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# Characterization of stationary phases based on monosubstituted benzene retention indices using correspondence factor analysis and linear solvation energy relationships in RPLC

Hassina Larbi<sup>1</sup> · Linda Didaoui<sup>1</sup> · Michel Righezza<sup>2</sup>

## Abstract

In reversed-phase liquid chromatography (RPLC), the comparison of experimental results obtained from different columns is a complex problem. A correspondence factor analysis (CFA) and a linear solvation energy relationship (LSER) were applied on retention data to characterize second-order intermolecular interactions responsible for retention on a set of RPLC columns. Seven octadecyl- $C_{18}$  columns with different packing materials are obtained from different manufacturers and one octyl- $C_8$  column. The retention data were determined under isocratic conditions using a methanol–water (65:35, v/v) mobile phase. The chromatographic retention indices based on alkan-2-ones and alkyl aryl ketones retention index scales are calculated using a multiparametric least-squares regressions iterative method. The CFA and LSER results permitted to highlight that the retention indices were appropriate for studying the second-order retention mechanisms on the eight chromatographic systems investigated and exhibited the best reproducibility. Although many earlier studies have reported the use of chemometric methods to characterize chemical factors affecting retention in RPLC using retention factors as retention parameters, this is the first study based on retention indices.

**Keywords** Retention indices · Correspondence factor analysis · Solvation parameter model · Monosubstituted benzenes · Characterization of RPLC stationary phases · Retention mechanism

## Introduction

Reversed-phase liquid chromatography (RPLC) is a powerful analytical technique commonly used for a wide range of practical chromatographic separations [1]. However, the main disadvantage of retention data in LC is the primary retention parameter (retention times or retention factors) which is system dependent. The variability in a mobile phase composition, its pH, ionic strength, temperature and instrumentation affect the reproducibility of retention parameters. To improve the transferability of LC data, numerous attempts have been made to develop the secondary retention

parameters—retention index system for LC analysis by analogy with data presentation in gas chromatography, where the  $n$ -alkane-based Kovàts retention indices play an important role to identify the complex compounds, and in quantitative structure–retention relationship (QSRR) studies [2, 3].

The standardization of LC results with different retention index standards have been investigated by many authors. Among the numerous retention index scales in LC, three have been widely applied: the alkan-2-ones, alkyl aryl ketones and 1-nitroalkanes. Good results concerning the linearity of  $\ln(k)$  versus carbon number plots of these three homologous series in RPLC have been observed as a base for the calculation of retention indices of many pharmaceuticals and drug compounds [4–6].

To elucidate the structural reasons governing the retention of solutes in RPLC, several mathematical models exist in the literature for studying the retention mechanisms. Among the models applied currently, the QSRR model has been widely used for studying different chromatographic systems and predict of primary retention data in LC [7–9], particularly, in chemometric methods as principal component analysis

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(PCA) and correspondence factor analysis (CFA) [10–13] and in the linear solvation parameter model based on the linear solvation energy relationships (LSER). A QSRR model has been also used for characterizing and comparing of stationary phases [14–16] and the elucidating of retention mechanisms in LC [17, 18]. The retentions of selected solutes are related to specific interactions by the following equation:

$$SP = c + vV + aA + bB + sS + eE, \quad (1)$$

where SP is a solute property of a series of selected probe solutes;  $V$  the McGowan characteristic volume in units of  $(\text{cm}^3 \cdot \text{mol}^{-1})/100$ ;  $S$  the solute dipolarity/polarizability;  $A$  and  $B$  are the hydrogen bond acidity and basicity, respectively;  $E$  the excess molar refraction (calculated from the refractive index of a molecule) and models polarizability contributions from  $n$  and  $\pi$  electrons. Coefficients  $c$ ,  $v$ ,  $a$ ,  $b$ ,  $s$  and  $e$  are the constants of the system which describe interactions related to the previous properties [19–22]. They are obtained through a multilinear regression of retention data for a certain number of solutes with known molecular descriptors. These methods allow the extraction of precise information from large amounts of retention data for a number of chromatographic systems.

The retention factors ( $k$ ) are without doubt the most frequently applied retention parameters used in QSRR studies to provide insights into the retention mechanism and understanding the types and relative strengths of chemical interactions controlling retention and selectivity in LC [23, 24]. The retention indices offer considerably better intra- and interlaboratory reproducibility than retention factors with small changes in the chromatographic conditions and have been used in QSRRs studied in RPLC [25–27].

The present paper is the continuation of our previous research, which involves the evaluation of retention indices, calculated using a multiparametric method to compare and evaluate chromatographic characteristics of different chromatographic systems in RPLC [28, 29].

The objective of this work is to study the applicability of retention indices of a set of monosubstituted benzenes with a variety of functional groups. This was undertaken to provide insight into secondary retention mechanism in RPLC to compare a set of chromatographic columns using as correspondence factor analysis and the linear solvation energy relationships. The results are compared to those obtained using the retention factors data.

The retention indices and retention factors of some selected monosubstituted benzenes with a variety of functional groups are calculated for eight chromatographic systems consisting in two types of commercially available columns: seven octadecyl- $C_{18}$  column with different packing materials and obtained from different manufacturers and one octyl- $C_8$  column. The retention data are determined under

isocratic conditions using a methanol–water (65:35, v/v) mobile phase. The retention indices of the test compounds are calculated using the multiparametric least-squares regression iterative method and based on alkan-2-ones and alkyl aryl ketones retention index scales [30, 31].

In the first part, the retention indices and retention factors of the monosubstituted benzenes calculated for eight columns studied are investigated using correspondence factor analysis. In the second part, the construction of a linear solvation energy relationships model based on the retention indices of the monosubstituted benzenes based on the alkan-2-ones retention index scale is investigated using the solute solvatochromic parameters. The correspondence factor analysis and the linear solvation energy relationship results using both retention indices and retention factors of selected monosubstituted benzenes are compared and then used for studying various interactions taking place on the eight RPLC columns studied in this work.

## Experimental

### Liquid chromatography

The retention measurements were performed on a Perkin Elmer (Perkin Elmer, Berlin, Germany) HPLC system equipped with a LC pump (250), a Rheodyne injector (7125) with 5  $\mu\text{l}$  sample loop and a variable wavelength UV detector (290) operated at 254 nm. Eurochrom 2000 chromatography data system was used for data collection and instrument control.

Standard monosubstituted benzenes (benzaldehyde, acetophenone, nitrobenzene, phenetole, chlorobenzene, toluene, bromobenzene and ethylbenzene) and benzene listed in Table 1 were purchased either from Promochem (Promochem, Wesel, Germany) and Fluka (Fluka, Buchs, Switzerland). Two homologous series were employed: alkan-2-ones (butan-2-one to nonan-2-one) and alkyl aryl ketones (acetophenone to valerophenone). The two homologous series were purchased from Merck (Merck, Nogent sur Marne Cedex, France) (Table 1).

The mobile phase consisted of methanol–water (65:35, v/v). Solvents used were HPLC grade methanol purchased from Merck (Merck, Darmstadt, Germany). Water was pre-treated in the Milli-Q Water Purification System (Millipore Corporation, Bedford, MA, USA).

The RPLC columns investigated in this study are eight commercially available reversed-phase  $C_{18}$  and  $C_8$  columns with different packing materials, purchased from different manufacturers. Eurospher  $C_{18}$  (Knauer, Berlin, Germany); Spherisorb-ODS2  $C_{18}$  (Hewlett Packard, Waldbronn, Germany);  $\mu$ Bondapak  $C_{18}$  (Waters, Paris, France); UltraSep-SEX  $C_{18}$  (SepServ, Berlin, Germany); Nucleosil 120-5  $C_{18}$ ;

**Table 1** Labels of columns and compounds investigated

Columns	Labels	Monosubstituted benzenes	Labels	Homologs	Labels
Eurospher C <sub>18</sub>	Ero	Benzaldehyde	CHO	Butan-2-one	C4
Spherisorb-ODS2 C <sub>18</sub>	Sph	Acetophenone	COCH <sub>3</sub>	Pentan-2-one	C5
μBondapak C <sub>18</sub>	Bpk	Nitrobenzene	NO <sub>2</sub>	Hexan-2-one	C6
UltraSepESEX C <sub>18</sub>	Esx	Benzene	H	Heptan-2-one	C7
Nucleosil 120-5 C <sub>18</sub>	N20	Phenetole	OC <sub>2</sub> H <sub>5</sub>	Octan-2-one	C8
Nucleosil 100-5 C <sub>18</sub> HD	Nhd	Chlorobenzene	Cl	Nonan-2-one	C9
Nucleosil 100-5 C <sub>18</sub>	N10	Toluene	CH <sub>3</sub>	Acetophenone	AC8
Nucleosil 100-5 C <sub>8</sub> HD	Nc8	Bromobenzene	Br	Propiophenone	AC9
		Ethylbenzene	C <sub>2</sub> H <sub>5</sub>	Butyrophenone	AC10
				Valerophenone	AC11

Nucleosil 100-5 C<sub>18</sub> (High Density); Nucleosil 100-5 C<sub>18</sub> and Nucleosil 100-5 C<sub>8</sub> (High Density). The four Nucleosil columns were obtained from (Machery & Nagel, Drenth, Germany). The different C<sub>18</sub> columns have dimension of (250 × 4.0 mm i.d.), 5-μm particle size, and 100 Å pore size, except Nucleosil 120 C<sub>18</sub> where the pore size is 120 Å. The names of the columns studied are presented in Table 1. The flow rate was 1.0 mL min<sup>-1</sup>. Each column was thermostated at 30 °C several hours before data collection. The differences between pre-selected temperature and effective temperature were less than 0.5 °C. A sample volume of 5 μL was injected into the HPLC system. For each column, all measurements were repeated four times and the average retention times were used in the calculations. The hold-up time ( $t_M$ ) was determined for each column used by multiparametric method based on the alkan-2-one homologues. Multiple linear regression analysis and correspondence factor analysis were performed using XLSTAT 2009 version 3.02 software from Addinsoft (New York, NY, USA).

## Methods

### Calculation of retention indices

The linearity of  $\ln(t'_R)$  versus carbon number plots for members of homologous series can be represented mathematically as follows:

$$\ln t'_R = \ln(t_{R_i} - t_M) = b Z_i + c, \quad (2)$$

where  $Z_i$  and  $t_{R_i}$  are the carbon atom number and the uncorrected retention time of the  $i$ -th homologue examined, respectively. In addition to the hold-up time ( $t_M$ ) calculation, Eq. 2 permits the determination of the slope  $b$  and intercept  $c$  of the homologous series retention time curve.

The multiparametric iterative non-linear least-squares adjustment method (MP) [28, 29] is based on the following equation:

$$t_{R_i} = t_M + A e^{B Z_i}, \quad A = e^c, \quad B = b \ln(10). \quad (3)$$

Using Eq. 3, one can obtain reliable estimation of standard deviations for the three parameters ( $t_M$ ,  $A$  and  $B$ ) and derived quantities (adjusted retention times and retention indices) are obtained by usual error propagation formulae. The retention factors ( $k$ ) were determined from the following relationship:

$$k = (t_{R_i} - t_M)/t_M. \quad (4)$$

The multiparametric method [28] was written in BASIC and run on a PC microcomputer. The retention factors ( $k$ ) for each compound were calculated using the retention time of unretained compound ( $t_M$ ) obtained by the multiparametric method based on the alkan-2-one homologues.

### Correspondence factor analysis

Among the various methods of factor analysis, the CFA method is more appropriate for studying second-order interactions, responsible for the selectivity in a given retention mechanism [10, 11].

In CFA, first the row and column margin values are calculated from the experimental data matrix. Then, the combination of the margin values divided by the sum of the experimental data matrix gives rise to the independence matrix. The difference between the experimental data matrix and the independence matrix leads to the residual matrix. Then, eigenvalues and eigenvectors are derived from the latter matrix. The abscissas of row and column designees, the column points after their projection in a two-dimensional space, i.e., compounds and chromatographic systems are recalculated in this reduced hyperspace and simultaneous projections are drawn [10, 11]. The CFA has many advantages in the study of retention mechanisms in chromatography, its main advantage is to reveal the effect of low intensities taking part in chromatographic retention. The main difference with PCA, which is very popular in Anglo-Saxon countries, is essentially due to the pre-treatment of

data which is centered and reduced before the search of the axes of inertia. This pre-treatment has two advantages; the first is to weight the values by the inverse of their sum (in row and column). This weighting increases the influence of low values and decreases the influence of high values. Thus, the low intensity effects intervening on the retention are better highlighted. The second allows a simultaneous projection of individuals and variables on the same map thus leading to a proximity analysis. In chromatography, CFA also offers the possibility of carefully exploiting the relations of proximity between the projections of the compounds and the chromatographic systems [25, 32, 33].

In this work, we have used CFA for studying the second-order intermolecular interactions presented by the hydrogen bond basicity ( $B$ ), bound energies on molar refractivity ( $E$ ) due to the presence of  $n$  and  $\pi$  electrons and the polarity/polarizability ( $S$ ) which have a low intensity responsible for a weak part of the chromatographic retention.

The 19 compounds, presented in (Table 1), include mono-substituted benzenes (MSB), alkane-2-ones and alkyl aryl homologous. These compounds were studied on two types of columns. The first group includes seven octadecyl- $C_{18}$  columns with different packing materials, while the second one includes one octyl- $C_8$  column (Table 1).

The retention factors ( $k$ ) were calculated for the 19 selected compounds on all eight stationary phases (Table 2). The retention indices ( $I$ ) of 9 monosubstituted benzenes were calculated using the multiparametric method and based on two index scales (alkane-2-ones and alkyl aryl ketones) (Table 3). The three different data matrices were analyzed using CFA.

### Solvation parameter model

In this study, two linear solvation energy relationship models (LSER) are applied and compared. The first one is based on the logarithm of retention factors (LSER- $\log k$ ), while the second is based on the retention indices (LSER- $I$ ) calculated using the multiparametric method based on the alkan-2-ones retention index scale as follows:

$$\log(k) = c + vV + bB + sS + eE, \quad (5)$$

$$I = c + vV + bB + sS + eE, \quad (6)$$

where  $B$  is the hydrogen bond basicity,  $V$  is the McGowan volume,  $S$  is the dipolarity/polarizability and  $E$  is the excess molar refraction of the solute. They are solute descriptors and reflect the structural features of a solute. The coefficients  $v$ ,  $a$ ,  $b$ ,  $s$ ,  $e$  and the constant  $c$  are determined by multiple

**Table 2** Retention factors ( $k$ ) of the alkan-2-one, alkyl aryl ketones homologs, the MSB and hold-up time ( $t_M$ ) on eight columns

	Columns							
	Ero	Sph	Bpk	Esx	N20	Nhd	N10	Nc8
Compound labels								
C4	0.43	0.30	0.25	0.41	0.28	0.37	0.33	0.41
C5	0.85	0.57	0.44	0.77	0.53	0.67	0.61	0.70
C6	1.66	1.06	0.76	1.41	0.99	1.22	1.11	1.19
C7	3.33	2.01	1.37	2.62	1.84	2.27	2.03	2.10
C8	6.62	3.83	2.43	4.86	3.46	4.24	3.69	3.66
C9	13.15	7.24	4.33	9.03	6.49	7.82	6.71	6.34
AC8	–	–	0.65	1.35	1.08	1.05	1.03	0.97
AC9	–	–	1.18	2.44	2.02	1.96	1.85	1.63
AC10	–	–	2.01	4.05	3.46	3.39	3.07	2.70
AC11	–	–	3.46	7.20	6.26	6.17	5.38	4.58
CHO	1.60	0.86	0.51	1.11	0.89	0.91	0.93	0.82
COCH <sub>3</sub>	1.73	0.86	0.63	1.35	1.09	1.05	1.03	0.96
NO <sub>2</sub>	2.08	1.45	0.85	1.91	1.63	1.47	1.60	1.25
H	3.78	2.09	1.11	2.78	2.44	2.65	2.21	1.92
OC <sub>2</sub> H <sub>5</sub>	5.94	3.27	1.74	4.41	3.81	3.94	3.44	2.78
Cl	7.18	3.94	1.98	5.19	4.53	4.67	3.91	3.29
CH <sub>3</sub>	7.47	3.94	2.02	5.19	4.96	4.95	3.98	3.29
Br	8.64	4.73	2.31	6.25	5.42	5.57	4.67	3.69
C <sub>2</sub> H <sub>5</sub>	13.15	6.66	3.25	8.60	7.54	8.31	6.37	5.37
Hold-up time (min)								
$t_M$	1.94	2.15	3.18	1.83	1.99	2.02	2.29	2.14

Condition: eluent methanol–water (65:35, v/v); column temperature 30 °C

**Table 3** Retention indices (*I*) of the MSB calculated using both alkan-2-one and alkyl aryl ketones scales on eight columns

Compound labels	Alkan-2-ones scale										Alkyl aryl ketones scale							
	Columns										Columns							
	Ero	Sph	Bpk	Esx	N20	Nhd	N10	Nc8	Bpk	Esx	N20	Nhd	N10	Nc8	V	S	B	E
CHO	593.3	566.4	534.8	560.2	582.3	550.0	569.3	530.3	765.2	756.4	760.0	769.8	776.9	766.5	0.873	1.000	0.390	0.820
COCH <sub>3</sub>	605.1	566.4	570.3	592.3	614.8	574.0	586.4	559.0	798.4	794.8	795.9	795.8	796.0	798.2	1.014	1.010	0.480	0.818
NO <sub>2</sub>	632.1	648.6	623.5	648.4	679.8	628.5	659.6	606.1	850.2	860.4	867.2	854.2	877.2	849.7	0.891	1.110	0.280	0.871
H	718.8	705.8	669.1	709.3	743.8	724.1	714.0	683.9	896.1	929.7	937.0	955.7	937.1	933.5	0.716	0.520	0.140	0.610
OC <sub>2</sub> H <sub>5</sub>	784.4	775.4	746.0	784.2	814.9	788.6	788.1	750.7	976.1	1013.1	1014.4	1023.7	1018.3	1004.6	1.057	0.700	0.320	0.681
Cl	811.9	804.9	768.5	810.3	842.7	816.2	809.7	781.2	1000.0	1042.0	1044.5	1052.7	1041.9	1036.9	0.839	0.650	0.070	0.718
CH <sub>3</sub>	817.8	804.9	771.1	810.3	857.1	825.6	812.4	781.2	1002.9	1042.0	1060.1	1062.5	1044.9	1036.9	0.857	0.520	0.140	0.601
Br	838.9	833.4	794.3	840.4	871.3	844.7	839.0	801.7	1027.6	1075.0	1075.5	1082.5	1074.0	1058.5	0.891	0.730	0.090	0.882
C <sub>3</sub> H <sub>5</sub>	900.0	886.9	853.3	892.2	923.8	909.6	891.2	869.6	1091.4	1131.1	1132.4	1150.4	1130.8	1129.8	0.998	0.510	0.150	0.613

Condition: eluent methanol–water (65:35, v/v); column temperature 30 °C

\*The solvatochromic parameters (*V*, *S*, *B* and *E*) of the selected solutes were collected from the literature [20–23]

linear regressions of Eqs. (5) and (6). They are system parameters and indicate the type of chemical interaction that control retention of a chromatographic system.

The monosubstituted benzene compound solvatochromic parameters used in the LSER-*I* and LSER-log *k* models were collected from the literature [19–22].

## Results and discussion

The retention indices calculated by the multiparametric method [29–31] of some monosubstituted benzenes (MSB) comprising various chemical functions have been studied on eight stationary phases (seven octadecyl-C<sub>18</sub> with different packing materials and one octyl-C<sub>8</sub>). Therefore, we used two homologous series as retention index scales (alkan-2-ones and alkyl aryl ketones). We note that the correlation coefficient was good for a linear relationship for ln *k* versus *Z<sub>i</sub>*, concerning both alkan-2-ones (0.9999) and alkyl aryl ketones (0.9997) homologues for all eight columns investigated. The retention factors (*k*) and retention indices (*I*) of the selected MSB are collected in Tables 2 and 3, respectively.

To evaluate the use of *I* of MSB compounds as retention parameters for the characterization of secondary interactions on the various columns studied, we have used correspondence factor analysis (CFA). For the comparison of the results, we have also submitted the *k* values of MSB compounds to CFA.

## Comparison of CFA results

We have selected for this part six columns: Nhd, N20, N10, Bpk, Esx and Nc8 (Table 1). Three different retention data matrices of MSB compounds were studied: the first corresponds to the retention factors (*k*) (Table 2), the second matrix concerns the *I* based on alkan-2-ones retention index scale and the third matrix related to *I* based on alkyl aryl ketones index scale (Table 3). The three data matrices were submitted to CFA and the simultaneous projection of the chromatographic systems and compounds on planes defined by factorial axes 1 and 2 are given in Figs. 1, 2 and 3, respectively.

By examining the three CFA maps, it can be seen that the first factorial axis represents the major part of the data; contributing to more than 75% of the information content (noted IC).

The CFA map of Fig. 1 gives the simultaneous projection of MSB and six selected columns on the first factorial plane which takes into account 92.3% of IC : 80.0% for axis 1 and 12.3% for axis 2. The compounds are projected on axis 1 according to their polarity. The most polar compounds, NO<sub>2</sub>, COCH<sub>3</sub> and CHO are projected on the left side, whereas the least polar compound C<sub>2</sub>H<sub>5</sub> is projected on the right side,

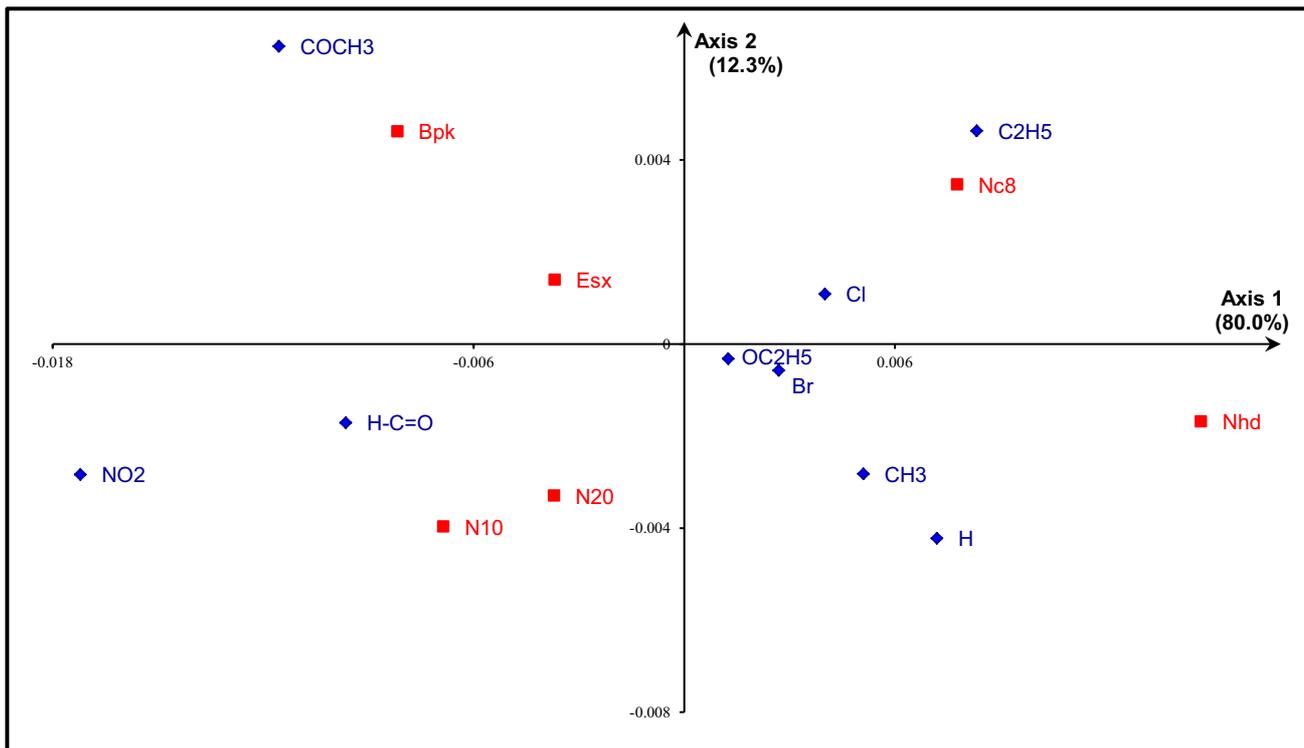


Fig. 1 CFA of the retention indices (*I*) of the MSB (filled diamond) based on alkan-2-ones on six columns (filled square)

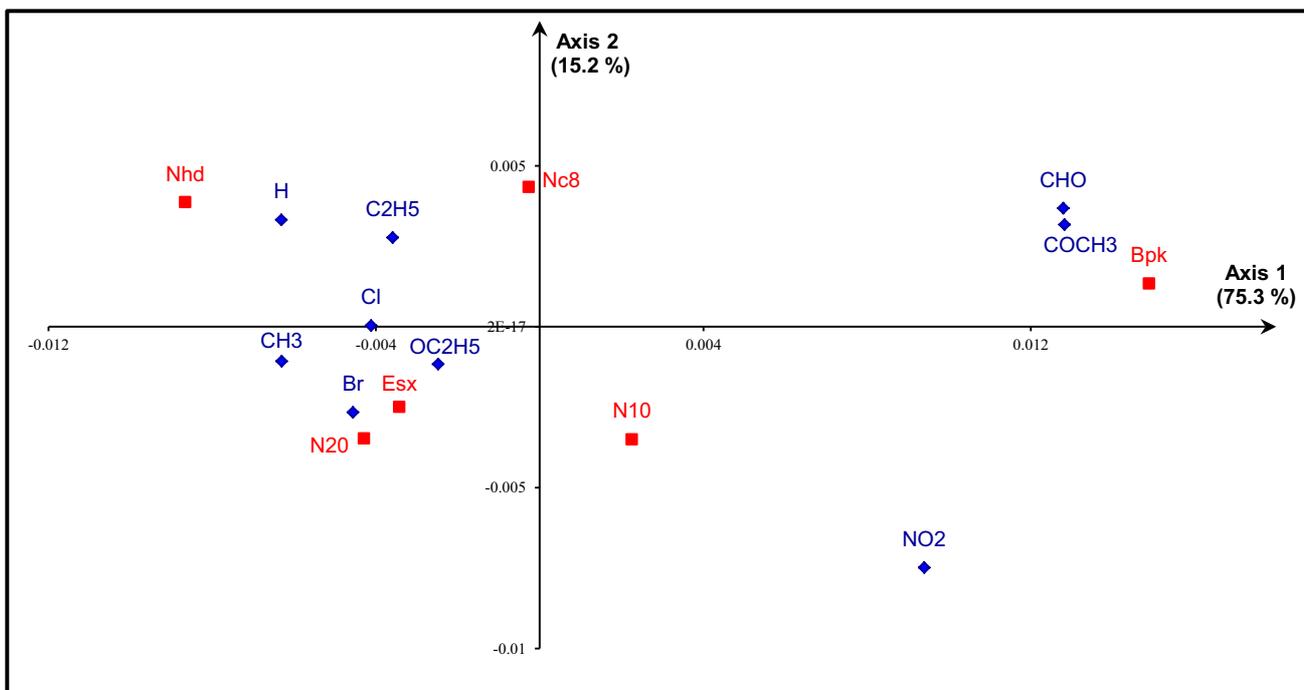
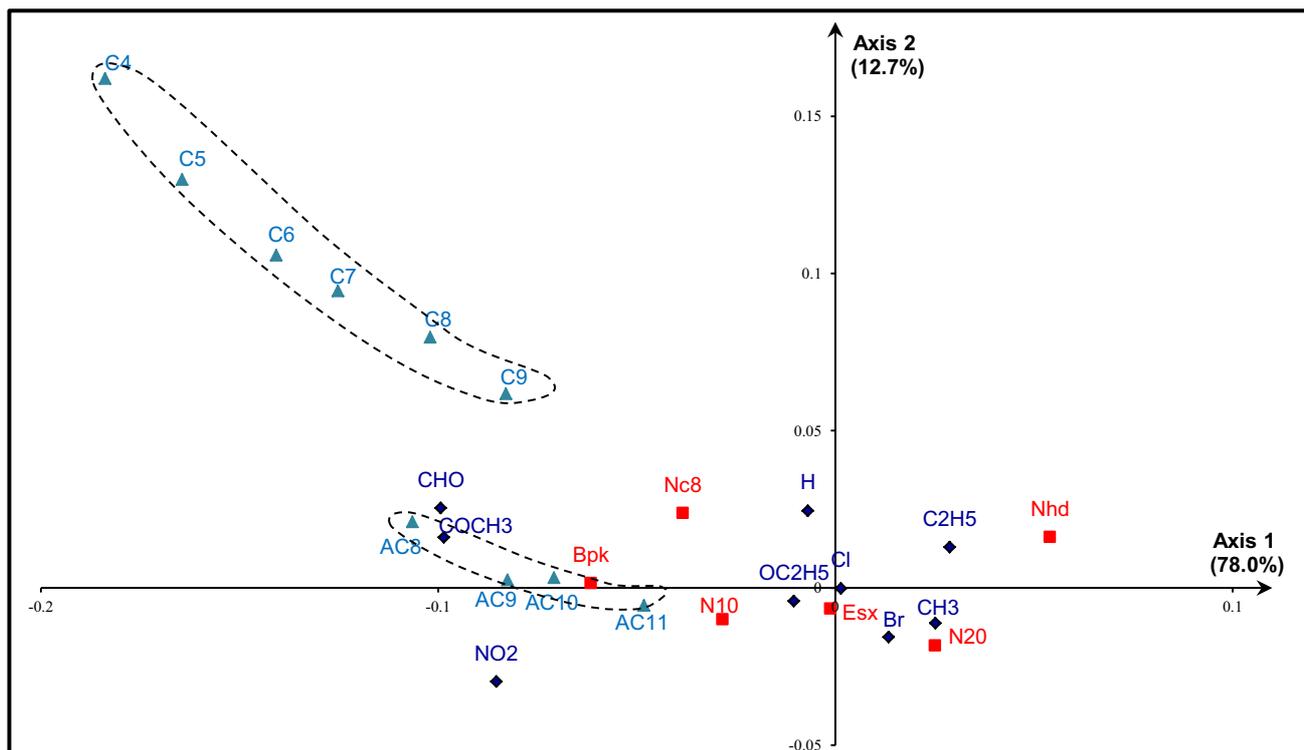


Fig. 2 CFA of the retention indices (*I*) of the MSB (filled diamond) based on alkyl aryl ketones on six columns (filled square)



**Fig. 3** CFA of the  $k$  values of the MSB (filled diamond) on six columns (filled square). The alkan-2-ones and alkyl aryl ketones (filled triangle) homologs are projected as supplementary compounds and do not contribute to the formation of the factorial plane

define mainly the first axis. The compounds Br, OC<sub>2</sub>H<sub>5</sub> and Cl which show an average retention are projected near the center of the first factorial plane. The second axis is determined by four compounds, namely COCH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>, H and CH<sub>3</sub>. The columns are projected according to their hydrophobicity. The column Nhd which contributes to 52.5% to define the first axis and it is projected on the same side as the hydrophobic compounds. This column permits a good selectivity of hydrophobic compounds. While the column Bpk is projected on the same side as the compounds COCH<sub>3</sub>, CHO and NO<sub>2</sub>, it allows a better separation of the compounds with a basic character. The column Esx shows an average behavior and it is projected near the center of the first factorial plane. The second axis is mainly defined by the columns Bpk, N10, Nc8 and N20.

Concerning the CFA map of Fig. 2, the axes 1 and 2 represent 75.3 and 15.3% of IC, respectively. Along the first factorial axis the compounds COCH<sub>3</sub>, CHO and NO<sub>2</sub> which define mainly the first axis projected on the right side of the first factorial plane. The column Bpk which contribute to 66.0% to the first axis is projected on the right side of this axis near the compounds CHO and COCH<sub>3</sub> and it permits a good separation of compounds with a basic character. The column Nhd which contribute to 23.2% to the first axis is projected on the same side (left) as the hydrophobic compounds and it allows a good selectivity of hydrophobic

compounds. The second axis is mainly defined by NO<sub>2</sub> that has a contribution of 50.5%, and the columns Nc<sub>8</sub>, Nhd, N10 and N20. The column Esx has a negligible contribution to the first factorial plane. The column Nc<sub>8</sub> has a very weak contribution (it is equal to 0.02%) to the inertia explained by axis 1. On the other hand, it contributes for 28.3% to the inertia explained by axis 2.

In the case of CFA map of Fig. 3, where the values of  $k$  for the MSB are projected, 78.0% of IC according to axis 1 and 12.7% of IC according to axis 2 are obtained. The first factorial axis is mainly defined by the most polar compounds, namely NO<sub>2</sub>, CHO, COCH<sub>3</sub> on the left side, and C<sub>2</sub>H<sub>5</sub> on the right side. This axis reflects the polarity for compounds. The medium polar compounds Cl, Br and OC<sub>2</sub>H<sub>5</sub> which show an average retention are projected in the center of the first factorial plane. The columns are projected according to their hydrophobicity. This is confirmed by the projection of the two columns Nhd and Bpk. Moreover, the column Nhd is projected near the hydrophobic compounds and Bpk is projected near the most polar compounds while the column Esx is projected near the center of the first factorial plane. The second axis is mainly defined by the compounds NO<sub>2</sub>, H, Br and C<sub>2</sub>H<sub>5</sub> and the columns Nc<sub>8</sub>, N20 and Nhd.

Considering the three data matrices using both  $I$  and  $k$ , the CFA maps lead to similar results. The first conclusion is

that MSB are projected along the first axis according to their polarity. This is confirmed by the projection of the alkan-2-ones and the alkyl aryl ketones homologs considered in the CFA analysis as additional individuals and do not contribute in the definition of the factorial plane. The homologous series are projected along axis 1 on the left towards the center of the map according to the carbon number of each compound. The columns are projected according to their hydrophobicity. This is confirmed by the projection of the two columns, Bpk and Nhd. The comparison of the three CFA graphs leads to the conclusion that the informational content extracted using  $I$  values can highlight the different physicochemical properties of selected compounds and stationary phases studied in this work (Table 1).

The second part concerns the comparison of retention mechanisms of the different chromatographic systems using both  $I$  and  $k$  values. CFA of the solvatochromic parameters of the MSB was undertaken and presented on Fig. 4. The most significant solvatochromic parameters of the MSB analyzed by CFA are:  $B$  and  $V$  defining axis 1. They account for 65.8 and 17.6%, respectively, to the inertia of the first axis. The second axis is mainly defined by  $V$  and  $S$  terms that contribute to the inertia of this axis to 38.5 and 33.2%, respectively.

Concerning the projection of MSB, the first factorial axis is defined with  $\text{COCH}_3$ , and  $\text{CHO}$  projected on the right side

which account for 27.5 and 18.2% to the inertia. Moreover, both  $\text{C}_2\text{H}_5$  and  $\text{CH}_3$  are projected near the parameter  $V$  that represents the hydrophobic property of the compounds. The first axis is defined by the two terms that influence mainly the retention mechanism, on the one side, the hydrogen bond basicity  $B$ , and on the other side, the molar volume  $V$ .

The molar volume measures the endoergic process of forming a cavity in the solvent. It is known that in RPLC mode, the retention combines the main mechanism, partition, which is the primary contributor to the retention [10, 11] and mechanisms or the secondary effects which have a low contribution. In this case, the main retention mechanism is presented by the molar volume  $V$  and the secondary retention mechanisms are presented by the polar interactions, especially hydrogen bond basicity  $B$  and the bound energies on molar refractivity  $E$  due to the presence of  $\pi$  electrons.

Furthermore, to compare the information content of  $I$  and  $k$  values, we studied the correlations between the projection of MSB in the factorial space matrices  $I$  and  $k$  and their projection in the factorial space obtained by the treatment of the solvatochromic properties matrix. The retention data of MSB obtained on seven selected columns (Esx, N20, Nhd, Ero, N10, Sph, Nc8) were considered. The MSB coordinates on axis 1 using retention factors or retention indices were correlated with the solvatochromic parameter coordinates. The study of the CFA coordinates of the used

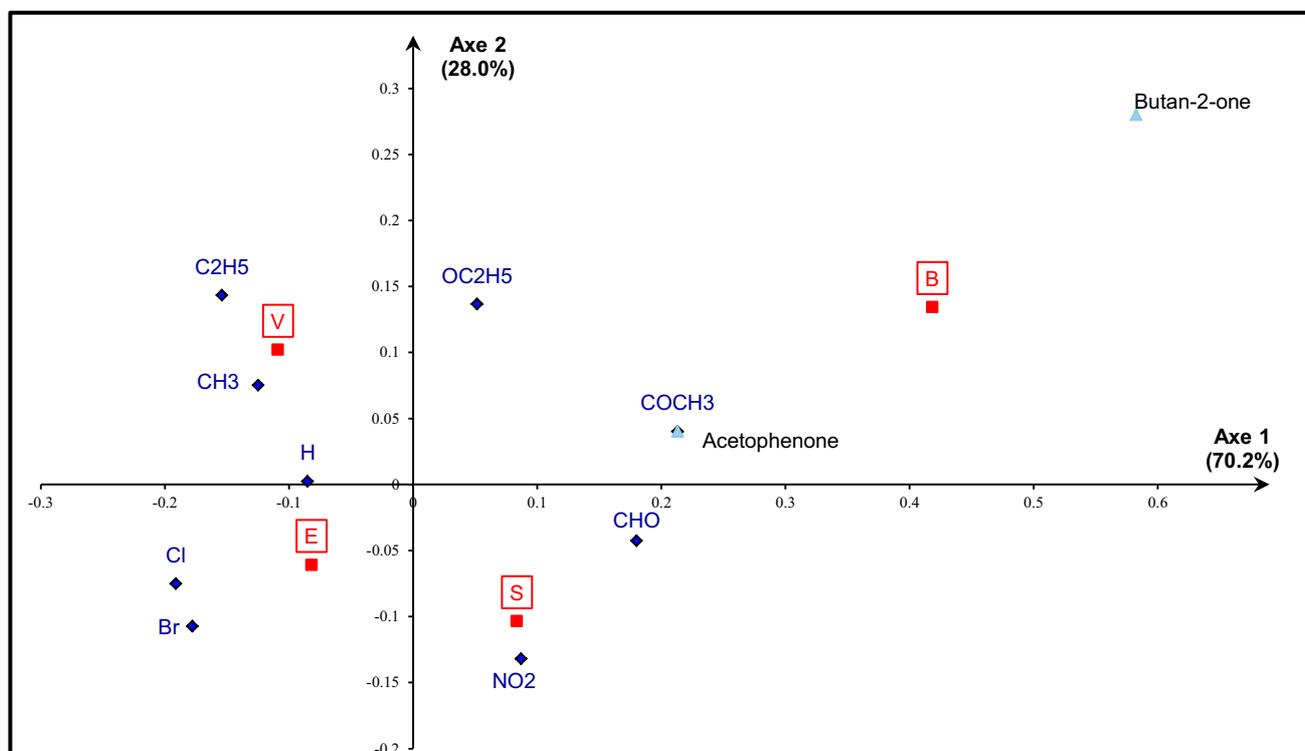


Fig. 4 CFA of the MSB solvatochromics parameters ( $V$ ,  $B$ ,  $S$  and  $E$ ). Acetophenone and butan-2-one are projected as supplementary compound and do not contributed to the formation of the factorial plane

solvatochromic parameters (axis 1, Fig. 4) as a function of the CFA coordinates (axis 1, Figs. 1, 3) obtained from  $I$  calculated with alkan-2-ones homologous series and  $k$  of MBS results in a correlation coefficient  $r$  equal to 0.683 and 0.845, respectively. The results show that the MSB coordinates on axis 1 ( $k$  and  $I$ ) can be explained by the coordinates on axis 1 of the solvatochromic parameters. Similarly, the study of the solvatochromic parameter  $B$  and  $S$  (two probes acting for secondary mechanisms in RPLC) with respect to the CFA coordinates (axis 1) obtained using the values of  $k$  results in a correlation coefficient equal to 0.716 and 0.858, respectively. While  $r$  is equal to 0.559 for  $B$  and 0.964, for  $S$  using the values of  $I$ .

### Evaluation of LSER model quality using retention indices

The different chromatographic systems were studied using linear solvation energy relationship based on the retention indices calculated with the multiparametric method. The results were compared with those of LSER obtained from the retention factors ( $\log k$ ). All calculated model coefficients and regression statistics for seven  $C_{18}$  and one  $C_8$  columns using both  $I$  based on alkan-2-one (LSER- $I$ ) and  $\log k$  (LSER- $k$ ) are presented in Table 4 and Fig. 5 a, b. As it can be seen from the statistics (Table 4), high correlation coefficients ranging from 0.993 to 0.999 and system coefficients significantly larger than their standard deviations were obtained for each column and indicate the goodness of fit concerning the two models. We note that the  $e$  coefficients are smaller than their uncertainty and considered not to be significant.

The coefficients of LSER- $I$  and LSER- $k$  show that only the coefficients of the solute molar volume  $v$  are positive, whereas the coefficients of the hydrogen bond basicity character  $b$  and the solute dipolarity/polarizability  $s$  are negative. The coefficients of the solute refractivity  $e$  are insignificant and positive or negative. It should be noted that the coefficients obtained using LSER- $I$  are more consistent than those obtained from LSER- $k$  (using the LSER- $I$  the coefficients with positive sign are larger while those of negative sign are smaller). For the LSER- $k$ , the  $v$  values obtained for five columns Esx, N20, Nhd, Ero and Sph are similar and are much higher than those obtained for N10 and Nc8 columns. For the LSER- $I$ , only the columns Esx, N20 and Nhd have a similar  $v$  values. For LSER- $k$ , column Bpk shows the lowest  $v$  values in comparison with other columns and the cavity formation is more difficult, it presents a polar character.

The coefficients of both LSER- $k$  and LSER- $I$  show that the retention expressed by  $\log k$  or  $I$  depends primarily on the solute molar volume  $v$  (positive sign), noting an overall attractive interaction with the stationary phase (increase the retention). For both models, the solute hydrogen bond

**Table 4** Coefficients of both LSER- $\log k$  and LSER- $I$  and their statistics for seven  $C_{18}$  and one  $C_8$  columns

Columns	LSER- $I$												
	LSER- $\log k$					LSER- $I$							
Coefficients					Coefficients					Correlation			
$c$	$v$	$s$	$b$	$e$	$c$	$v$	$s$	$b$	$e$	$r$	$r^2_{adj}$	$F$ test	
Esx	-0.42 (0.10)	1.82 (0.11)	-0.40 (0.14)	-1.94 (0.14)	0.05 (0.20)	388 (39)	680 (40)	-149 (52)	-724 (54)	19 (75)	0.9984	0.9968	313
N20	-0.41 (0.16)	1.86 (0.17)	-0.36 (0.22)	-2.08 (0.23)	-0.09 (0.32)	450 (60)	683 (62)	-129 (80)	-767 (84)	-35 (117)	0.9965	0.9930	141
Nhd	-0.35 (0.11)	1.81 (0.12)	-0.56 (0.15)	-1.94 (0.16)	0.06 (0.22)	433 (43)	679 (44)	-210 (57)	-728 (60)	23 (83)	0.9984	0.9968	313
N10	-0.43 (0.14)	1.73 (0.14)	-0.27 (0.18)	-1.95 (0.19)	-0.09 (0.27)	415 (52)	667 (53)	-106 (69)	-750 (73)	-35 (101)	0.9970	0.9941	168
Nc8	-0.42 (0.07)	1.61 (0.07)	-0.40 (0.09)	-1.69 (0.10)	-0.01 (0.14)	392 (29)	667 (29)	-167 (38)	-702 (40)	-3 (56)	0.9992	0.9983	591
Ero	-0.26 (0.14)	1.80 (0.14)	-0.73 (0.18)	-1.71 (0.19)	0.32 (0.26)	438 (45)	603 (46)	-245 (60)	-575 (63)	105 (88)	0.9977	0.9953	213
Sph	-0.48 (0.16)	1.83 (0.16)	-0.29 (0.21)	-2.14 (0.22)	-0.09 (0.31)	418 (57)	659 (59)	-103 (76)	-774 (80)	-36 (111)	0.9965	0.9931	143
Bpk	-0.33 (0.10)	1.35 (0.11)	-0.25 (0.14)	-1.38 (0.15)	-0.02 (0.21)	358 (41)	674 (42)	-102 (54)	-708 (57)	-34 (79)	0.9960	0.9920	249

The LSER coefficients are given with their standard deviation (the numbers in italics)

$r$  is the multiple correlation coefficients;  $r^2_{adj}$  is the adjusted correlation coefficient and  $F$  is Fisher's test

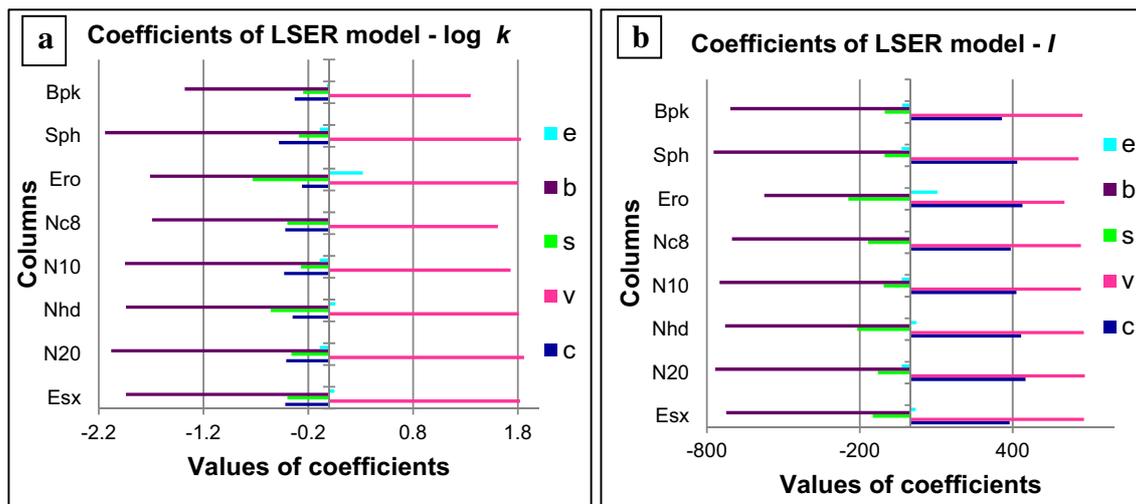


Fig. 5 Coefficient values using two LSER models

basicity  $b$  is negative. The Sph column shows the lowest  $b$  values (more negative). This indicates that the Sph column is lower hydrogen bond donor than the other columns used in this study. The coefficient  $s$  which measures the ability of the phase to interact with dipolar and/or polarizable solute is negative in two models, denoting a dipole–dipole interaction is strong between the solute and the mobile phase than the stationary phase. The  $e$  coefficient which measure the ability to interact by electron pair (n or  $\pi$  electrons) are positive for three columns Esx, Nhd and Ero and positive for other columns using both models. The highest  $e$  coefficient value is obtained for Ero column; this interaction type affects the retention of analyte (increase the retention).

The molar volume ( $V$ ) associated with the energy of formation of cavity contributes to the principal retention mechanism which is a partition mechanism. The other terms represent the contribution to the secondary retention mechanism concerning the polar interactions ( $B$ ,  $S$  and  $E$ ).

The evaluation of LSER models was also performed by comparing the experimentally determined  $\log k$  ( $\log k_{(\text{exp})}$ ) and  $I$  ( $I_{(\text{exp})}$ ) values versus the calculated values ( $\log k_{(\text{cal})}$ ) and  $I_{(\text{cal})}$ ) from LSER equations (Fig. 6a, b). As expected, there is a good correlation between calculated and experimental values on each column using both  $\log k$  and  $I$  as retention parameter ( $r > 0.9920$ ).

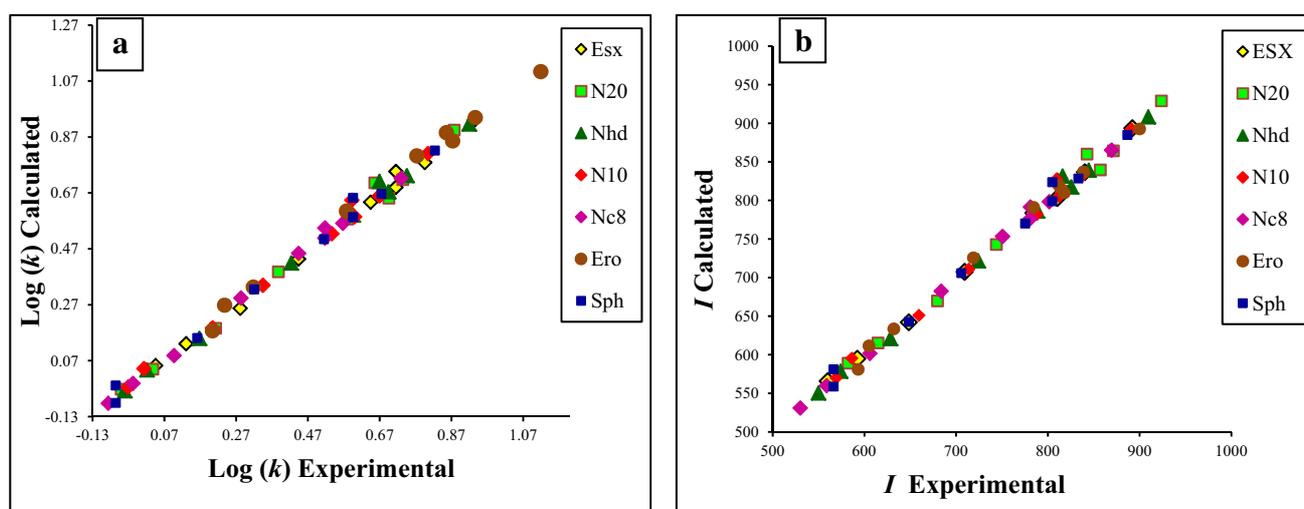


Fig. 6 Plots of the calculated  $\log k_{(\text{cal})}$  and  $I_{(\text{cal})}$  and experimental  $\log k_{(\text{exp})}$  and  $I_{(\text{exp})}$  of MSB on seven columns **a** calculated from Eq. (5); **b** calculated from Eq. (6)

## Conclusion

The use of correspondence factor analysis (CFA) and linear solvation energy relationships (LSER) allowed us to evaluate some secondary interactions affecting the retention behavior of a set of eight non-polar columns (seven octadecyl- $C_{18}$  with different packing materials and obtained from different manufacturers and one octyl- $C_8$ ) that have been studied. The retention parameters used were retention indices ( $I$ ) based on alkan-2-ones and alkyl aryl ketones retention index scales calculated using a statistical multiparametric method and retention factors ( $k$ ) of some monosubstituted benzenes with a variety of functional groups.

The comparison of CFA graphs and LSER results leads to the conclusion that the informational content extracted using  $I$  values as retention parameters can highlight the different physicochemical properties of the selected monoaromatics (CHO, COCH<sub>3</sub>, NO<sub>2</sub>, H, OC<sub>2</sub>H<sub>5</sub>, Cl, CH<sub>3</sub>, Br, C<sub>2</sub>H<sub>5</sub>) and the eight studied columns (Ero, Sph, Bpk, Esx, N20, Nhd, N10 and Nc8). Therefore, the retention indices calculated using the multiparametric method can be used for studying chromatographic characteristics of different columns, and in particular, for quantifying the second-order interactions and comparing of the retention mechanisms in different stationary phase's chromatographic systems in RPLC.

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