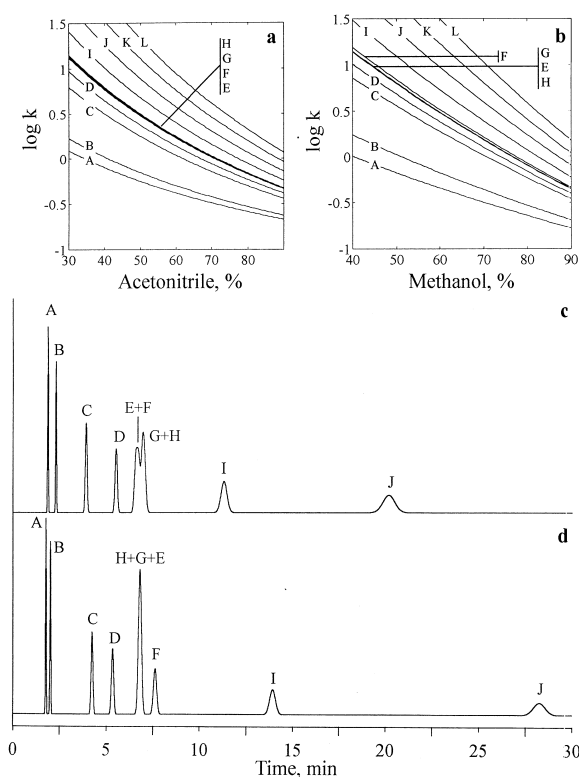


Fig. 6. Retention behaviour of a set of phenones eluted with: (a) acetonitrile–water, and (b) methanol–water mixtures. The chromatograms were drawn for: (c) 40% acetonitrile, and (d) 50% methanol. Compounds: (A) 4-hydroxyacetophenone, (B) 3-hydroxyacetophenone, (C) acetophenone, (D) 2-hydroxyacetophenone, (E) 4-methylacetophenone, (F) propiophenone, (G) 3-methylacetophenone, (H) 2-methylacetophenone, (I) butyrophenone, (J) valerophenone, (K) hexanophenone, and (L) heptanophenone. Peaks (K) and (L) are not drawn in the chromatograms due to their long retention times.

and the  $p$  values associated to both solvent systems (acetonitrile and methanol) are the following: 4-hydroxyacetophenone (A, 1.93, 1.99), 3-hydroxyacetophenone (B, 2.16, 2.36), acetophenone (C, 3.14, 3.35), 2-hydroxyacetophenone (D, 3.44, 3.59), 4-methylacetophenone (E, 3.69, 3.81), propiophenone (F, 3.70, 3.88), 3-methylacetophenone (G, 3.72, 3.82), 2-methylacetophenone (H, 3.74, 3.80), butyrophenone (I, 4.19, 4.36), valerophenone (J, 4.70, 4.90), hexanophenone (K, 5.24, 5.46), and heptanophenone (L, 5.78, 6.06).

Fig. 6a,b shows the retention behaviour of each phenone as a function of the mobile phase com-

position for each solvent system. The chromatograms in Fig. 6c,d correspond to 40% acetonitrile and 50% methanol, respectively, for which the mobile phase polarity parameter,  $P_m^N$ , is about 0.46. The chromatograms were drawn using the true (experimental)  $\log k$  data, but the peaks shown are Gaussian simulations assuming efficiencies of  $N=4000$  and asymmetry factors of  $B/A=1$ , for all compounds. A dead time of  $t_0=1$  min was arbitrarily taken. The two less polar compounds (hexanophenone and heptanophenone), that eluted at times above 30 min, are not included in the chromatograms. The experimental retention times for these compounds were 37.4 and 61.5 min for hexanophenone and 60.4 and 133.4 min for heptanophenone, in acetonitrile–water and methanol–water mixtures.

As observed, the elution order agrees with the  $p$  values and those compounds with similar polarity are overlapped. Thus, for example, compounds E, F, G and H in acetonitrile–water mixtures ( $p=3.69$ – $3.74$ ), and E, G and H in methanol–water ( $p=3.80$ – $3.82$ ) elute at similar retention times. Consequently, the  $p$  parameter constitutes a good descriptor of the retention, and can be used to obtain approximate predictions of the elution in a chromatogram. The experimental and predicted retention factors of the studied phenones were: A (0.88, 0.80), B (1.31, 1.05), C (2.9, 3.1), D (4.5, 4.4), E (5.6, 5.9), F (5.7, 5.9), G (5.9, 6.1), H (6.0, 6.2), I (10.3, 10.3), J (19.2, 18.3), K (36.4, 33.8), L (60.5, 62.3) for acetonitrile–water, and A (0.8, 0.7), B (1.02, 1.06), C (3.2, 3.6), D (4.3, 4.8), E (5.8, 6.3), F (6.6, 6.9), G (5.8, 6.4), H (5.8, 6.3), I (12.9, 12.5), J (27.2, 24.5), K (59.4, 49.1), L (132, 102), for methanol–water. As observed, the predictions are usually satisfactory.

## 5. Conclusions

The proposed algorithm, based on solute, column and mobile phase polarity parameters, can be successfully applied to predict retention data of solutes having diverse polarity. The retention can be transferred between solvent systems and columns. The results obtained in different columns, and acetonitrile–water and methanol–water systems, confirm that  $p$  is a relative measurement of solute polarity, which depends on the environment inside the col-

umn. Accordingly, the  $p$  values for the data reported by several authors, which are given in Tables 1a,b and 2, can be used to predict the retention in new columns and solvent systems. The study can be extended to other sets of compounds to add new  $p$  values and, eventually, develop a polarity database.

### Acknowledgements

This work was supported by the Ministerio de Ciencia y Tecnología of Spain (Projects BQU2001-2882 and BQU2001-3047), Generalitat de Catalunya (1999SGR00047), and Generalitat Valenciana (GR01-63). JR TL thanks the MCYT for a Ramón y Cajal position.

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