Generalized criterion of solvent polarity as a tool for control of chromatographic process

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The generalized (reductive) criterion of solvent polarity was obtained by the method of multiparametric optimization of the Snyder index P', Hildebrand parameter δ_T, permittivity ε_r, and solvatochromism parameter $E_T(30)$. Possibilities of employing this criterion for estimation of the elution power of normal and reversed mobile phases used in high-performance liquid chromatography were considered.

Key words: generalized (reductive) criterion of solvent polarity, high-performance liquid chromatography, retention parameters, phenols, chemometrics.

In liquid chromatography, solvent polarity implies its ability to solvate sorbate molecules and immobile phase surface. A sequence of criteria of polarity is presently employed in chromatographic studies, among which permittivity[1] (ε_r) can be given the priority. Its value characterizes the solvent ability to separate charges and dipole orientation. It is most appropriate for the description of the dissociation power of the liquid. However, the permittivity cannot help in describing interactions between the solvent and solute at the molecular level.[2] In several cases, an inconsistency between the elution strength and permittivity is observed. For example, dioxane is close in $\varepsilon_r = 2.2$ to low-polar alkanes ($\varepsilon_r \approx 1.9$) but under normal-phase chromatographic (NPC) conditions manifests a much higher elution strength.

With the development of chromatographic methods, the proposed criteria of polarity became more differentiated.[3,4] The Snyder index (P') was proposed for partition chromatography, the solvent strength criterion ($\varepsilon°$) was proposed for NPC, and the elution strength parameter (S) was proposed for reversed-phase chromatography (RPC). However, some facts[5,6] indicate that these criteria are not optimal and their use sometimes can result in erroneous estimation of the chromatographic properties of the mobile phase.

The P' parameter, being the sum of logarithms of the partition coefficients of standard substances (ethanol, dioxane, and nitromethane) between the vapor phase and tested solvent,[2] is rarely used in liquid chromatography (LC). It is based on the empirical data but does not always adequately estimate the real polarity of solvents observed in LC.[1—6] Although, according to this criterion, MeCN is less polar than MeOH, and the former is most appropriate for RPC.

Another criterion is the Hildebrand parameter of solubility (δ_T) ($\delta_T = c^{1/2}$, where c is the cohesion energy density[3]). When this criterion is used, the polarities of MeCN and MeOH coincide with those observed in LC. The total cohesion energy density is the sum of contributions from dispersion, orientational, induction, and acid-base interactions. Unlike the permittivity, δ_T characterizes the ability of the liquid to dissolve both electrolytes and nonelectrolytes. The closer the δ_T values of the solvent and solute, the higher the dissolution power of the certain solvent. Among disadvantages of this criterion is an excessive contribution of the dispersion component to the total index, whereas the dispersion component changes insignificantly on going from one solvent to another.

One more criterion of polarity is the Dimroth—Reichardt solvatochromism parameter ($E_T(30)$). It is calculated from the spectroscopic measurements of interactions of the solvent with standard *N*-phenoxypyridiniumbetaine dye.[2] The electron transition energy of the charge transfer band characterizes the degree of solvent polarity.

The sequences of solvents in different polarity scales (elution sequences) constructed using various criteria are sufficiently close. The typical solvents are arranged in such sequences between nonpolar alkanes and polar water. Only perfluoroalkanes are less polar by all criteria, but their employment is restricted by ecological and economic

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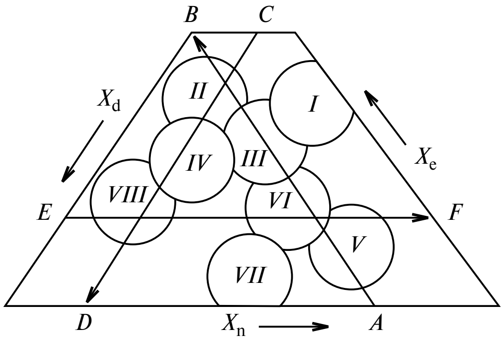

Fig. 1. Triangular diagram of the Snyder selectivity[3]: *I—VIII* (see clarification in the text), regions in which solvents are grouped by selectivity. (X_e, X_d, and X_n are the abilities to proton-releasing, proton-withdrawing, and dipole-dipole interactions, respectively. *AB*, *CD*, and *EF* are the trends by which the sequences of solvents were selected to estimate correlations (3) and (4)).

considerations. Formamide and secondary amides are more polar than water (in term of ε_r).[2,7]

The solvent polarity can be divided into partial components characterizing this or another mechanism of interactions (dipole-dipole, proton-releasing, or proton-withdrawing) between the solvent and solute. Snyder distinguished eight groups of solvents with similar selectivity toward the interactions indicated[3]: *I*, aliphatic ethers; *II*, aliphatic alcohols; *III*, pyridine derivatives, THF, sulfoxides; *IV*, glycols, AcOH; *V*, dichloromethane, 1,2-dichloroethane; *VI*: *a*, aliphatic ketones and esters, dioxane; *b*, sulfons, nitriles; *VII*, arenes, haloarenes, nitro compounds, aromatic esters; and *VIII*, fluoroalkanols, water. This classification demonstrates the tendency of a solvent to act as a proton donor or acceptor or enter into strong dipole-dipole interactions (Fig. 1).

Possibilities of estimating polarities from the statistically averaged chemometric parameters, which are a linear combination of various physicochemical and chemical properties of solvents, were considered.[2,8,9]

Summary tables with different polarity scales are usually presented in the literature and allow researchers to choose this or another criterion for interpretation of experimental data.[2—7] In this work we attempted to find the generalized criterion of solvent polarity, which would be appropriate for different variants of LC and suitable for comparison of results obtained using mobile phases different in qualitative and quantitative compositions. This criterion is based on the P', δ_T, ε_r, and $E_T(30)$ parameters known for the most important solvents.

The estimation of variants by the generalized criterion is a standard method of computer search for optimum solutions.[10] The first scale of the generalized criterion of polarity of the listed four parameters was tested in determination of solvent efficiencies for specific chromatographic problems[11] and in analysis of the influence of polarity of binary mobile phases on their boiling points and azeotropic compositions.[12] This scale was plotted from the data for 32 solvents applied mainly in HPLC. In this work we considered 42 solvents, which are used in both column and planar LC.

Experimental

Parameters of chromatographic retention of sorbates were measured on a Milikhrom-4 instrument (Russia) in steel microcolumns (2×62 mm) packed with the Silasorb 600 and Silasorb C_{18} sorbents with a particle size of 5 μm. Hexane was used as diluent in the mobile phase in NPC, and Pr^iOH (volume fraction $\varphi_2 = 0.001—0.30$), AcOEt ($\varphi_2 = 0.025—0.50$), and dioxane ($\varphi_2 = 0.027—0.52$) were used as modifiers. The water—MeCN and water—MeOH mobile phases ($\varphi_2 = 0.5—1$) were used for RPC. In all cases, the flow rate was 100 $\mu L\ min^{-1}$. The retention volumes of phenols used in this work as sorbates were monitored in the two-wave regime at $\lambda = 254$ and 272 nm.

Results and Discussion

The generalized parameter was obtained by the transformation of the P', δ_T, $E_T(30)$, and ε_r parameters into dimensionless values using the equation

$$P_i = (D_i - D_{\min})/(D_{\max} - D_{\min}), \qquad (1)$$

where P_i is the normalized parameter for the ith solvent, D_i is the initial parameter of the ith solvent, and $D_{\max}$ and $D_{\min}$ are the maximal and minimal D_i values. Then the arithmetic mean P_i was found. Since none of the solvents for which all four parameters are minimal or maximal got into the set, the normalization procedure was repeated. The maximal polarity criterion for water was accepted as 100, and the minimal criterion for decane was taken as 0 (Table 1). In the proposed variant of generalized criterion, the weight coefficients for the partial parameters are the same.

The generalized index P_N is named reductive to emphasize that it can be obtained by the chemometric method approach implying the reduction of the number of criteria.

In the scale framework, the polarity of most solvents does not change dramatically, and only the smoothening effect is achieved for anamalously low or, on the contrary, high polarity values of particular solvents, which was observed in the initial criteria due to their specific sensitivity to one of the partial polarities.

A linear correlation between the elution strength of solvents on SiO_2 and Al_2O_3 is known[2,13—15] in NPC

$$\varepsilon°(SiO_2) = 0.77\varepsilon°(Al_2O_3). \qquad (2)$$

The elution ability $\varepsilon°$ is a dimensionless value, which is determined as the adsorption energy of the solvent referred to the adsorbent surface area occupied by the sol-

Table 1. Generalized criterion of polarity P_N, partial parameters P', δ_T, ε_r, and $E_T(30)$, and criteria of elution strength $\varepsilon°(SiO_2)$, $\varepsilon°(Al_2O_3)$, and S for various solvents

Solvent	P_N	P'	δ_T /MPa$^{1/2}$	ε_r	$E_T(30)$ /kJ mol^{-1}	$\varepsilon°(SiO_2)$	$\varepsilon°(Al_2O_3)$	S
Decane	0	−0.3	15.95	2.00	130.1	0.03	0.04	—
Isooctane	0.32	0.1	14.99	1.94	130.1	0.01	0.01	—
Pentane	0.45	0	15.65	1.84	129.7	0	0	—
Cyclohexane	0.71	−0.2	16.77	2.02	129.4	0.02	0.04	—
Hexane	0.85	0.1	15.83	1.88	129.7	0.01	0.01	—
Heptane	1.44	0.2	16.18	1.93	130.1	0.01	0.01	—
Et_3N	6.24	1.9	15.34	2.42	134.3	0.42	0.54	—
CCl_4	7.29	1.6	17.59	2.23	135.5	0.11	0.18	—
CS_2	8.25	1.0	20.45	2.60	137.2	0.12	0.15	—
Diisopropyl ether	9.02	2.4	14.52	3.88	142.7	0.28	0.28	—
Diethyl ether	11.73	2.8	16.20	4.27	144.4	0.43	0.38	4.8[a]
Toluene	12.07	2.4	19.49	2.37	141.8	0.23	0.30	—
Benzene	13.44	2.7	19.86	2.23	143.5	0.25	0.32	—
Chlorobenzene	16.65	2.7	19.40	5.62	156.9	0.24	0.31	—
Bromoethane	16.72	3.1	18.00	5.40	157.3	0.29	0.38	—
THF	21.00	4.0	20.21	7.39	156.5	0.44	0.51	4.4
Dioxane	21.71	4.8	21.78	2.21	150.6	0.60	0.61	3.5
AcOEt	21.84	4.4	19.58	6.02	159.5	0.48	0.60	4.3[a]
$CHCl_3$	22.00	4.1	20.19	4.72	163.5	0.26	0.36	—
CH_2Cl_2	23.04	3.1	21.85	8.93	170.3	0.30	0.40	—
1,2-Dichloroethane	24.88	3.5	21.76	10.38	172.8	0.32	0.44	—
Octan-1-ol	28.85	3.4	21.70	10.00	194.4	0.42[b]	0.55[b]	4.0[a]
Butanone	29.03	4.7	20.37	18.51	172.8	0.40	0.51	3.9[a]
Pyridine	29.04	5.3	21.27	12.40	169.5	0.55	0.71	3.9[a]
Bu^tOH	29.12	4.1	21.70	12.47	183.6	0.54	0.70	3.9[a]
Pentan-1-ol	31.25	3.5	20.05	14.30	205.4	0.47	0.61	3.8[a]
Benzonitrile	31.72	4.6	21.89	25.20	173.6	0.46[b]	0.60[b]	—
Acetone	32.18	5.1	21.50	20.54	176.6	0.50	0.58	3.4
Nitrobenzene	33.00	4.5	22.70	35.50	165.8	0.48[b]	0.62[b]	—
BuOH	36.29	3.9	23.30	17.10	210.1	0.53[b]	0.69[b]	3.6[a]
Propan-2-ol	36.72	3.9	25.30	19.13	202.5	0.55	0.82	4.2
AcOH	38.45	6.0	20.70	6.30	216.4	0.56[b]	0.73[b]	3.5[a]
Propan-1-ol	39.09	4.0	25.10	20.33	212.2	0.55	0.82	3.4[a]
DMF	42.88	6.4	24.14	36.71	183.3	0.63[b]	0.81[b]	3.3[a]
EtOH	43.97	4.3	27.92	24.55	217.1	0.60	0.88	3.6
MeCN	44.66	5.8	26.90	35.94	190.8	0.60	0.55	3.1
Nitromethane	46.72	6.0	27.70	37.78	193.3	0.49	0.64	3.1[a]
DMSO	48.41	6.4	26.18	48.50	188.7	0.58	0.75	3.0[a]
MeOH	54.34	5.1	32.42	32.66	231.8	0.70	0.95	3.0
1,2-Ethanediol	62.77	6.9	34.77	37.70	235.6	0.85	1.11	2.3[a]
Formamide	83.83	7.3	36.61	111.00	237.2	1.22[b]	1.58[b]	1.2[a]
Water	100	10.2	52.20	78.54	264.0	1.50	1.95	0

[a] The S values were calculated from Eq. (6).

[b] The $\varepsilon°$ values were calculated from Eqs. (3) and (4).

vent. The elution power depends on the solvent and also on the adsorbent and other conditions accepted as standard. Presently, $\varepsilon°$ is more often used in TLC where modified silica gels prepared using modern technologies are less popular and where Al_2O_3 is used as the immobile phase. On going to new chromatographic systems, the $\varepsilon°$ values need to be refined or established again. To increase the massive of analyzed data, let us calculate the tentative $\varepsilon°(SiO_2)$ or $\varepsilon°(Al_2O_3)$ values by Eq. (2) and find linear correlations (3) and (4) between the P_N parameter and $\varepsilon°$ for 37 solvents

$$\varepsilon°(SiO_2) = 0.0146P_N, \quad (3)$$

$n = 37$, $r = 0.92$;

$$\varepsilon°(Al_2O_3) = 0.0189P_N, \quad (4)$$

$n = 37$, $r = 0.94$.

The calculations show that the generalized criterion correlates with the elution power on both sorbents more tightly than the initial partial polarities included in the generalized criterion. If the correlations are considered not in the whole massive of solvents but according to Snyder´s classification (only among isolated groups of solvents in which either the parameter of the proton donor $X_e = \log K''_e/P'$ or the parameter of the proton acceptor $X_d = \log K''_d/P'$, or the dipole-dipole interaction parameter $X_n = \log K''_n/P'$ monotonically increases), then correlations (3) and (4) become much better. For example, in the sequence nonpolar alkanes—*II*, *III*, *V*, and *VIa* selectivity group solvents—water oriented primarily to the X_e parameter (see Fig. 1, trend *AB*), correlations (3.1) and (4.1) are fulfilled

$$\varepsilon°(SiO_2) = 0.0152P_N, \quad (3.1)$$
$n = 23, r = 0.97;$

$$\varepsilon°(Al_2O_3) = 0.020P_N, \quad (4.1)$$
$n = 23, r = 0.98.$

Considering the sequence, which reflects changes in *CD* (see Fig. 1) and proton acceptor parameter X_d (alkanes, *II* and *IV* group solvents, water), we obtain

$$\varepsilon°(SiO_2) = 0.0145P_N, \quad (3.2)$$
$n = 19, r = 0.98;$

$$\varepsilon°(Al_2O_3) = 0.0193P_N, \quad (4.2)$$
$n = 19, r = 0.98.$

Analysis of the *FE* sequence parallel to a change in the parameter of dipole-dipole interaction X_n (alkanes, solvents of *V*—*VII* groups, water) leads to the following results:

$$\varepsilon°(SiO_2) = 0.0147P_N, \quad (3.3)$$
$n = 22, r = 0.96;$

$$\varepsilon°(Al_2O_3) = 0.0184P_N, \quad (4.3)$$
$n = 22, r = 0.97.$

Thus, the P_N criterion agrees well with Snyder´s classification of solvents and, being used in combination, the criterion helps to solve the problem of choosing the solvent for LC because it takes into account both the strength and selectivity of the solvent.

The correlations obtained make it possible to estimate the approximate ε° values for some solvents by the P_N value (see Table 1). For AcOH the calculated ε° values are underestimated because, as follows from experiment, its elution power is very high ($\varepsilon° \geq 1$).[13,14]

The elution strength *S* in RPC is determined empirically from the equation

$$\log k' = \log k'_1 - S\varphi_2, \quad (5)$$

where $\log k'_1$ is the retention factor when water is used as eluent, and φ_2 is the volume fraction of the organic modifier in the mobile phase. Equation (5) obeys well when the eluent composition changes within 30%, and the *S* index is sensitive to the sorbate nature.[3,5]

It is found that the known *S* values are inversely proportional to P_N

$$S = 5.39 - 0.05P_N, \quad (6)$$
$n = 8, r = 0.93.$

This provides evidence that the P_N parameter is appropriate for the estimation of the elution strength of solvents in both the NPC and RPC regimes. Unlike the *S* parameter, the reductive criterion P_N is averaged *a priori* and is not referred to specific RPC conditions. The *S* values predicted by Eq. (6) for solvents, which are unrestrictedly or partially soluble in water (≥7%), MeCN, and MeOH, are presented in Table 1. For example, additives of 4—14% pentan-1-ol or octan-1-ol to reversible phases with $\varphi_2 \geq 50\%$ in some cases enhance the selectivity of sorbate separation.[16] Therefore, the calculated *S* values are also of interest for solvents restrictedly soluble in water but highly soluble in MeCN and MeOH.

Mobile phases of individual solvents are rarely used. Binary or multicomponent phases including an inactive solvent (diluent) and a certain fraction of active solvents (modifiers) are employed. One of the methods for checking the applicability of the generalized criterion of polarity is the establishment of a single relation between the retention in one column of the same sorbate and the polarity in several series of mobile phases with a variable composition differed by the type of modifier.

For example, MeCN and MeOH are predominantly used as modifiers in RPC. If we accept, as in partition LC, for the P' [3] and δ_T [5] parameters that the total polarity in mixtures of these solvents with water is additive, then

$$P_N = \Sigma\varphi_i P_{N_i}, \quad (7)$$

where P_{N_i} and φ_i are the polarity and volume fraction of the *i*th solvent, respectively. The plot of ε_r *vs.* composition in MeCN—water and MeOH—water mixtures is also almost linear.[17] In a narrow region at $\varphi_2 = 0.98—1.0$, the $E_T(30)$ parameter changes jumpwise due to the specificity of the solvatochromic effect. However, in a wide range ($\varphi_2 = 0—0.98$), as shown by our calculations using known data,[18] the $E_T(30)$ parameter almost linearly depends on the volume fraction of water ($r > 0.98$). In the ideal case, based on the isoelutropism principle, the retention of a particular sorbate in a column should be the same if mobile phases different in composition have the same P_N value and, hence, the same strength.

Let us consider as an example the behavior of several phenols in binary mobile phases for RPC. Phenols are often used as standard sorbates to verify retention models in chromatographic systems under study.[5] The elution strength of water in RPC tends to zero. Therefore, it can

Table 2. Shatts criterion (H), coefficients in Eq. (8), and correlation coefficient r for phenols in the water—modifier mobile phases (Silasorb C_{18} as sorbent)

Compound	H	Modifier	φ_2	Coefficients		
				a	b	r
Pyrocathechol	0.3	MeCN	0.5—1	1.95	0.006	0.991
	0.3	MeOH	0.5—1	1.73	0.009	0.966
	0.3	—*	0.5—1	1.91	0.007	0.905
Phenol	2.0	MeCN	0.5—1	1.93	0.007	0.993
	2.0	MeOH	0.5—1	1.71	0.010	0.982
	2.0	—*	0.5—1	1.87	0.008	0.959
o-Cresol	3.0	MeCN	0.5—1	1.66	0.013	0.974
	3.0	MeOH	0.5—1	1.50	0.014	0.966
	3.0	—*	0.5—1	1.64	0.012	0.902
p-Cresol	3.0	MeCN	0.5—1	1.72	0.012	0.996
	3.0	MeOH	0.5—1	1.23	0.018	0.968
	3.0	—*	0.5—1	1.60	0.013	0.921
Eugenol	4.3	MeCN	0.5—1	1.56	0.015	0.994
	4.3	MeOH	0.5—1	0.63	0.030	0.981
	4.3	—*	0.5—1	1.21	0.021	0.939
2-Naphthol	6.0	MeCN	0.5—1	1.50	0.018	0.967
	6.0	MeOH	0.5—1	0.66	0.029	0.980
	6.0	—*	0.5—1	1.32	0.020	0.890
p-*tert*-Butylphenol	6.0	MeCN	0.6—1	1.15	0.026	0.982
	6.0	MeOH	0.6—1	0.20	0.038	0.939
	6.0	—*	0.6—1	1.13	0.025	0.826
Ionol	11.3	MeCN	0.75—1	0.65	0.039	0.992
	11.3	MeOH	0.75—1	1.08	0.066	0.997
	11.3	—*	0.75—1	0.41	0.042	0.929
3-(2,4-Dimethylphenyl-1-(2-hydroxypenyl)propan-1-one	12.0	MeCN	0.75—1	0.48	0.044	0.998
	12.0	MeOH	0.75—1	0.70	0.058	0.998
	12.0	—*	0.75—1	0.90	0.033	0.791
3-(4-*tert*-Butylphenyl)-1-(2-hydroxyphenyl)propan-1-one	13.3	MeCN	0.75—1	0.36	0.046	0.998
	13.3	MeOH	0.75—1	0.90	0.063	0.996
	13.3	—*	0.75—1	0.51	0.041	0.906
3-(Biphenil-4-yl)-1-(2-hydroxyphenyl)propan-1-one	15.3	MeCN	0.75—1	0.19	0.049	0.975
	15.3	MeOH	0.75—1	0.65	0.058	0.988
	15.3	—*	0.75—1	0.68	0.038	0.841

* General correlation taking into account the values for both modifiers.

be expected that the retention volumes (V_r) increase with an increase in the strength.

In fact, analysis of the experimental data showed (Table 2) satisfactory general correlations for phenols with different compositions in the MeCN—water and MeOH—water elution sequences in the interval φ_2 = 1—0.5

$$\log V_r = a + bP_N. \quad (8)$$

If the isoelutropism principle does not obey, individual correlations (8) found from particular methanolic or acetonitrile sequences would substantially differ in the a and b coefficients.

Retention of phenols is primarily affected by the total polarity of the eluent and, to a less extent, the type of modifier, which agrees with the universal character of the criterion. At the same time, according to the solvophobic mechanism of retention on reversible immobile phases, the V_r values increase in accordance with an increase in the sorbate hydrophobicity. The latter is often expressed in the form of the Shatts criterion (H).[6] There are correlations between the retention parameters of phenols and their hydrophobicity in isoelutropic and close in polarity mobile phases (Table 3)

$$\log V_r = c + dH. \quad (9)$$

The explicit correlations between the phenol retention and polarity of the mobile phase expressed as an additive generalized criterion of polarity and between the structure (hydrophobicity) of sorbates and their retention in an eluent isoelutropic by a certain criterion points to a possibility of its use in studying the chromatographic be-

Table 3. Coefficients in Eq. (9) and correlation coefficient (*r*) for phenols* in the water—MeCN and water—MeOH mobile phases (Silasorb C_{18})

Modifier	φ_2	P_N	Coefficients		
			c	*d*	*r*
MeCN	1	44.66	2.22	0.015	0.957
MeOH	1	53.34	2.22	0.015	0.924
MeCN	0.8	55.73	2.22	0.049	0.968
MeOH	0.8	62.67	2.18	0.059	0.933
MeCN	0.75	58.50	2.26	0.061	0.988
MeOH	0.75	65.01	2.21	0.069	0.971
MeCN	0.6	66.80	2.29	0.076	0.923
MeOH	0.6	72.00	2.29	0.098	0.900
MeCN	0.5	72.33	2.35	0.071	0.926
MeOH	0.5	76.67	2.39	0.092	0.908

* See Table 2.

havior of substances at different polarities of the mobile phase and structural peculiarities of the sorbate. However, some distinctions in selectivity of mobile phases with MeCN and MeOH are obvious and expressed in the fact that individual correlations (8) are better fulfilled than general correlations, and the general correlations exhibit systematic deviations caused by the type of modifier (Fig. 2).

Correlations (8) and (9) are practically significant: they allow one to estimate the retention characteristics of phenols under the chosen RPC conditions at an arbitrary composition of the mobile phase, to calculate V_r on going from one eluent to another, and to predict the possibility of separation of phenols with different hydrophobicities in the mobile phase with a specified polarity.

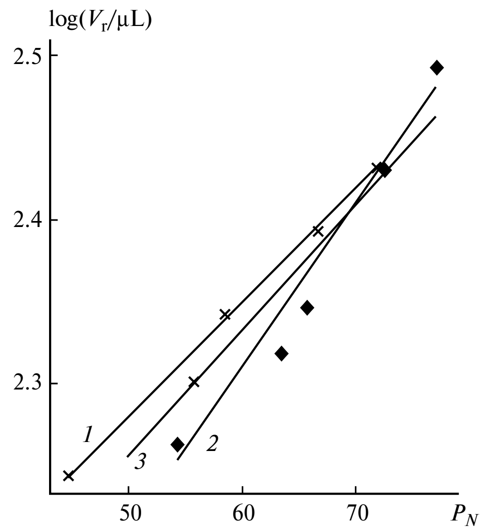

Fig. 2. Correlations (8) for phenol in the water—modifier mobile phases (V_r is the retention volume, P_N is the generalized criterion of polarity): modifiers MeCN (*1*) and MeOH (*2*), and general correlation (*3*).

It can be useful to apply the generalized criterion for the isocratic variant of RPC and also for optimization of the program of the gradient of the mobile phase composition by the Snyder method[3,5] when the linear gradient character is considered optimal.

Let us substitute the function of the mobile phase composition (φ) *vs.* time *t* ($\varphi = A + Bt$, where *A* and *B* are coefficients) by the function

$$P_N = P_0 - kt, \qquad (10)$$

where P_0 is the mobile phase polarity in the beginning of the gradient ($t = 0$), and *k* is the specified coefficient of the gradient program. The sign minus means that the gradient program begins from the more polar composition of the mobile phase with a lower elution strength.

The linear gradient of the strength can be expressed through the correlation

$$\log V_{\text{in}} = \log V_0 - g(t/t_0), \qquad (11)$$

where V_{in} is the retention volume of the sorbate under isocratic conditions corresponding to the composition at the inlet of the column in the moment *t* from the time of obtaining the initial gradient, V_0 is the retention volume corresponding to the composition of the mobile phase in the onset of the gradient ($t = 0$), *g* is the gradient slope, and t_0 is the "dead" time of the column. Let us insert expression (11) into Eq. (8)

$$\log V_{\text{in}} = a + b(P_0 - kt) = a + bP_0 - bkt. \qquad (12)$$

Let us compare Eqs. (11) and (12)

$$g = (\log V_0 - a - bP_0 + bkt)(t_0/t) \qquad (13)$$

and since $\log V_0 = a + bP_0$, we get

$$g = bkt_0. \qquad (14)$$

Thus, the *g* parameter is a function of solvent (through the *b* coefficient) and specified characteristics of the gradient (through *k*) and column (through t_0). Equation (14) was derived on the basis of the dependence of Eqs. (5) and (11) in which $\log k'$ is used instead of $\log V_r$.[5] Given that the optimum *g* value lies in the 0.2—0.4 range and t_0 of the particular column at a flow rate of 100 μL min^{-1} equals ~1.6 min, the gradient program can be planned varying the *k* value.

Let us consider the applicability of additive Eq. (7) for prediction of the strength of mixed mobile phases under the NPC conditions. With an increase in the fraction of the polar modifier in the mobile phase, the adsorption retention mechanism competes more strongly with the partition mechanism. Therefore, the plot of the retention parameters under the NPC conditions on the eluent composition is nonlinear.[3,5,6] The greater the difference in polarities of the diluent and modifier, the more pronounced the nonadditivity effect of the strength. For example, when the concentration of a polar modifier, *e.g.*, Pr^{i}OH in hexane (φ_2 = 0.0001—0.01) increases insignificantly, the strength of the mobile phase increases sharply; the further increase in φ_2 results in a smooth increase in the elution power (saturation effect).

Analysis of the empirical functions $\varepsilon° = f(\varphi_2)$ for mixed solvents[3,5,6] shows that Eq. (7) adequately describes the isotherms of strength in NPC if the modifier polarity insignificantly differs from the diluent polarity when the nonadditivity of the $\varepsilon° = f(\varphi_2)$ function can be neglected. Equation (7) is appropriate as the first approximation in partition LC on polar immobile phases if φ_2 is high and the range of its variation is narrow. Correlation (7) is applied for partition LC to the P' and δ_T indices,[3,5,6] which are included in the generalized criterion P_N. The ε_r and $E_T(30)$ parameters of binary mixtures of nonpolar and polar solvents can noticeably deviate from additivity, especially the latter.[2,17,18] Therefore, the linear change in the isotherm of mixed eluent polarity for NPC is a particular case of the ideal mobile phase.

The additive P_N value calculated from Eq. (7) can be employed in another way, namely, to use it instead of the volume fractions of the modifier. In this case, P_N is the normalized linear function of the eluent composition, which is expressed not in the volume or weight fractions but in polarity units. This scale is convenient because it allows one to compare sequences of mobile phases containing modifiers different in nature and concentration or their mixtures in the same system of coordinates.

Analogously to $\varepsilon° = f(\varphi_2)$, the $V_r = f(P_N)$ functions demonstrate the saturation effect, which is more intense for a hexane—Pr^{i}OH system and a less intense for hexane—dioxane and hexane—AcOEt systems. The V_r values decreases drastically with an increase in P_N and then decrease monotonically with an increase in the eluent polarity (Fig. 3). The retention volumes approach the retention volume of the nonsorbed compound (V_0). The saturation effect is especially pronounced for hydrophobic phenol derivatives and phenols in which the OH group is shielded by a bulky substituent in the *ortho*-position or a substituent forming an intramolecular hydrogen bond with this OH group.[19] The runs of the $V_r = f(P_N)$ plots mirrors the $\varepsilon° = f(\varphi_2)$ trends. As can be seen in Fig. 3, in mobile phases isoelutropic in P_N, the retention volumes of phenol are close if the modifiers refer to one group of selec-

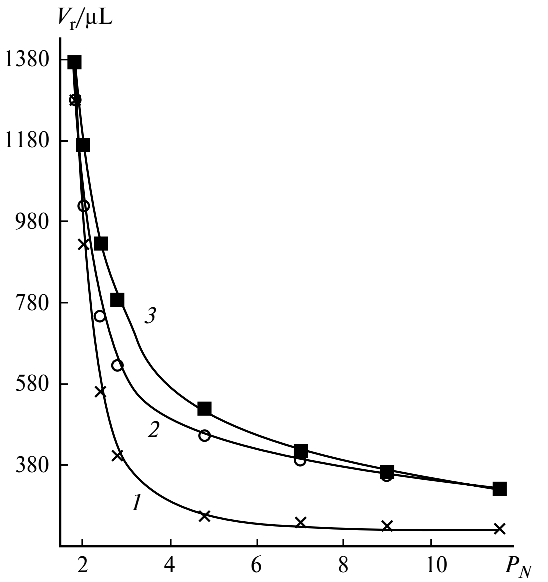

Fig. 3. Relation (15) for phenol in the hexane—modifier mobile phases (V_r is the retention volume, P_N is the generalized criterion of polarity): modifiers Pr^{i}OH (*1*), AcOEt (*2*), and dioxane (*3*).

Table 4. Coefficients in Eq. (15) and correlation coefficient (*r*) for phenols in the hexane—modifier mobile phases (Silasorb 600, V_0 = 160 μL, P_N = 0.89—11.57)

Compound	Modifier	Coefficients			
		$a_1 \cdot 10^{-3}$	$b_1 \cdot 10^{-3}$	$c_1 \cdot 10^{-3}$	r
Phenol	Pr^{i}OH	1.21	−6.76	14.78	0.997
	AcOEt	2.45	−7.64	12.23	0.985
	Dioxane	2.04	−2.70	5.31	0.994
Eugenol	Pr^{i}OH	2.28	−15.95	30.14	0.994
	AcOEt	2.62	−14.94	31.15	0.993
	Dioxane	1.84	−7.12	14.47	0.989
2-Naphthol	Pr^{i}OH	1.49	−5.89	10.32	0.986
	Dioxane	3.24	−9.66	12.14	0.980
3-(2,4-Dimethylphenyl-1-	Pr^{i}OH	0.54	−3.54	5.41	0.988
(2-hydroxypenyl)propan-1-one	AcOEt	0.84	−3.54	6.46	0.996
3-(4-*tert*-Butylphenyl)-1-	Pr^{i}OH	0.47	−2.80	4.53	0.986
(2-hydroxyphenyl)propan-1-one	AcOEt	0.82	−3.57	5.70	0.987
3-(Biphenil-4-yl)-1-	Pr^{i}OH	0.64	−4.20	7.15	0.988
(2-hydroxyphenyl)propan-1-one	AcOEt	0.53	−0.60	7.64	0.983

tivity (AcOEt and dioxane). Systematic deviations in elution strength are observed between the mobile phases with Pr^{i}OH and hexane—AcOEt and hexane—dioxane phases.

Computer processing of the experimental curves for $V_r = f(P_N)$ showed that they are adequately described by an inversion equation of the third order (Table 4)

$$V_r = V_0 + a_1/P_N + b_1/(P_N)^2 + c_1/(P_N)^3, \qquad (15)$$

where V_0, a_1, b_1, and c_1 are empirical coefficients, and P_N is the total polarity determined using Eq. (7). The V_0 value approaches the minimum, which lies between the extrapolated retention volume at $\varphi_2 = 1$ and the "dead" volume. Let V_0 = 160 μL, which corresponds to V_r of poorly sorbed benzene on a given column in the hexane—Pr^{i}OH eluent (φ_2 = 0.3, P_N = 11.61). The initial region of the $V_r = f(P_N)$ function in the interval φ_2 = 0.001—0.10 is well approximated by an inversion equation of the second order with a systematic deviation from experiment in the region of $\varphi_2 > 0.2$ in which chromatography is not performed, as a rule, because of low selectivity. We have recently considered[19] in detail the influence of the polarity of the normal mobile phase and structure of phenols on their retention. The P_N criterion and initial criterion P^0 [11,12] are related by a distinct linear function

$$P_N = 101.22P^0 - 0.28, \qquad (16)$$
$$r = 0.999,$$

therefore, the qualitative conclusions made previously[11,12,19] are valid for this reductive scale.

Thus, a comparison of the reductive criterion of polarity with the empirical parameters of strength and analysis of experimental data on retention of phenols, depending on the mobile phase polarity under RPC and NPC conditions, show that this criterion is promising for application in chromatographic practice to predict the elution properties and study "retention—properties of mobile phase—sorbate structure" models.

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