



ELSEVIER

Journal of Chromatography A, 942 (2002) 237–248

JOURNAL OF
CHROMATOGRAPHY A

www.elsevier.com/locate/chroma

Solute–solvent interactions in micellar electrokinetic chromatography

III. Characterization of the selectivity of micellar electrokinetic chromatography systems[☆]

Elisabet Fuguet^a, Clara Ràfols^a, Elisabeth Bosch^a, Michael H. Abraham^b, Martí Rosés^{a,*}

^aDepartament de Química Analítica, Universitat de Barcelona, Diagonal 647, E-08028 Barcelona, Spain

^bChemistry Department, University College London, 20 Gordon Street, London WC1H 0AJ, UK

Received 12 June 2001; received in revised form 9 October 2001; accepted 9 October 2001

Abstract

Several micellar electrokinetic chromatography (MEKC) systems (sodium dodecyl sulfate, lithium dodecyl sulfate, lithium perfluorooctanesulfonate, sodium cholate, sodium deoxycholate, tetradecyltrimethylammonium bromide and hexadecyltrimethylammonium bromide) have been characterized by means of the solvation parameter model. It has been observed that the coefficients of the correlation equations depend strongly on the particular set of compounds analyzed. Principal component analysis has been used to characterize the 2975 compounds with available solute descriptors and to select an appropriate subset of compounds to be analyzed by MEKC. With this set of compounds, the MEKC systems have been characterized. Principal component analysis has also been used to show the similarities and differences between the properties of the surfactants characterized by MEKC. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Micellar electrokinetic chromatography; Solute descriptors; Linear solvation energy relationships; Principal component analysis; Micelles; Selectivity; Surfactants

1. Introduction

Micellar electrokinetic chromatography (MEKC) is a powerful technique for the separation of mixtures of uncharged and/or charged compounds [1–

3]. The uncharged molecules are separated according to their distribution between the aqueous phase and the micellar phase. In the case of charged solutes a combination of distribution between phases and electrophoretic mobility is the reason of their separation. Migration behaviour and separation by MEKC can be easily modified through proper selection of the surfactant type, adding different complexing agents (cyclodextrins, urea, chiral additives, etc.) or adding organic solvents to the separation buffer [4–6]. Since the chemical nature of the pseudo-stationary phase has a major influence on solute–micelle interaction, it is generally agreed that the

[☆]Presented at the 30th Scientific Meeting of the Spanish Group of Chromatography and Related Techniques/1st Meeting of the Spanish Society of Chromatography and Related Techniques, Valencia, 18–20 April 2001.

*Corresponding author. Tel.: +34-93-402-1796; fax: +34-93-402-1233.

E-mail address: marti@apolo.qui.ub.es (M. Rosés).

choice of surfactant is the most important consideration to optimize selectivity [3,4], whereas surfactant concentration and the addition of organic solvents in small percentages (<10%) have a small effect on the selectivity [5]. It is important to know the nature of these interactions to achieve a better understanding of the factors that control selectivity.

The solvation parameter model is an appropriate model for characterizing the distribution of neutral solutes between a micellar phase and an aqueous buffer in MEKC. It is based on linear free energy relationships (LFERs), and it can be written as:

$$\log k = c + eE + sS + aA + bB + vV \quad (1)$$

where k is the MEKC retention factor and E , S , A , B and V are the Abraham solute descriptors. This model has been demonstrated to be extremely useful in the characterization of many physicochemical and biological processes [7,8]. E is an excess molar refraction, S the solute dipolarity/polarizability, A and B are parameters characterizing the effective hydrogen-bond acidity and hydrogen-bond basicity, respectively, and V is McGowan's characteristic volume. The values of the coefficients of the correlation reflect the system properties that interact with the corresponding solute property: e depends on the difference in capacity of the buffer and micellar phase to interact with solute n - or π -electrons; s is a measure of the difference in dipolarity/polarizability between the two phases, a and b are measures of the difference in hydrogen-bond basicity and acidity, respectively, between the buffer and micellar phase and v is a measure of the relative ease of forming a cavity for the solute in the buffer and micellar phase.

The solvation parameter model has been applied to the characterization of many MEKC systems [3–6,9–15]. The coefficients of the equation can be obtained by multiple linear regression analysis between the experimental $\log k$ values acquired for a group of solutes and their solute descriptors. This set of solutes with known descriptors must have properties sufficiently varied to define properly all interactions in Eq. (1) and be of sufficient size to establish the statistical validity of the model. Proper selection of an adequate set of solutes is one of the aspects we shall examine in detail in this work. By means of the selected group we characterize some

surfactants: sodium dodecyl sulfate (SDS), lithium dodecyl sulfate (LDS), lithium perfluorooctanesulfonate (LPFOS), sodium cholate (SC), sodium deoxycholate (SDC), tetradecyltrimethylammonium bromide (TTAB) and hexadecyltrimethylammonium bromide (HTAB). The similarities and differences between the different surfactants characterized are also discussed in terms of the fundamental interactions reflected in Eq. (1).

2. Experimental

2.1. Apparatus and conditions

All separations were performed with a Beckman P/ACE System 5500 with a UV diode array detector. The fused-silica separation capillaries were 40 cm effective length \times 50 μm I.D. When the surfactant was changed, the capillary was conditioned in the following sequence: 5 min of water, 20 min of 1 M hydroxide solution, 10 min of water, 10 min of 0.1 M hydroxide solution and 20 min of separation buffer. Prior to each separation the capillary was flushed with 5 min of separation buffer. Retention measurements were made at 25°C and +15 kV for anionic surfactants or –15 kV for cationic ones. Detection was at 214 nm. For LDS (40 mM) and LPFOS (40 mM) the separation buffers were prepared by solving the surfactants in water, adding H_3PO_4 , and neutralizing with LiOH up to pH 7.0. SDS (40 mM), SC (80 mM), TTAB (20 mM) and HTAB (20 mM) separation buffers were prepared by solving the surfactants in sodium phosphate buffer at pH 7.0, and SDC (40 mM) in sodium phosphate–sodium tetraborate buffer at pH 8.0. All separation solutions were 20 mM in buffer. Surfactant concentrations were similar to the ones used by other authors [3–5,9,13], and they were chosen to be well above the critical micelle concentration (CMC) to obtain a reasonable volume of pseudo-stationary phase and an acceptable elution window. Solute were solved in methanol (used as electroosmotic flow marker) and contained ca. 2 mg ml^{-1} of dodecanophenone as micellar marker. The injection of methanol produces a local disruption of the micellar phase. For low micellar concentrations, the disruption causes peak splitting [16], which can be

avoided working at higher concentrations such as the ones used in this work. The concentration of the solutes was 2 mg ml⁻¹, except for the alcohols which were 40% (v/v) in order to obtain a measurable absorbance. All solutions were filtered through 0.45- μ m nylon syringe filters (Albet). Samples were introduced into the capillary by a pressure of 0.5 p.s.i. during 1 s (1 p.s.i.=6894.76 Pa). The efficiency of the capillary was between 50 000 and 100 000 plates. All measurements were taken in triplicate.

2.2. Reagents and materials

Phosphoric acid (85% in water), lithium hydroxide (98%), sodium dihydrogenphosphate monohydrate (G.R.), disodium hydrogenphosphate (G.R.), disodium tetraborate anhydrous (G.R.), sodium hydroxide (G.R.), SDS (>99%), LDS (>99%) and methanol (for chromatography) were from Merck. SC (>98%), TTAB (>98%), HTAB (>99%) and LPFOS (25% in water) were from Fluka. SDC (98%) was from Aldrich. Water was Milli-Q plus (Millipore) with a resistivity of 18.2 M Ω cm. The test solutes were reagent grade or better and obtained from several makers.

2.3. Calculation

LFERs require a dependent variable directly related to the free energy change of the process (ΔG^0). In MEKC, as in common high-performance liquid chromatography (HPLC), the most convenient variable is the retention factor, k , which was calculated using Eq. (2) with the migration time of methanol used to determine the electroosmotic flow (t_{eo}), and dodecanophenone the migration time of the micelles (t_{mc}). t_R is the solute migration time:

$$k = (t_R - t_{eo}) / (1 - t_R/t_{mc}) t_{eo} \quad (2)$$

In addition, the use of k increases reproducibility since it minimizes the variation of t_R , t_{eo} and t_{mc} between the different replicates of the same sample.

Principal component analysis (PCA) was done with Matlab package version 4.2b from MathWorks (Natick, MA, USA).

3. Results and discussion

3.1. Selection of appropriate solutes

The accurate determination of the coefficients of Eq. (1) requires the determination of the MEKC retention of a set of solutes of known descriptors. The literature gives the recommendations to select an appropriate collection of solutes [4]: they have to embrace a wide range of descriptor values, there should be an absence of significant cross-correlation among the descriptors, and clustering of individual descriptor values should be avoided. In addition, in MEKC systems the solutes should have a reasonable absorbance between 200 and 250 nm for convenient detection and be neutral at the working pH.

The current database available contains more than 4000 solutes characterized by some of their descriptors. 2975 of these solutes have all the five descriptors needed for correlation through Eq. (1). Some procedure is required to select a subset of solutes appropriate for characterization of MEKC systems. PCA is a powerful chemometric technique widely used to characterize differences and similarities between the individual components of large sets of data [17]. We have applied PCA here to the solute properties database in order to select an adequate subset. The aim of the principal components (PCs) study is to provide a tool (PC values) to select compounds with properties that may contribute to solute–solvent interactions with different relative weights of the descriptors. This requires a pretreatment of the solute descriptor data because direct PCA with the original solute descriptors only points out differences between solutes with extreme descriptor values. For instance, two alkanes with very different volumes, such as methane and hexacotane, will have very different PC values although they behave the same type of solute–solvent interactions.

The most common and efficient data pretreatment in PCA is column and/or row normalization. Column (or descriptors) normalization transforms each descriptor to have a mean of zero and a standard deviation (SD) of one for the whole set of compounds. However, this pretreatment does not solve the problem of the extreme values and in fact it does not alter significantly the data and the PC results

Table 1

Contribution of the solute descriptors to the principal components (loadings matrix) and percentage of variance explained for each component

	<i>E</i>	<i>S</i>	<i>A</i>	<i>B</i>	<i>V</i>	Variance (%)
PC1	0.02	2.07	-6.13	-2.40	6.45	67
PC2	-4.22	-3.14	1.82	2.03	3.51	19
PC3	2.78	-3.00	1.85	-3.17	1.54	9
PC4	-2.16	2.58	2.25	-2.91	0.23	5

because the original descriptors are already more or less normalized between zero and one.

In row (or compound) normalization, the descriptors of each compound are normalized to have a mean of zero and standard deviation of one for each compound. With this pretreatment, all compounds

with proportional descriptors have the same normalized descriptors (e.g., methane and hexacontane). Therefore, the compounds are evaluated according to the different weights of the original descriptors. The original data set has been normalized according to this method. Table 1 and Fig. 1 show the results obtained. Four PCs explain the compounds properties. PC1 explains 67% of the variance. Solute volume (*V*) and hydrogen-bond acidity (*A*) are the solute properties that have the largest contributions to this component. *V* has a positive contribution and *A* has a negative one. So, compounds with high hydrogen-bond acidity and low volume values present the lowest PC1 values. This is the case of water, methanol, thiourea and formic acid which have PC1 values lower than -0.05. Some polyhydroxybenzenes with a larger volume but also larger hydrogen-

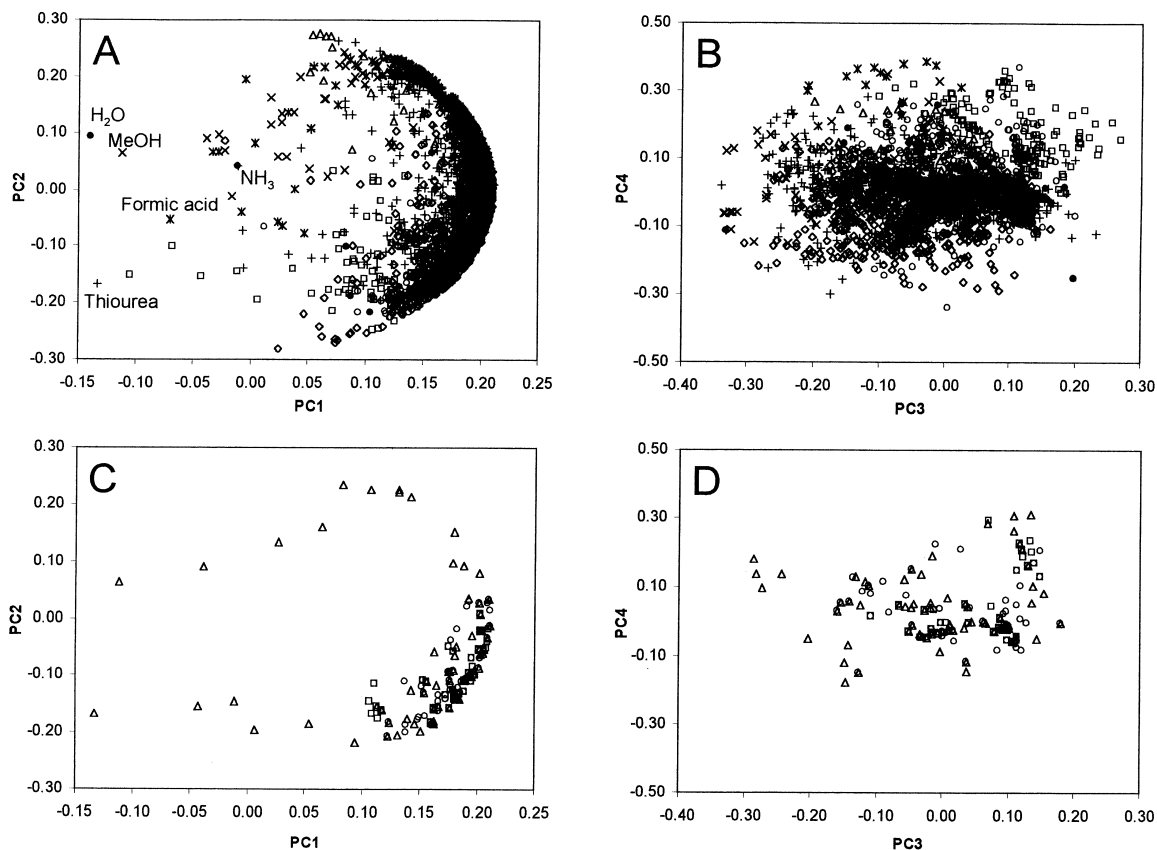


Fig. 1. Scores plots of the four principal components of solute descriptors: (A) and (B) for the all database available (2975 solutes): (•) inorganic compounds, (×) aliphatic alcohols, (Δ) fluoroalkanes, (*) aliphatic acids, (+) other aliphatic compounds, (□) phenols, (○) other aromatic compounds, (◇) heterocyclic compounds. (C) and (D) plots for selected sets: (Δ) this work, (○) Ref. [4], (□) Ref. [11].

bond acidity ($A \gg 1.0$) have very low PC1 values too.

PC2 explains 19% of the variance. The main contributions to this component are polarizability (E), dipolarity (S) and volume (V). High PC2 values correspond to solutes with low E and S and high V values. Fig. 1A shows that aliphatic compounds and specially polyfluoroalkanes have high PC2 values whereas the most polarizable, and in general larger, aromatic compounds have lower PC2 values.

PC3 and PC4 (Fig. 1B) explain only 9 and 5% of variance, respectively. PC3 is mostly related to hydrogen-bond basicity and dipolarity, which decrease its value, and also to polarizability that increases PC3. Aromatic compounds, which are quite polarizable, present high PC3 values. All the descriptors, except V , contribute to a similar degree to PC4. The combination of descriptors seems to concentrate heterocyclic compounds in the range of low PC4 values.

The compounds we have finally selected for MEKC systems are given in Table 2 with their descriptors [4,7,18,19] and PC values. The selected set is plotted in Fig. 1C and D, and compared with some other sets of compounds selected by other authors [4,13]. In comparison with the other sets, our compounds embrace a wider range of PC values. The compounds proposed in the literature, which are similar to the ones we used in previous work [15], are aromatic compounds with high PC1 and low PC2 values. We have enlarged these sets mainly with small hydrogen-bond donors (thiourea, alcohols, polyhydroxybenzenes) of low PC1 values and with aliphatic compounds of high PC2 values. It would have been interesting to select also some compounds with PC1 and PC2 values close to zero, like carboxylic acids, urea or ammonia, but these compounds did not absorb in the UV and/or were ionized at the working pH. However, we propose these compounds for other techniques not limited by these constraints, such as HPLC with refractive index detection.

The cross-correlation matrix between the PC values of the selected set of solutes is given in Table 3. It can be observed that all correlation coefficients are low and therefore there is no cross-correlation between the principal components of the selected set of solutes.

3.2. Characterization of MEKC systems

SDS, LDS, LPFOS, SC, SDC, TTAB and HTAB have been characterized with the solvation parameter model through Eq. (1) by analysis of the $\log k$ data of the 71 solutes selected. Fig. 2 presents the chemical structures of the monomers of the tensioactive compounds studied.

The k values obtained in the different MEKC systems are presented in Table 4. In consonance with previous work [11,15], methanol and dodecanophenone have been used as electroosmotic flow and micellar markers, respectively. Propan-1-ol, propan-2-ol, propan-1,3-diol and butan-1,4-diol coelute with methanol in the systems studied (except butan-1,4-diol in SDS). SDC presents a low solubility at pH 7.0, and the experimental data have been obtained at pH 8.0. At this pH the solutes with pK_a values between 9 and 10 (hydroquinone, resorcinol, catechol, 1,2,3-trihydroxybenzene, 2-naphthol and 4-chlorophenol) are partially ionized and their retention has not been measured. The cationic systems present an elution window smaller than that of the anionic systems, and some solutes of high volume values coelute with the micellar marker. In these systems almost all alcohols coelute with methanol.

The system constants and the statistics for the fit of the solvation parameter model to the experimental $\log k$ data are summarized in Table 5. The coefficients obtained for each system are similar to the ones obtained for other authors in similar conditions [4,5,13,15]. The slight differences observed in some cases may come from the differences in the selection of the analyzed set of compounds. The largest differences are observed for LPFOS. In this case, the correlation constants given in Table 5 are quite different from the ones we have published in a previous paper [15] with a smaller set of solutes. For the same surfactant, other authors [13] have found correlations that do not agree with the one we published previously, or with the ones we present in Table 5. We believe that these discrepancies stem from the different sets of solutes analyzed, although we cannot discard some differences on the purity of the tensioactive compound used. This points out the importance of proper solute selection, which seems to be much more significant for LPFOS than for the other surfactants analyzed, where there is a major

Table 2
 Descriptors and principal components of the selected solutes

Solute	<i>E</i>	<i>S</i>	<i>A</i>	<i>B</i>	<i>V</i>	PC1	PC2	PC3	PC4
Methanol	0.278	0.44	0.43	0.47	0.3082	-0.112	0.065	-0.273	0.099
Propan-1-ol	0.236	0.42	0.37	0.48	0.5900	0.107	0.226	-0.124	0.046
Propan-2-ol	0.212	0.36	0.33	0.56	0.5900	0.083	0.234	-0.143	-0.069
Butan-1-ol	0.224	0.42	0.37	0.48	0.7309	0.131	0.221	-0.057	0.045
Pentan-1-ol	0.219	0.42	0.37	0.48	0.8718	0.141	0.214	-0.018	0.041
Pentan-3-ol	0.218	0.36	0.33	0.56	0.8718	0.131	0.225	-0.035	-0.035
Propan-1,3-diol	0.397	0.91	0.77	0.85	0.6487	-0.038	0.091	-0.286	0.180
Butan-1,4-diol	0.395	0.93	0.72	0.90	0.7860	0.026	0.133	-0.283	0.139
Pentan-1,5-diol	0.388	0.95	0.72	0.91	0.9305	0.065	0.160	-0.244	0.137
Thiourea	0.840	0.82	0.77	0.87	0.5696	-0.133	-0.167	-0.149	-0.120
Benzene	0.610	0.52	0.00	0.14	0.7164	0.194	-0.096	0.078	-0.028
Toluene	0.601	0.52	0.00	0.14	0.8573	0.201	-0.053	0.086	-0.019
Ethylbenzene	0.613	0.51	0.00	0.15	0.9982	0.203	-0.021	0.096	-0.022
Propylbenzene	0.604	0.50	0.00	0.15	1.1391	0.203	0.009	0.100	-0.017
Butylbenzene	0.600	0.51	0.00	0.15	1.2800	0.202	0.028	0.101	-0.010
<i>p</i> -Xylene	0.613	0.52	0.00	0.16	0.9982	0.203	-0.021	0.091	-0.022
Naphthalene	1.340	0.92	0.00	0.20	1.0854	0.163	-0.158	0.106	-0.059
Chlorobenzene	0.718	0.65	0.00	0.07	0.8388	0.189	-0.107	0.087	0.012
Bromobenzene	0.882	0.73	0.00	0.09	0.8914	0.180	-0.130	0.094	-0.007
Anisole	0.708	0.75	0.00	0.29	0.9160	0.201	-0.086	0.017	-0.024
Benzaldehyde	0.820	1.00	0.00	0.39	0.8730	0.183	-0.140	-0.046	-0.011
Acetophenone	0.818	1.01	0.00	0.48	1.0139	0.195	-0.103	-0.051	-0.029
Propiophenone	0.804	0.95	0.00	0.51	1.1548	0.205	-0.061	-0.031	-0.044
Butyrophenone	0.797	0.95	0.00	0.51	1.2957	0.209	-0.033	-0.016	-0.037
Valerophenone	0.795	0.95	0.00	0.50	1.4366	0.211	-0.011	-0.001	-0.029
Heptanophenone	0.720	0.95	0.00	0.50	1.7184	0.210	0.034	0.010	-0.010
Dodecanophenone	0.720	0.95	0.00	0.50	2.4229	0.202	0.081	0.043	0.000
Benzophenone	1.447	1.50	0.00	0.50	1.4808	0.185	-0.140	0.009	-0.021
Methyl benzoate	0.733	0.85	0.00	0.46	1.0726	0.206	-0.055	-0.024	-0.046
Benzyl benzoate	1.264	1.42	0.00	0.51	1.6804	0.202	-0.087	0.010	-0.009
Benzonitrile	0.742	1.11	0.00	0.33	0.8711	0.180	-0.137	-0.067	0.046
Aniline	0.955	0.96	0.26	0.50	0.8162	0.163	-0.184	-0.008	-0.034
<i>o</i> -Toluidine	0.970	0.90	0.23	0.59	0.9751	0.184	-0.131	-0.005	-0.085
3-Chloroaniline	1.050	1.10	0.30	0.36	0.9390	0.163	-0.181	0.038	0.043
4-Chloroaniline	1.060	1.10	0.30	0.35	0.9390	0.161	-0.183	0.034	0.051
2-Nitroaniline	1.180	1.37	0.30	0.36	0.9904	0.151	-0.197	0.007	0.071
3-Nitroaniline	1.200	1.71	0.40	0.35	0.9904	0.131	-0.204	-0.034	0.137
4-Nitroaniline	1.220	1.91	0.42	0.38	0.9904	0.123	-0.206	-0.049	0.151
Nitrobenzene	0.871	1.11	0.00	0.28	0.8906	0.177	-0.156	-0.028	0.033
2-Nitroanisole	0.965	1.34	0.00	0.38	1.0902	0.181	-0.142	-0.048	0.038
Benzamide	0.990	1.50	0.49	0.67	0.9728	0.139	-0.177	-0.117	0.117
4-Aminobenzamide	1.340	1.94	0.80	0.94	1.0726	0.094	-0.216	-0.132	0.129
Acetanilide	0.870	1.36	0.46	0.69	1.1137	0.176	-0.107	-0.112	0.106
4-Chloroacetanilide	0.980	1.50	0.64	0.51	1.2357	0.165	-0.117	-0.016	0.193
Phenol	0.805	0.89	0.60	0.30	0.7751	0.117	-0.160	0.121	0.209
3-Methylphenol	0.822	0.88	0.57	0.34	0.9160	0.157	-0.111	0.129	0.165
2,3-Dimethylphenol	0.850	0.90	0.52	0.36	1.0569	0.181	-0.065	0.138	0.104
2,4-Dimethylphenol	0.840	0.80	0.53	0.39	1.0569	0.182	-0.048	0.153	0.083
Thymol	0.822	0.79	0.52	0.44	1.3387	0.192	0.035	0.134	0.053
4-Chlorophenol	0.915	1.08	0.67	0.20	0.8975	0.113	-0.153	0.116	0.229
Catechol	0.970	1.10	0.88	0.47	0.8338	0.054	-0.185	0.107	0.265
Resorcinol	0.980	1.00	1.10	0.58	0.8338	-0.011	-0.144	0.133	0.312
Hydroquinone	1.000	1.00	1.16	0.60	0.8338	0.006	-0.195	0.068	0.287

Table 2. Continued

Solute	<i>E</i>	<i>S</i>	<i>A</i>	<i>B</i>	<i>V</i>	PC1	PC2	PC3	PC4
2-Naphthol	1.520	1.08	0.61	0.40	1.1441	0.124	−0.183	0.179	−0.002
1,2,3-Trihydroxybenzene	1.165	1.35	1.35	0.62	0.8925	−0.042	−0.154	0.107	0.307
Furan	0.369	0.53	0.00	0.13	0.5363	0.198	−0.094	−0.019	0.053
2,3-Benzofuran	0.888	0.83	0.00	0.15	0.9053	0.183	−0.137	0.062	0.000
Quinoline	1.268	0.97	0.00	0.51	1.0443	0.167	−0.154	0.036	−0.117
Pyrrrole	0.613	0.73	0.41	0.29	0.5774	0.146	−0.185	−0.059	0.121
Pyrimidine	0.606	1.00	0.00	0.65	0.6342	0.143	−0.126	−0.204	−0.051
Antipyrine	1.320	1.50	0.00	1.48	1.5502	0.162	−0.059	−0.146	−0.177
Caffeine	1.500	1.60	0.00	1.33	1.3632	0.154	−0.129	−0.127	−0.149
Corticosterone	1.860	3.43	0.40	1.63	2.7389	0.179	−0.091	−0.142	0.058
Cortisone	1.960	3.50	0.36	1.87	2.7546	0.175	−0.093	−0.159	0.029
Hydrocortisone	2.030	3.49	0.71	1.90	2.7975	0.176	−0.092	−0.154	0.053
Estradiol	1.800	3.30	0.88	0.95	2.1988	0.203	−0.063	0.066	−0.005
Estratriol	2.000	3.36	1.40	1.22	2.2575	0.195	−0.029	0.036	−0.143
Monuron	1.140	1.50	0.47	0.78	1.4768	0.198	−0.090	−0.045	0.049
Myrcene	0.483	0.29	0.00	0.21	1.3886	0.188	0.092	0.110	−0.044
α-Pinene	0.446	0.14	0.00	0.12	1.2574	0.178	0.096	0.143	−0.052
Geraniol	0.513	0.63	0.39	0.66	1.4903	0.179	0.152	0.032	−0.016
Average	0.894	1.116	0.328	0.538	1.1296	0.147	−0.063	−0.008	0.037
SD	0.430	0.742	0.362	0.389	0.5122	0.074	0.121	0.112	0.105

agreement between the results obtained from different sets of compounds. The PCA shows that the set we have selected embraces a larger variety of compound properties than those previously proposed, and we strongly recommend to characterize MEKC systems with compound sets similar to the one of Table 2.

The comparison between the coefficients of each system shows that solute volume and hydrogen-bond basicity are the two descriptors that present the largest coefficients (*v* and *b*, respectively). In all the systems the cavity contribution is more favourable to partition to the micelle than to water ($v > > 0$). The negative *b* coefficient indicates the hydrogen-bond acidity of the micelles is lower than the hydrogen-bond acidity of water. The least acidic are cationic micelles, whereas LPFOS is only slightly less acidic

than water. LDS, SDS, SDC and SC have an acidity intermediate between those of the other systems. The contribution of the solute hydrogen-bond acidity term (*a* coefficient) depends on the type of surfactant. The cationic ones have the largest positive values, so they should be the most basic of the systems studied and they are also more basic than water. SC has a value of hydrogen-bond basicity lower than the cationic surfactants, but it is still a better hydrogen-bond acceptor than water. The *a* coefficient for the SDC system is very close to 0, which indicates that the hydrogen-bond acceptor ability of SDC micelles is similar to that of water. SDS, LSD and LPFOS have negative *a* coefficients, showing that all these systems are less hydrogen-bond basic than water. LPFOS has the lowest *a* value, so it is much less hydrogen-bond basic than LDS, SDS, water and the other surfactants.

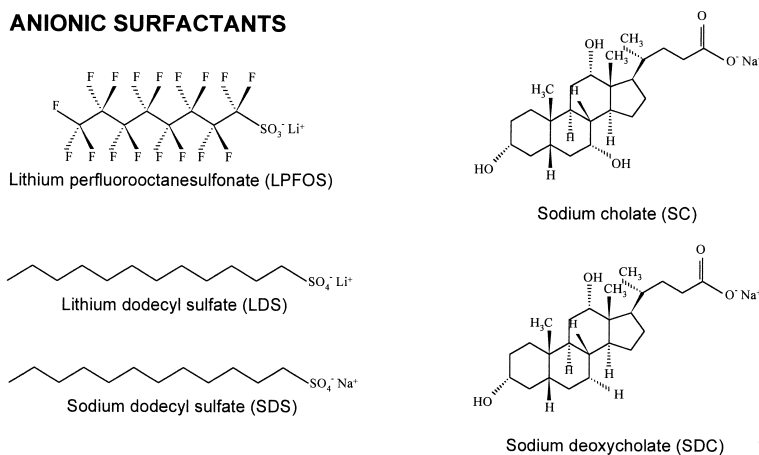
All the systems have negative *s* coefficient values, which show that they are less dipolar than water. There are no large differences in dipolarity between systems because all of them show moderate *s* values. Regarding the *e* coefficient, all surfactant systems have positive values except LPFOS. The most polarizable surfactants are TTAB, HTAB and SDC, while LDS, SDS and SC have moderate *e* values.

Table 3

Correlation matrix between the solute principal components (r^2)

	PC1	PC2	PC3	PC4	PC5
PC1	1				
PC2	0.002	1			
PC3	0.135	0.054	1		
PC4	0.226	0.038	0.004	1	
PC5	0.049	0.034	0.039	0.005	1

ANIONIC SURFACTANTS



CATIONIC SURFACTANTS

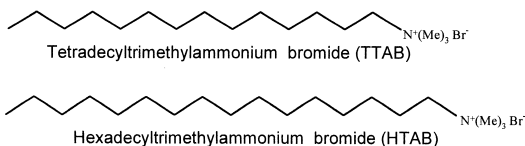


Fig. 2. Chemical structures of the monomers of the tensioactive compounds studied.

LPFOS is slightly less polarizable than water and quite less polarizable than the rest of the systems. This behaviour can be attributed to the high electronegativity of the fluorine atoms in the alkylic chain, compared to the hydrocarbon chains or rings of the other surfactants [3,15]. The constant c of the correlations is related to the phase ratio for the separation system, and it depends on the critical micelle concentration, the overall surfactant concentration and the molar volume of the surfactant [4,9,15].

The analysis of the coefficients of Table 5 shows that LPFOS, TTAB and HTAB systems, which have large absolute values of the a coefficient, would be very appropriate to separate mixtures of compounds differing in their hydrogen-bond acidity. LPFOS system has a low absolute b value as compared with the other systems, therefore it would be the least convenient system to separate mixtures of compounds with different hydrogen-bond basicity. It would also be the least convenient system to separate compounds by their polarity (s coefficient) and polarizability (e coefficient). All systems show a

similar ability (similar v coefficient) to separate compounds according to their size.

In order to characterize the similarities and differences between the surfactants studied, we have applied PCA to the coefficients of Eq. (1) given in Table 5. PCA has been applied in two modalities: direct analysis of the coefficients e , s , a , b , and v ; and PCA after row normalization of these coefficients. The first modality should identify correlations between the surfactant descriptors (coefficients), whereas the second method should classify the surfactants according to their ability to interact with solutes, as it has been previously explained for solute selection. In fact, both methods give very similar results, as can be observed in the PC2 vs. PC1 plots of Fig. 3. This figure shows that the MEKC systems are clustered according to the chemical nature of the surfactant: TTAB and HTAB, SC and SDC, and SDS and LDS, whereas LPFOS shows very different PC values.

The contributions of the coefficients to the different PCs are given in Table 6 (for PCA without normalization). According to the F -test and to the

Table 4
Solute retention factors in the studied systems

Solute	<i>k</i>						
	LPFOS	LDS	SDS	SC	SDC	TTAB	HTAB
Methanol	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Propan-1-ol	~0	~0	~0	~0	~0	~0	~0
Propan-2-ol	~0	~0	~0	~0	~0	~0	~0
Butan-1-ol	0.53	0.49	0.50	0.44	0.28	~0	~0
Pentan-1-ol	0.82	0.82	0.82	0.67	0.39	0.26	~0
Pentan-3-ol	0.60	0.56	0.57	0.46	0.30	~0	~0
Propan-1,3-diol	~0	~0	~0	~0	~0	~0	~0
Butan-1,4-diol	~0	~0	0.20	~0	~0	~0	~0
Pentan-1,5-diol	0.35	0.27	0.27	0.26	0.23	~0	~0
Thiourea	~0	0.24	0.24	0.33	0.25	0.22	0.24
Benzene	0.60	0.95	0.90	0.94	0.68	0.85	0.97
Toluene	0.83	1.48	1.41	1.53	1.19	1.31	1.52
Ethylbenzene	1.10	2.20	2.10	2.33	1.94	1.91	2.24
Propylbenzene	1.52	3.54	3.42	3.61	3.07	2.98	3.42
Butylbenzene	2.11	5.75	5.62	4.97	4.40	4.57	4.58
<i>p</i> -Xylene	1.13	2.28	2.23	2.35	2.00	1.97	2.33
Naphthalene	1.12	3.04	2.90	2.75	2.47	3.04	3.61
Chlorobenzene	0.82	1.66	1.60	1.74	1.34	1.55	1.79
Bromobenzene	0.84	1.91	1.88	2.04	1.63	1.83	2.14
Anisole	0.87	1.23	1.14	1.00	0.77	1.01	1.13
Benzaldehyde	0.94	1.02	0.93	0.63	0.55	0.68	0.76
Acetophenone	1.24	1.23	1.12	0.72	0.64	0.77	0.85
Propiophenone	1.60	1.70	1.55	1.00	0.87	1.12	1.26
Butyrophenone	2.12	2.43	2.23	1.43	1.24	1.62	1.84
Valerophenone	2.85	3.61	3.35	2.13	1.93	2.44	2.85
Heptanophenone	5.62	9.05	8.98	4.48	— ^a	— ^a	— ^a
Dodecanophenone	~∞	~∞	~∞	~∞	~∞	~∞	~∞
Benzophenone	2.85	3.90	3.61	2.29	2.02	2.60	2.97
Methyl benzoate	1.48	1.68	1.54	1.06	0.87	1.09	1.22
Benzyl benzoate	3.34	6.88	7.34	3.82	3.68	5.04	— ^a
Benzonitrile	0.98	1.01	0.94	0.64	0.54	0.71	0.79
Aniline	0.53	0.73	0.68	0.48	0.40	0.62	0.70
<i>o</i> -Toluidine	0.68	0.99	0.93	0.62	0.51	0.86	0.96
3-Chloroaniline	0.57	1.08	1.20	0.98	0.69	1.49	1.71
4-Chloroaniline	0.59	1.29	1.24	1.04	0.71	1.44	1.64
2-Nitroaniline	0.85	1.30	1.21	0.94	0.73	1.41	1.62
3-Nitroaniline	0.64	0.99	0.94	0.76	0.59	1.11	1.27
4-Nitroaniline	0.60	1.02	0.97	0.88	0.67	1.20	1.36
Nitrobenzene	0.97	1.26	1.02	0.83	0.64	0.90	1.02
2-Nitroanisole	1.33	1.32	1.22	0.90	0.70	1.08	1.20
Benzamide	0.63	0.75	0.69	0.55	0.50	0.56	0.62
4-Aminobenzamide	0.39	0.54	0.50	0.51	0.47	0.28	0.34
Acetanilide	0.66	0.92	0.83	0.67	0.57	0.73	0.81
4-Chloroacetanilide	0.88	1.77	1.59	1.45	1.02	1.63	1.85
Phenol	0.41	0.71	0.68	0.64	0.52	1.04	1.18
3-Methylphenol	0.58	1.06	1.00	0.88	0.67	1.54	1.80
2,3-Dimethylphenol	0.73	1.48	1.41	1.28	0.91	2.18	2.62
2,4-Dimethylphenol	0.78	1.59	1.50	1.32	0.95	2.24	2.67
Thymol	1.18	2.66	2.62	2.10	1.44	3.55	4.65
4-Chlorophenol	0.51	1.34	1.32	1.41	— ^b	2.37	2.85
Catechol	0.33	0.55	0.59	0.60	— ^b	1.09	1.35

Table 4. Continued

Solute	<i>k</i>						
	LPFOS	LDS	SDS	SC	SDC	TTAB	HTAB
Resorcinol	0.29	0.50	0.49	0.64	– ^b	1.16	1.34
Hydroquinone	0.17	0.42	0.39	0.57	– ^b	0.66	0.78
2-Naphthol	0.79	2.25	2.15	1.94	– ^b	– ^a	– ^a
1,2,3-Trihydroxybenzene	0.31	0.41	0.44	0.57	– ^b	1.06	1.39
Furan	0.46	0.51	0.49	0.41	0.34	0.43	0.49
2,3-Benzofuran	0.86	1.66	1.60	1.60	1.25	1.64	1.88
Quinoline	2.04	1.85	1.85	1.00	0.91	1.04	1.18
Pyrrrole	0.29	0.41	0.40	0.38	0.30	0.52	0.58
Pyrimidine	0.50	0.32	0.30	0.34	0.27	0.17	~0
Antipyrine	2.23	1.14	1.00	0.50	0.49	0.34	0.41
Caffeine	0.89	0.83	0.74	0.58	0.59	0.33	0.42
Corticosterone	5.31	7.21	7.51	1.34	1.54	3.88	4.48
Cortisone	4.05	4.30	4.12	1.07	1.18	2.31	2.66
Hydrocortisone	2.51	4.37	4.34	1.19	1.29	2.95	3.32
Estradiol	2.38	8.44	8.26	3.06	2.89	– ^a	– ^a
Estratriol	1.04	3.30	3.14	1.95	1.91	– ^a	3.87
Monuron	1.06	1.63	1.45	1.17	0.85	1.28	1.41
Myrcene	2.79	7.03	7.27	10.79	6.32	4.19	3.80
α-Pinene	3.43	8.17	8.66	7.40	6.22	4.42	4.99
Geraniol	2.25	3.45	3.29	1.99	1.51	2.03	2.48

^a Solutes that coelute with dodecanophenone.

^b Solutes with pK_a values between 9 and 10 and therefore partially ionized at pH 8.

indicator (IND) function [17], two PCs suffice to explain the data. These two PCs explain more than 99% of the variance. The main contributions to PC1 are differences on lipophilicity (v) and on hydrogen-bond acidity (b) between surfactant micelle and water. The main contribution to PC2 is the difference between the hydrogen-bond basicities of surfactant and water (a coefficient).

The above results indicate a strong correlation between the properties of the MEKC systems, and therefore between the properties of the surfactant micelles. Two MEKC coefficients are enough to

describe the differences between all the systems. One is undoubtedly the v coefficient which is the main contribution to PC1 and which does not show good correlations with the other coefficients. The second coefficient may be b or a , which show the largest variability and have major contributions to PC1 and PC2, respectively. This has been confirmed by target factor analysis [17] of the coefficient data which gives combinations of v and b or v and a as the best target factors.

The relationships between the polarizability (e), dipolarity (s), hydrogen-bond basicity (a) and hydro-

Table 5

Constants for the micellar separation systems (standard deviations in parentheses)

System	Coefficient						Statistics			
	c	e	s	a	b	v	n	r	SD	F
LPFOS (40 mM)	–1.410 (0.087)	–0.113 (0.132)	–0.243 (0.096)	–0.876 (0.078)	–0.455 (0.111)	1.966 (0.095)	62	0.970	0.190	180
LDS (40 mM)	–1.575 (0.056)	0.586 (0.086)	–0.595 (0.067)	–0.317 (0.052)	–1.565 (0.074)	2.609 (0.064)	63	0.989	0.128	526
SDS (40 mM)	–1.680 (0.052)	0.558 (0.079)	–0.596 (0.063)	–0.266 (0.049)	–1.674 (0.071)	2.717 (0.061)	63	0.991	0.120	618
SC (80 mM)	–1.408 (0.085)	0.691 (0.127)	–0.693 (0.097)	0.117 (0.078)	–1.937 (0.111)	2.274 (0.104)	62	0.962	0.191	139
SDC (40 mM)	–1.833 (0.120)	0.926 (0.202)	–0.867 (0.146)	0.070 (0.143)	–1.785 (0.146)	2.422 (0.130)	58	0.949	0.260	94
TTAB (20 mM)	–1.851 (0.051)	0.902 (0.083)	–0.617 (0.051)	0.766 (0.042)	–2.410 (0.059)	2.634 (0.047)	53	0.994	0.089	746
HTAB (20 mM)	–1.833 (0.055)	1.112 (0.089)	–0.755 (0.051)	0.824 (0.040)	–2.437 (0.057)	2.710 (0.049)	49	0.994	0.081	690

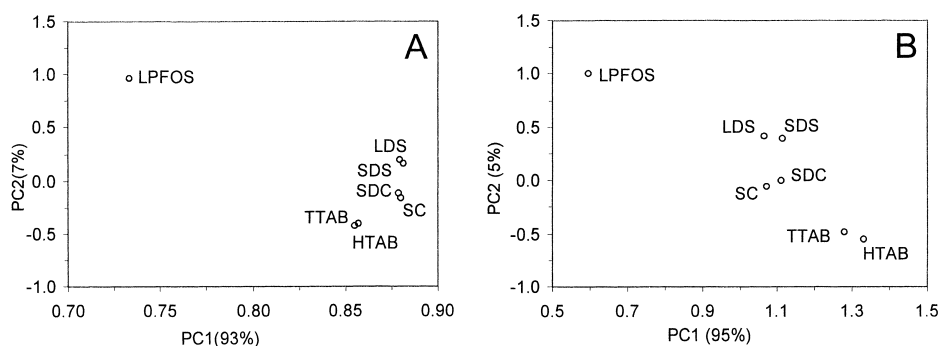


Fig. 3. Scores plots of the two principal components of the coefficients of the solvation parameter model applied to MEKC systems: (A) after row normalization, (B) without any pretreatment.

gen-bond acidity (b) of the micelles can be observed in Fig. 4, where e , s , and a coefficients have been plotted against the b coefficient. When the hydrogen-bond acidity of the surfactant increases, the dipolarity (s) increases too, but the polarizability (e) and the hydrogen-bond basicity (a) decrease. These good correlations would be reasonable if all surfactants studied would belong to the same chemical family, but they are surprising for compounds of such different nature as sulfates, sulfonates, cholates and quaternary ammoniums.

Also surprising are the large differences on hydrogen-bond acidity (b coefficient) between the different MEKC systems, for instance LPFOS has a hydrogen-bond acidity quite similar to that of water when in fact, it has no hydrogen-bond donor group. It has been argued that the hydrogen-bond acidity of LPFOS stems from the inductive effect of the fluorine atoms on the water molecules in contact with the surfactant [3,15]. The same argument can explain the good correlations observed between the e , s , a , and b coefficients of the surfactants. Interstitial water in the micelles would cause most of the dipole and hydrogen-bond interactions between sol-

utes and micelles. These would be affected by the water environment (i.e., the micellar surfactant), which would favour some interactions and not favour other ones.

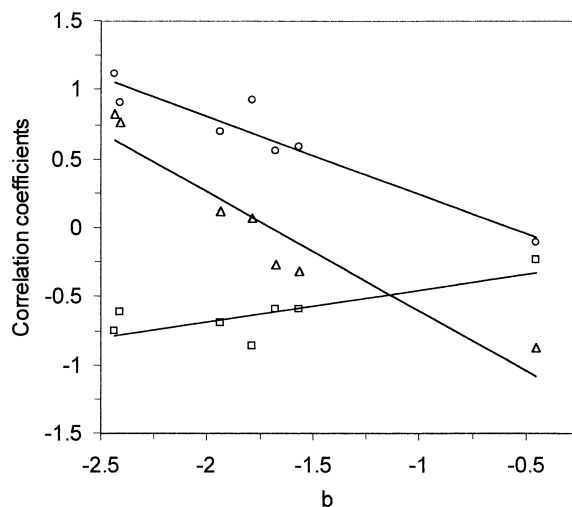


Fig. 4. Correlations between the coefficients of the solvation parameter model applied to MEKC systems: (○) e vs. b , (□) s vs. b , (△) a vs. b .

Table 6

Contribution of the system coefficients to the principal components (loadings matrix) and percentage of variance explained for each component

	e	s	a	b	v	Variance (%)
PC1	0.654	-0.579	0.131	-1.663	2.236	95.16
PC2	-0.418	0.036	-1.046	-0.516	0.576	4.54
PC3	0.381	-0.431	-0.246	0.040	-0.179	0.23
PC4	-0.189	-0.013	-0.191	-0.332	-0.184	0.06
PC5	0.163	0.199	-0.089	-0.039	-0.020	0.01

Acknowledgements

The financial support of the DGICYT (project PB98-1257) of the Spanish Government and the CIRIT (1999SGR00047) of the Catalan Government is gratefully acknowledged. We also acknowledge the helpful assistance of Dr. Anna de Juan in the principal component analysis.

References

- [1] S. Terabe, N. Chen, K. Otsuka, *Adv. Electrophoresis* 7 (1994) 87.
- [2] D.R. Baker, *Capillary Electrophoresis*, Wiley–Interscience, New York, 1995.
- [3] C.F. Poole, S.K. Poole, *J. Chromatogr. A* 792 (1997) 89.
- [4] C.F. Poole, S.K. Poole, M.H. Abraham, *J. Chromatogr. A* 798 (1998) 207.
- [5] S.K. Poole, C.F. Poole, *Analyst* 122 (1997) 267.
- [6] S.K. Poole, C.F. Poole, *Anal. Commun.* 34 (1997) 57.
- [7] M.H. Abraham, *Chem. Soc. Rev.* 22 (1993) 73.
- [8] M.H. Abraham, H.S. Chadha, F. Martins, R.C. Mitchell, M.W. Bradbury, J.A. Gratton, *Pestic. Sci.* 55 (1999) 78.
- [9] S. Yang, M.G. Khaledi, *Anal. Chem.* 67 (1995) 499.
- [10] S.K. Poole, C.F. Poole, *J. High Resolut. Chromatogr.* 20 (1997) 174.
- [11] M. Rosés, C. Ràfols, E. Bosch, A.M. Martínez, M.H. Abraham, *J. Chromatogr. A* 845 (1999) 217.
- [12] M.D. Trone, M.G. Khaledi, *Anal. Chem.* 71 (1999) 1270.
- [13] M.D. Trone, M.G. Khaledi, *J. Chromatogr. A* 886 (2000) 245.
- [14] P.G. Muijselaar, H.A. Claessens, C.A. Cramers, *Anal. Chem.* 69 (1997) 1184.
- [15] E. Fuguet, C. Ràfols, E. Bosch, M. Rosés, M.H. Abraham, *J. Chromatogr. A* 907 (2001) 257.
- [16] C. Ràfols, A. Poza, E. Fuguet, M. Rosés, E. Bosch, in preparation.
- [17] E.R. Malinowski, *Factor Analysis in Chemistry*, Wiley, New York, 1991.
- [18] M.H. Abraham, H.S. Chadha, G.S. Whiting, R.C. Mitchell, *J. Pharm. Sci.* 83 (1994) 1085.
- [19] M.H. Abraham, *The UCL Database*, University College London, 1997.