THEORETICAL INTERPRETATION OF HIGH-PERFORMANCE CHROMATOGRAPHIC DATA FOR A HETEROGENEOUS SERIES OF COMPOUNDS

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A new approach to theoretical evaluation of the Gibbs free energy of solvation was applied for estimation of retention data in high-performance liquid chromatography on reversed phases (RP-HPLC). Simple and improved models of stationary and mobile phases in RP-HPLC were employed. Statistically significant correlations between the calculated and experimental data were obtained for a heterogeneous series of twelve compounds.

Chromatographic methods afford many experimental data and consequently, requirement for their correct and rapid interpretation has emerged. At the same time, it is necessary to understand and to learn elementary processes ruling the course of chromatographic separation, this being a condition for more effective utilization of this experimental technique. Therefore, one has to understand individual interaction forces at molecular level in the chromatographic process[1]. The capacity factors or retention indexes are most frequently used for identification of compounds from their retention behaviour in the liquid or gas chromatography[2]; these indexes are considered to be the most reproducible and most precise tools for definition of retention. They found a broad utilization in both theoretical studies predicting the retention behaviour from their structures and conversely, when determining structure from retention characteristics obtained. A study concerning the relationship between the structure and retention data – capacity factors (QSRR – Quantitative Structure Retention Relationship) is presented in this paper for a series of 12 compounds (benzene derivatives) separated by Kaliszan et al.[3,4] on a well characterized chemically bonded stationary phases of various surface coverage with octadecyl chains and mixed mobile phases. This paper verifies to what extent the elaborated model can be employed for interpretation of variously polar compounds constituting a heterogeneously structural series. Simultaneously, a composition change of the mobile phase at various C_{18} suface coverage of the stationary phase was modelled, thereby interpreting theoretically the experimentally obtained capacity factors at the given composition of the mobile phase and C_{18} coverage of the stationary phase. This paper considers possibilities of modelling the stationary chemically bonded C_{18} phase and mobile phase (water–methanol). The calculated individual contributions of Gibbs solvation energy were further correlated with the experimental capacity factors; basing on this correlation analysis and employing the least squares method, the predictivity of this method was judged.

THEORETICAL

The capacity factor k', characterizing the chromatographic separation, is given by relation

$$\log k' = -\Delta G^{s/m}/(2{\cdot}3\, \boldsymbol{R}T) + \log (V_s/V_m)\,, \tag{1}$$

where $\Delta G^{s/m}$ is the Gibbs retention energy for the given stationary (s) and mobile (m) phases, V_s and V_m are volumes of the corresponding phases, $\boldsymbol{R}$ is the gas constant and T temperature.

The total Gibbs energy is expressed as a difference between interaction solvation Gibbs energies in stationary and mobile phases:

$$\Delta G^{s/m} = \Delta G^{s}_{solv} - \Delta G^{m}_{solv}\,. \tag{2}$$

Modelling in this paper is based upon a continuum model; the Gibbs energies in single phases have to be expressed afterwards. The total Gibbs retention energy with various contributions is

$$\Delta G^{s/m} = (\Delta G^{s}_{el} - \Delta G^{m}_{el}) + (\Delta G^{s}_{d} - \Delta G^{m}_{d}) + (\Delta G^{s}_{cav} - \Delta G^{m}_{cav})\,, \tag{3}$$

where ΔG_{el}, ΔG_d and ΔG_{cav} stand for electrostatic, dispersion-repulsion and cavitation terms, respectively; the coulombic part[2,5-7] was calculated for the electrostatic contribution. The CNDO/2 semiempirical quantum chemical method[8] was applied to the calculation of pure charges on atoms of the respective compound molecule needed for expressing the electrostatic contribution. The dispersion and repulsion contributions to the Gibbs solvation energy can be expressed by the London relation for the dispersion term[9] and the Born relation for the repulsion term[10]. The dispersion-repulsion contribution in this paper was calculated according to the elaborated model[2,11,12]. The cavitation contribution was calculated by the modified Pierotti[12,14] and Sinanoglu approaches[12,13].

The Gibbs solvation energies were taken from tabulated values of physicochemical characteristics for the solute and solvent entering the relation for expressing electrostatic, dispersion–repulsion and cavitation terms.

Physicochemical characteristics of the model solvent octanol–water were considered at the first approximation in the separation processes.

The second approach in these processes involved values of characteristics of the mixed mobile phase methanol–water obtained either by a simple calculation of the weighted average of these values, or from the measured dependence of these parameters, especially from the methanol to water ratio in the mixture[15,16].

Contributions to the Gibbs solvation energy thus obtained were inserted in Eq. (*3*), the total Gibbs solvation energy was calculated, the correlation equations between experimental log k' and calculated Gibbs retention energy values (or individual contributions) of the type (compare with Eq. (*1*)):

$$\log k' = a \,.\, \Delta G^{s/m} + b \qquad (4)$$

were constructed. The correlations were then statistically evaluated with respect to the accordance between theoretical and experimental data and their statistical significance. For this purpose correlation coefficient r was applied and the linearity or correlation function were tested according to F-criterion[17] (S.R.).

RESULTS AND DISCUSSION

Standard geometries of compounds of the heterogeneous series under investigation were taken from[18]. Individual contributions of Gibbs solvation energy were calculated for the simpliest system octanol–water; further calculations concerned modelling of the mixed mobile and stationary phases. These results were correlated with capacity factors of compounds at the given composition of the mobile phase and at C_{18} surface coverage degree of the stationary phase[3,4] (cf. Table I).

Comparison of individual contributions to the Gibbs solvation energy was calculated in the first step for the simpliest model of mobile and stationary phases for the system octanol–water. Parameters listed in Table II were employed to the calculation of Gibbs solvation energies in water and octanol for the series of compounds studied. Table III presents contributions of Gibbs solvation energies and differences of Gibbs solvation energies $\Delta G^{o/w}$.

These values evidence that the individual contributions of Gibbs solvation energy for the heterogeneous series of 12 compounds have markedly different size. This series contains compounds of a more polar character than that of alkylbenzenes[2]; this was also observed in greater absolute values of electrostatic contributions in comparison with those of the series of alkylbenzenes. Comparison of the electrostatic ΔG_{el} and dispersion-repulsion ΔG_d contribution data computed for water and octanol were shown to be qualitatively correct. Differences between Gibbs solvation energies $\Delta G^{o/w}$ obtained by calculation for octanol and water are negative (cf. Table III) and seemed to be correct.

Modelling of the Mobile Phase Composition and C_{18} Surface Coverage of the Stationary Phase

To approximate the model to experimental conditions a refined modelling of the mobile phase composition and C_{18} surface coverage of stationary phase were accomplished. Modelled were following compositions of the mobile phase water–methanol: *a*) 55 : 45, *b*) 45 : 55, *c*) 35 : 65.

Relative permittivity ε, microscopic cavitation factor of the solvent k_b (l), surface tension γ_b, thermal expansion coefficient A_b from the experimentally estimated relations[13,15,16,20,21] radius of the mixed mobile phase r_s, polarizability α (ref.[19]), HOMO energy and change of the surface tension on temperature $\delta \ln \gamma / \delta \ln T$ as weighted average values for pure solvents were introduced for modelling the mixed mobile phase of the given composition.

The stationary chemically bonded C_{18} phase was modelled as pure solvent (either octanol or heptane). The second model solvent heptane represents one of lower relative permittivity $\varepsilon = 1{\cdot}92$; the value for octanol is higher ($\varepsilon = 10{\cdot}3$). Heptane should represent the stationary phase with a greater coverage degree; in fact, the

TABLE I

Capacity factors of compounds under investigation[3,4] obtained on columns of varying C_{18} coverage of the chemically bonded stationary phase and various composition of the mobile phase water–methanol

Number	Compound	C_{18} surface covergae					
		$4{\cdot}96 . 10^{-4}$ g (C_{18}/g)			$6{\cdot}6 . 10^{-4}$ g (C_{18}/g)		
		55 : 45[a]	45 : 55[a]	35 : 65[a]	55 : 45[a]	45 : 55[a]	35 : 65[a]
1	Phenol	1·54	0·88	0·47	1·86	0·94	0·61
2	Aniline	1·57	0·94	0·53	1·71	1·00	0·67
3	*p*-Cresol	3·23	1·82	0·79	3·97	1·89	1·06
4	Acetophenone	3·66	1·85	0·91	4·34	2·17	1·21
5	N-Methylaniline	3·80	2·12	1·12	4·71	2·43	1·39
6	Nitrobenzene	4·40	2·35	1·21	5·57	2·83	1·55
7	4-Ethylphenol	6·66	3·00	1·35	8·69	3·74	1·85
8	Methyl benzoate	7·66	3·53	1·62	10·51	4·54	2·18
9	3-Chloroacetophenone	10·03	4·44	1·97	13·60	5·60	2·61
10	4-Propylphenol	15·11	5·94	2·38	20·94	7·86	3·33
11	4-sec-Butylphenol	26·71	9·35	3·38	38·80	13·00	5·03
12	3,4-Dichloroacetophenone	25·00	9·88	3·94	36·14	13·14	5·45

[a] Water : methanol.

polarity of C_{18} chemically bonded phase should lies between both limit values (cf. Table II).

The computation results are listed in Tables III to V. Tables III and IV show that the electrostatic contributions calculated for the mixed mobile phase water–methanol dropped slightly (in absolute values) towards values of electrostatic contributions computed for water. This is, however, in accordance with the lower polarity of the mixed mobile phase water–methanol towards water.

The values of dispersion-repulsion contributions $\Delta G_d^{w:m}$ calculated for the mobile phase decreased towards the ΔG_d values computed for a pure solvent (water) and are, therefore, of stabilizing effect.

Decrease of the value for cavitation contribution seemed to be qualitatively correct for the change of mobile phase (water) for the less polar mixture (water–methanol). The least decrease revealed phenol, the greatest one 4-sec-butylphenol, all this being in line with the known fact[22] that the separation equilibrium of a less polar compound between polar and non-polar phases is shifted towards the less polar one. The values for individual contributions of the Gibbs solvation energy as calculated for heptane (cf. Tables III to V) were roughly by one half lower than the corresponding values computed for octanol and, as a consequence, the $\Delta G_s^{h/w:m}$ values were positive,

TABLE II

Parameters for calculation of individual contributions of Gibbs solvation energy of the compound in octanol, heptane, water and water–methanol

Parameter	Octanol	Heptane	Water	Water : Methanol		
				55 : 45	45 : 55	35 : 65
Solvent radius $r_s \cdot 10^{10}$, m	4·2	3·71	1·9	2·15	2·21	2·26
Microscopic cav. factor $k_b(l)$	1·280	0·869	1·302	2·390	2·305	2·144
Surface tension γ_b, mNm^{-1}	21·95	25·36	73·05	36·60	34·13	27·75
$\partial \ln \gamma / \partial \ln T$	−1·33	−1·505	−0·657	−0·881	−0·930	−0·980
Thermal expansion coefficient $A_b \cdot 10^3$, K	0·245	1·656	0·180	0·653	0·753	0·852
E_{HOMO}, kJ mol^{-1}	2 074·6	2 575·0	2 638·6	2 499·7	2 468·8	2 437·9
Polarizability $\alpha \cdot 10^{30}$, m^3	16·17	13·68	1·47	2·29	2·47	2·65
Rel. permittivity ε	10·3	1·92	80·0	57·33	51·33	45·63

TABLE III

Calculated contributions to the Gibbs free energy of solvation (kJ mol^{-1}) in water and octanol and differences of the Gibbs solvation energies $\Delta G^{o/w}$. Indexes P and S refer to the cavitation contribution calculated according to Pierotti or Sinanoglu, respectively

Number	ΔG^{w}_{el}	ΔG^{o}_{el}	ΔG^{w}_{d}	ΔG^{o}_{d}	$\Delta G^{w}_{cav,S}$	$\Delta G^{o}_{cav,S}$	$\Delta G^{w}_{cav,P}$	$\Delta G^{o}_{cav,P}$	$\Delta G^{o/w}_{S}$	$\Delta G^{o/w}_{P}$
1	−23·20	−21·22	−59·57	−55·63	57·73	23·78	110·46	62·97	−28·02	−41·55
2	−19·92	−18·21	−60·54	−56·58	60·82	24·72	117·89	67·15	−30·44	−45·08
3	−22·55	−20·62	−68·30	−63·47	67·53	26·77	132·91	75·66	−34·01	−50·49
4	−25·02	−22·88	−81·46	−75·66	76·93	29·63	152·53	86·88	−39·36	−57·71
5	−15·98	−14·61	−69·16	−64·43	69·72	27·43	138·06	78·53	−36·19	−53·40
6	−93·95	−85·91	−65·90	−61·89	64·96	25·98	124·06	70·87	−26·92	−41·13
7	−22·83	−20·88	−77·85	−72·00	76·99	29·65	154·53	87·87	−39·54	−58·59
8	−60·29	−55·13	−81·68	−76·00	76·73	29·57	151·15	86·16	−36·33	−54·15
9	−37·88	−34·64	−104·47	−101·44	79·56	30·43	152·04	87·09	−42·86	−58·68
10	−22·35	−20·44	−88·57	−81·50	87·55	32·86	178·82	101·58	−45·70	−68·25
11	−22·60	−20·66	−95·48	−87·65	94·15	34·88	193·92	110·12	−49·51	−74·04
12	−42·14	−38·53	−121·58	−121·81	86·16	32·44	161·05	92·64	−50·33	−65·03

TABLE IV

Calculated values of the Gibbs solvation energies and individual contributions (kJ mol^{-1}) in water-methanol and differences of the Gibbs solvation energies $\Delta G^{o/w:m}$ between octanol and water-methanol at composition of the mobile phase water : methanol = 35 : 65 and C_{18} surface coverage of the stationary phase 4·96 . 10^{-4} g of C_{18} ligand per gram of silica substrate

Number	$\Delta G_{el}^{v:m}$	$\Delta G_{d}^{w:m}$	$\Delta G_{cav,S}^{w:m}$	$\Delta G_{S}^{w:m}$	$\Delta G_{el}^{o/w:m}$	$\Delta G_{d}^{o/w:m}$	$\Delta G_{cav,S}^{o/w:m}$	$\Delta G_{S}^{o/w:m}$
1	−22·98	−47·05	33·57	−36·45	1·77	−8·58	−9·80	−16·61
2	−19·73	−47·83	34·81	−32·75	1·52	−8·76	−10·09	−17·33
3	−22·33	−53·86	37·49	−38·70	1·71	−9·71	−10·72	−18·62
4	−24·78	−64·17	41·24	−47·62	1·91	−11·49	−11·61	−21·20
5	−15·83	−54·58	38·36	−32·05	1·22	−9·86	−10·93	−19·57
6	−93·06	−52·10	36·46	−108·69	7·15	−9·79	−10·48	−13·12
7	−22·61	−61·29	41·27	−42·64	1·72	−12·66	−13·24	−24·18
8	−59·72	−64·37	41·16	−82·93	4·59	−11·64	−11·59	−18·64
9	−37·52	−83·20	42·29	−78·44	2·88	−18·24	−11·86	−27·21
10	−22·14	−69·61	45·48	−47·18	1·70	−11·88	−12·62	−24·79
11	−22·48	−72·81	48·11	−48·35	1·72	−12·66	−13·24	−24·18
12	−41·73	−97·65	44·92	−94·46	3·21	−24·16	−12·48	−33·44

TABLE V

Calculated values of the Gibbs solvation energies and individual contributions (kJ mol^{-1}) between heptane and water-methanol at two C_{18} surface coverages of the stationary phase

Number	$\Delta G_{el}^{h/w:m}$	$\Delta G_{d}^{h/w:m}$	$\Delta G_{cav,S}^{h/w:m}$	$\Delta G_{S}^{h/w:m}$
1	11·72	22·42	−21·80	12·34
2	10·06	22·92	−22·70	10·81
3	11·39	25·87	−22·96	14·31
4	12·64	30·79	−24·06	19·38
5	8·07	26·28	−23·21	11·15
6	47·47	24·74	−22·65	49·56
7	11·54	29·61	−24·07	17·08
8	30·46	30·79	−24·04	37·22
9	19·04	38·48	−24·37	33·15
10	11·29	33·81	−25·31	19·80
11	11·42	36·47	−26·08	21·80
12	21·29	44·37	−25·14	40·52

whilst the $\Delta G_S^{o/w:m}$ values were negative. It is difficult to say what is the correct sign for the $\Delta G_S^{o/w:m}$ value. The accessible experimentally obtained values of partition coefficients[23] in the system heptane–water reported the negative sign of the logarithms of partition coefficients for aniline, phenol and 4-cresol in the −0·13 to −0·87 range; this is, then, in accordance with the positive $\Delta G_S^{h/w}$ value.

Statistical Evaluation and Prediction for Further Similar Derivatives

For statistical evaluation of the simpliest model octanol–water, values for the individual contributions of the Gibbs solvation energy and Gibbs retention energy were correlated with the experimental capacity factors for the series of compounds under examination at three compositions of the mixed mobile phase and two C_{18} surface coverages stages of the stationary phase (see Table VI). Correlation equations of type I, II and III for composition of the mobile phase water–methanol 35 : 65 and C_{18} surface coverage of stationary phase $4{\cdot}96 \,.\, 10^{-4}$ g of C_{18} ligand per gram of silica substrate are presented for illustration.

TABLE VI

Characteristics of correlation equations obtained on correlation of Gibbs retention energy $\Delta G_S^{o/w}$ (kJ mol^{-1}) and their contribution for the simpliest model water–octanol with experimental capacity factors k' at various composition of the mobile phase and two C_{18} surface coverages of the stationary phase

Parameter	C_{18} surface coverage					
	$4{\cdot}96 \,.\, 10^{-4}$ g (C_{18}/g)			$6{\cdot}6 \,.\, 10^{-4}$ g (C_{18}/g)		
	55 : 45[a]	45 : 55[a]	35 : 65[a]	55 : 45[a]	45 : 55[a]	35 : 56[a]
Correlation eq. I						
r	0·878	0·890	0·874	0·893	0·886	0·883
S.R.	40·41	38·18	32·44	39·39	36·60	35·47
1 − α (%)	>99·5	>99·5	>99·5	>99·5	>99·5	>99·5
Correlation eq. II						
r	0·975	0·971	0·976	0·971	0·972	0·970
S.R.	51·91	43·23	53·73	45·42	46·73	43·08
1 − α (%)	>99·99	>99·99	>99·99	>99·99	>99·99	>99·99
Correlation eq. III						
r	0·918	0·902	0·880	0·914	0·907	0·897
S.R.	53·72	43·83	35·47	50·57	46·69	41·12
1 − α (%)	>99·99	>99·99	>99·99	>99·99	>99·99	>99·99

[a] Water : methanol.

Correlation equations of type I are one-parameter equations considering differences of Gibbs solvation energies in stationary and mobile phases. The correlation equations of type II are three-parameter equations, which consider the difference of electrostatic $\Delta G_{\mathrm{el}}^{\mathrm{s/m}}$, dispersion-repulsion $\Delta G_{\mathrm{d}}^{\mathrm{s/m}}$ and cavitation $\Delta G_{\mathrm{cav}}^{\mathrm{s/m}}$ contribution values of the Gibbs solvation energy in stationary and mobile phases. Correlation equations of type III are one-parameter equations considering differences of cavitation contribution $\Delta G_{\mathrm{cav}}^{\mathrm{s/m}}$ values in stationary and mobile phases.

Following correlation equations for statistical parameters (see Table VI) were obtained when applying the cavitation contribution calculated according to Sinanoglu.

$$\text{I} \qquad \log k' = -0{\cdot}2677\Delta G_{\mathrm{S}}^{\mathrm{o/w}} - 0{\cdot}1365 \qquad (5)$$

$$\text{II} \qquad \log k' = 0{\cdot}0317\Delta G_{\mathrm{el}}^{\mathrm{o/w}} - 0{\cdot}0471\Delta G_{\mathrm{d}}^{\mathrm{o/w}} - 0{\cdot}0399\Delta G_{\mathrm{cav,S}}^{\mathrm{o/w}} - 1{\cdot}5677 \qquad (6)$$

$$\text{III} \qquad \log k' = -0{\cdot}0344\Delta G_{\mathrm{cav,S}}^{\mathrm{o/w}} - 1{\cdot}4418 \qquad (7)$$

Following correlation equations were obtained applying the cavitation term computed according to Pierotti.

$$\text{I}' \qquad \log k' = -0{\cdot}0238\Delta G_{\mathrm{P}}^{\mathrm{o/w}} - 1{\cdot}1988 \qquad (8)$$

$$r = 0{\cdot}839 \quad n = 12 \quad \text{S.R.} = 23{\cdot}82 \quad 1 - \alpha > 99{\cdot}5\%$$

$$\text{II}' \qquad \log k' = 0{\cdot}0393\Delta G_{\mathrm{el}}^{\mathrm{o/w}} - 0{\cdot}0604\Delta G_{\mathrm{d}}^{\mathrm{o/w}} - 0{\cdot}0298\Delta G_{\mathrm{cav,P}}^{\mathrm{o/w}} - 1{\cdot}591 \qquad (9)$$

$$r = 0{\cdot}983 \quad n = 12 \quad \text{S.R.} = 77{\cdot}91 \quad 1 - \alpha > 99{\cdot}99\%$$

$$\text{III}' \qquad \log k' = -0{\cdot}0233\Delta G_{\mathrm{cav,P}}^{\mathrm{o/w}} - 1{\cdot}3495 \qquad (10)$$

$$r = 0{\cdot}843 \quad n = 12 \quad \text{S.R.} = 34{\cdot}65 \quad 1 - \alpha > 99{\cdot}99\%$$

Increase of methanol concentration in the mixed mobile phase water–methanol resulted in a decrease of regression significance and thereby also in the accordance between the model and actual separation process (cf. Table VIII).

Signs of the absolute terms in equations of type I are in line with their physicochemical sense. The problem of the absolute term arises when comparing Eqs (*5*) and (*8*) with the corresponding Eq. (*1*). Evidently, criterion for the physicochemical correctness of the correlation equation of I, or I′ type (see Eq. (*4*)), is also the magnitude of regression coefficients (a and b values), which should ideally be equal to $-0{\cdot}434/\boldsymbol{R}T$ and $\log V_{\mathrm{s}}/V_{\mathrm{m}}$, respectively (cf. Eq. (*1*)). Constant a equals $-0{\cdot}17432$ at the temperature of compounds being separated $T = 298{\cdot}15$ K. The value of constant b crosses zero. Discrepancy between the absolute term values encountered in equations of type I or I′ in comparison with Eq. (*1*) could be rationalized by the fact that further additional effects in the chromatographic column, as e.g. adsorption, steric effect etc. have to be considered in addition to distribution process of the solute.

Our aim was to express explicitly the relationship of retention on the interaction and Gibbs energies and settle this value as most exactly as possible. To do this, the set of individual contributions corresponding to the total Gibbs retention energy was calculated theoretically but not empirically. Thus, it is more suitable to investigate relative trends in a series of substances i.e. differences in the contributions of Gibbs solvation energy in stationary and mobile phases when evaluating the relationships between structure and retention. The statistical evaluation of one-parameter equations embodying $\Delta G_{cav}^{s/m}$, $\Delta G_{dr}^{s/m}$ and $\Delta G_{el}^{s/m}$ makes it possible to ascertain the weight (statistical) of each contribution to retention of the compound separated in the chromatographic system.

Generally speaking, the correlation equations of the series of compounds under investigation have lower statistical parameters than those of the series of alkylbenzenes[2]. Table VII indicates that interpretation of type I equation is unsatisfactory for the most of compounds of this series. Table VI shows that correlation equations of type I are of less regression significance. The poor correlation of type I equation is due to values of electrostatic contributions of some compounds of this series mainly of those as nitrobenzene and methyl bezoate. Obviously, this would need a more exact calculation of electrostatic contribution than in this case, when only coulombic energy was considered. Interpretation of log k' values by

TABLE VII

Experimental and theoretically calculated values of capacity factors according to correlation equations of types I and II (Sinanoglu) or II′ (Pierotti), respectively. Experimental capacity factors k' refer to the mobile phase water–methanol 35 : 65 and 4·96 . 10^{-4} g of C_{18} ligand per gram of silica substrate

Number	k'_{exp}	k'^{I}_{calc} (Eq. (5))	k'^{II}_{calc} (Eq. (6))	$k'^{II'}_{calc}$ (Eq. (9))
1	0·47	0·62	0·46	0·46
2	0·53	0·74	0·55	0·56
3	0·79	0·97	0·79	0·79
4	0·91	1·45	1·31	1·25
5	1·12	1·15	0·88	0·89
6	1·21	0·57	1·14	1·17
7	1·35	1·47	1·29	1·32
8	1·62	1·16	1·64	1·61
9	1·97	1·89	2·28	1·95
10	2·38	2·34	2·22	2·29
11	3·38	3·12	3·13	3·24
12	3·94	3·32	3·72	4·02

TABLE VIII

Characteristics of correlation equations obtained on correlation of Gibbs retention energy $\Delta G_S^{o/w:m}$ and $\Delta G_S^{h:w/m}$ (kJ mol^{-1}) and their contributions with experimental capacity factors at various composition of the mobile phase and two C_{18} surface coverages of the stationary phase

Parameter	C_{18} surface coverage							
	4·96 . 10^{-4} g (C_{18}/g)				6·6 . 10^{-4} g (C_{18}/g)			
	55 : 45[a]	45 : 55[a]	35 : 65[a]	35 : 65[b]	55 : 45[a]	45 : 55[a]	35 : 65[a]	35 : 65[b]
Correlation eq. I								
r	0·782	0·773	0·749	0·450	0·775	0·667	0·703	0·460
S.R.	15·7	14·85	13·01	12·80	15·37	12·97	14·56	12·76
$1 - \alpha$ (%)	>99·5	>99·5	>99·5	>99·5	>99·5	>99·5	>99·5	>99·5
Correlation eq. II								
r	0·963	0·976	0·990	0·970	0·960	0·979	0·992	0·974
S.R.	34·43	52·64	132·01	42·76	31·79	60·77	198·40	49·22
$1 - \alpha$ (%)	>99·99	>99·99	>99·99	>99·99	>99·99	>99·99	>99·99	>99·99
Correlation eq. III								
r	0·940	0·934	0·919	9·20	0·936	0·938	0·930	0·930
S.R.	76·53	68·76	53·61	53·55	70·63	72·64	63·95	63·86
$1 - \alpha$ (%)	>99·99	>99·99	>99·99	>99·99	>99·99	>99·99	>99·99	>99·99

Mobile phase water: methanol; [a] model stat. phase octanol, [b] model stat. phase heptane.

correlation equation of type II, where cavitation contribution was calculated according to Sinanoglu, is satisfactory e.g. for phenol, aniline, 4-cresol, nitrobenzene, methyl benzoate, 4-ethylphenol; like results, but somehow better can be obtained employing equations of type II′ for which the cavitation contribution was calculated according to Pierotti (see Eq. (*9*)).

Statistical evaluation of improved models octanol/water–methanol and heptane//water–methanol (Table VIII) showed that the presumption to consider the radius of the mixed phase as a weighted average of radii of pure solvents (water and methanol) for calculation of dispersion-repulsion contributions for the mixed mobile phase water–methanol was not quite correct. Similarly, presumption to consider the radius of mobile phase as a weighted average of pure solvent radii for water and methanol was also incorrect for calculation of either dispersion-repulsion or cavitation contributions according to Pierotti. On the other hand, calculation of cavitation model for the mixed mobile phase according to Sinanoglu led unambiguously to correlation equations of higher regression significance. As shown, the computation process for cavitation contribution by substitution of single constants for experimental dependence was correct. Correlations, where the stationary phase was modelled as heptane (Table VIII) did not afford correlation equations of better quality than those for octanol. In other words, heptane is not a suitable model for C_{18} chemically bonded stationary phase.

Correlation equations of types II and III, especially those satisfying the criterion for physicochemical correctness of correlation equation can be applied for prediction of log k' values of isomers, and possibly for further similar isomers. Thus, correlation equation of type II (Table VIII):

$$\text{II} \qquad \log k' = 0{\cdot}0364\Delta G_{\text{el}}^{\text{o/w:m}} - 0{\cdot}0096\Delta G_{\text{d}}^{\text{o/w:m}} - 0{\cdot}2396\Delta G_{\text{cav,S}}^{\text{o/w:m}} - 2{\cdot}8033 \qquad (11)$$

$$r = 0{\cdot}99 \quad n = 12 \quad \text{S.R.} = 132{\cdot}01$$

bears signs of single contributions in accordance with physicochemical sense. Log k' values for 2-cresol, 3-cresol and 3,4,5-trichloroacetophenone (1·45, 0·81 and 2·10, respectivelly) can be calculated employing Eq. (*11*) at C_{18} surface coverage of the stationary phase 4·96 . 10^{-4} g of C_{18} per gram of silica substrate and water–methanol 35 : 65 mobile phase composition.

It could finally be concluded that the described process is more successful for a series of homogeneous compounds than for a heterogeneous one, where the possibilities are restricted due to the non-ballanced individual contributions. Correctness of modelling, mainly of the cavitation contribution according to Sinanoglu, in the mixed mobile phase water–methanol leading to correlation equations of higher quality was verified by comparing the simple and improved models. As shown, octanol, in contrast to heptane, is a suitable model for the C_{18} chemically bonded stationary phases in the RP-HPLC.

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