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Structure–retention correlations of isomeric alkylphenols in gas–liquid chromatography

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ABSTRACT

Correlations of the chromatographic retention of alkylphenols with their boiling points, molecular refraction and ionization constants were studied. The correlations were obeyed better for the alkylphenol groups which differ in the degree of shielding of the hydroxyl group. The dependences are approximated most exactly for alkylphenols with substituents at positions 2 and 6 by a four-factor equation and for the other phenols by a eight-factor equation which include the Van der Waals volume and connectivity indices of the first five orders as independent variables.

INTRODUCTION

Correlations of chromatographic retention with the physico-chemical and structural characteristics of substances are of significance for the identification of components of complex mixtures. A comprehensive analysis of the potential of different structure–chromatographic retention relationships, calculation schemes and their use in chromatographic investigations has been given in several reviews[1–6].

Studies of the structure–retention relationship are based on the principle of additivity of free energies of intermolecular interactions of the substances with the stationary phase, which are determined according to the dependence

$$\Delta G^0 = -RT \ln K \tag{1}$$

where K is the chromatographic distribution coefficient.

The widely used Kováts retention indices[7] can be expressed in units of free energy of sorption of n-alkanes:

$$I = 100 \cdot \frac{\Delta G^0 - \Delta G_n^0}{\Delta G_{n+1}^0 - \Delta G_n^0} + 100\, n \tag{2}$$

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where n is the number of carbon atoms in the n-alkane molecule.

The additive scheme suggested by Berezkin[8] for calculating the characteristics of retention by structural increments of the compound assumes additivity of retention indices[9]:

$$I = \sum_{i=1}^{n} a_i x_i + b \tag{3}$$

where x_i represents physico-chemical and structural characteristics of compound i and a_i and b are constants. Eqn. 3 may be simplified if we consider the linear correlation of the retention index to be dependent on the parameter:

$$I = ax + b \tag{4}$$

A number of workers who have studied the dependence of alkylphenol retention on different physico-chemical parameters have considered eqn. 4.

Franc[10] derived an empirical relationship between the relative retention volume and the dipole moment of isomeric alkylphenols. Karger and co-workers[11,12] showed that the Hammet equation can be used to characterize specific interaction forces between phenols and the stationary phase. Extension of the field of application of the Hammet equation permitted essential information on the mechanism of intermolecular interactions of phenols with different solvents to be obtained[13,14]. Lille[15] reported a linear dependence of retention indices and their increments on the number of carbon atoms in the side-chain of alkylphenols and induction constants of substituents. Correlation dependences of retention indices on the boiling temperature, molecular refraction and Hammet and Taft constants of alkyl substituents have been determined for a comparatively restricted number of alkylphenols[16,17]. It was shown that the linear dependence of the logarithm of the retention volume of different series of monosubstituted n-alkylphenols on the number of carbon atoms has a "break point" corresponding to n-propylphenols[18]. Hall and Kier[19] reported a direct influence of the structure of alkylphenols on their toxicity. Dmitrikov and Nabivach[20] established a correlation dependence of the relative retention times of alkylphenol in high-performance liquid chromatography on molecular connectivity indices of the first order. It has been shown that correlations for alkylphenols may be described by multi-factor equations[21].

EXPERIMENTAL

Retention indices of C_6–C_{12} alkylphenols obtained on a column packed with 5% hexaphenyl ether (HPE) on Chromatone N AW HMDS (0.16–0.20 mm) at 160°C were used[22].

Boiling temperature (t_b), molecular refraction (R_M), ionization constant (pK_a) in water and methanol and structural parameters (Van der Waals volume[23] and molecular connectivity index) were used as the variable x in eqns. 3 and 4.

The Van der Waals volumes (V_w) were calculated according to Bondi[23] by summation of the volume contributions of certain groups that form molecules of alkylphenols. For example, V_W for 3-ethyl-5-methylphenol is given by

$$V_W = V_W(\text{benzene ring}) + V_W(OH) + V_W(C_2H_5) + V_W(CH_3)$$

$$= 40.80 + 8.04 + 23.90 + 13.67 = 86.41 \text{ ml/mol}$$

The path (χ_p) and cluster ($^3\chi_c$, χ_{pc}) connectivity indices of the first five orders were calculated according to Kier and Hall[24]. Having combined the indicated indices, it is possible to obtain the total path and cluster index, *e.g.*, $^3\chi_{p+c} = {}^3\chi_p + {}^3\chi_c$, $^4\chi_{p+pc} = {}^4\chi_p + {}^4\chi_{pc}$, etc. To characterize more completely the structure of alkylphenols, the sums of connectivity indices of several orders were calculated, *e.g.*,

$$^{1-3}\chi_p = {}^1\chi + {}^2\chi + {}^3\chi_p$$

$$^{1-3}\chi_{p+c} = {}^1\chi + {}^2\chi + {}^3\chi_{p+c}$$

$$^4\chi_p = {}^1\chi + {}^2\chi + {}^3\chi_p + {}^4\chi_p$$

$$^{1-4}\chi_{p+pc} = {}^1\chi + {}^2\chi + {}^3\chi_{p+c} + {}^4\chi_{p+pc}$$

RESULTS AND DISCUSSION

Preliminary calculations of the coefficients in eqn. 4 for certain homologous series of alkylphenols with the use of connectivity indices of different orders made it possible to evaluate their significance and to choose the type of index that could provide the highest correlation. Table I shows that the sums of the path indices $^{1-3}\chi_p$, $^{1-4}\chi_p$ and $^{1-5}\chi_p$ correlate better with the retention index than the analogous path and cluster indices. Among the path indices studied, the sum of path indices of four orders, $^{1-4}\chi_p$, which simultaneously with the high level of correlation permits minimum standard deviations of the calculated retention indices to be obtained, is preferable.

The retention indices used and the physico-chemical and structural parameters of alkylphenols are given in Table II.

TABLE I

CORRELATION COEFFICIENTS AND STANDARD DEVIATIONS (i.u.) FOR EQNS. 4

Series of alkylphenols[a]	*Value of x*						
	$^1\chi$	$^{1-3}\chi_p$	$^{1-4}\chi_p$	$^{1-5}\chi_p$	$^{1-3}\chi_{p+c}$	$^{1-4}\chi_{p+pc}$	$^{1-5}\chi_{p+pc}$
3-MePh, 2,5-DiMePh, 2-Et-5-MePh,	0.9995	0.9978	0.9993	0.9992	0.9992	0.9933	0.9948
3-Me-6-*n*-PrPh	2.9	6.1	3.4	3.8	11.6	10.8	9.5
2-MePh, 2,3-DiMePh,	1.0000	0.9999	1.0000	0.9992	0.9999	0.9999	0.9997
2,3,4-TriMePh, 2,3,4,5-TetraMePh	0.9	1.9	0.4	5.1	1.8	2.8	3.1
Ph, 2-MePh, 2-EtPh, 2-*n*-PrPh	0.9987	0.9988	0.9996	0.9998	0.9968	0.9942	0.9938
	4.9	4.6	2.5	1.7	7.7	10.3	10.6
2,6-DiMePh, 2,3,6-TriMePh,	1.0000	0.9992	1.0000	0.9999	0.9994	0.9999	1.0000
2,3,5,6-TetraMePh	0.9	5.2	1.0	1.8	4.7	1.2	0.6

[a] Ph = Phenol; Me = methyl; Et = ethyl; Pr = propyl; Bu = butyl; Pe = pentyl; Hex = hexyl.

TABLE II

RETENTION INDICES AND PHYSICO-CHEMICAL CHARACTERISTICS OF PHENOLS

Compound	I_{160}^{HPE}	t_b (°C)	V_W (*ml/mol*)	$^{1-4}\chi_p$
Ph	1281	182.0	53.88	4.65402
2-MePh	1354	190.8	65.03	6.01632
3-MePh	1386	202.2	65.03	6.03592
4-MePh	1385	201.9	65.03	5.95925
2-EtPh	1430	206.0	75.26	7.27618
3-EtPh	1483	217.0	75.26	7.22427
4-EtPh	1473	218.0	75.26	7.20186
2,3-DiMePh	1495	217.1	76.18	7.50694
2,4-DiMePh	1456	211.3	76.18	7.40925
2,5-DiMePh	1453	211.5	76.18	7.33564
2,6-DiMePh	1416	200.6	76.18	7.45318
3,5-DiMePh	1489	221.7	76.18	7.45866
3,4-DiMePh	1530	226.9	76.18	7.44628
4-iso-PrPh	1527	229.1	85.48	8.65355
2-*n*-PrPh	1502	220.0	85.49	8.49285
3-*n*-PrPh	1565	233.5	85.49	8.42072
4-*n*-PrPh	1563	233.1	85.49	8.44838
2-Et-4-MePh	1523	223.3	86.41	8.62139
2-Et-5-MePh	1529	224.2	86.41	8.60257
2-Et-6-MePh	1485	213.0	86.41	8.67171
3-Et-5-MePh	1581	235.6	86.41	8.62160
4-Et-2-MePh	1539	227.0	86.41	8.60364
4-Et-3-MePh	1608	229.0	86.41	8.77046
2,3,4-TriMePh	1638	237.0	87.33	9.00709
2,3,5-TriMePh	1593	235.3	87.33	8.90280
2,3,6-TriMePh	1551	234.0	87.33	8.98058
2,4,5-TriMePh	1593	232.0	87.33	8.85882
3,4,5-TriMePh	1667	251.9	87.33	9.01393
4-*sec.*-BuPh	1612	242.1	95.71	10.09579
2-*n*-BuPh	1600	235.0	95.72	9.72462
3-*n*-BuPh	1668	250.5	95.72	9.64683
4-*n*-BuPh	1661	248.0	95.72	9.67448
2-Me-4-*n*-PrPh	1623	242.6	96.64	9.85476
2-Me-6-*n*-PrPh	1553	241.3	96.64	9.90766
3-Me-6-*n*-PrPh	1602		96.64	9.81922
4-Me-2-*n*-PrPh	1593	241.0	96.64	9.89444
2,4-DiEtPh	1602	229.0	96.64	9.90136
2,5-DiEtPh	1624	242.5	96.64	9.82030
3,4-DiEtPh	1682	252.5	96.64	10.06733
2,3,4,5-TetraMePh	1782	260.0	98.48	10.53318
2,3,4,6-TetraMePh	1690	250.0	98.48	10.60606
2,3,5,6-TetraMePh	1683	248.0	98.48	10.43240
2-Et-4,5-DiMePh	1656		97.56	10.07748
2-*n*-PePh	1700	256.2	105.95	11.02640
4-*n*-PePh	1765	266.6	105.95	10.97626
4-*tert.*-PePh	1703	264.0	105.94	11.43578
2-Et-5-*n*-PrPh	1706	257.6	106.87	11.07143
2-*n*-HexPh	1800	272.2	116.18	12.30673
4-*n*-HexPh	1871	281.3	116.18	12.26253
3-*n*-Bu-6-EtPh	1807	275.7	117.10	12.29754

TABLE III

CORRELATION COEFFICIENTS AND STANDARD DEVIATIONS (i.u.) FOR EQNS. 4

Eqn. No.	*Series of alkylphenols*	t_b		V_W		$^{1-4}\chi_p$	
		r	*s*	*r*	*s*	*r*	*s*
1	2,4-DiMePh, 2-Me-4-EtPh, 2-Me-4-*n*-PrPh	0.9999	0.4	1.0000	0.4	1.0000	0.2
2	3-MePh, 3,5-DiMePh, 2,3,5-TriMePh	0.9945	10.0	1.0000	0.3	1.0000	0.2
3	2-MePh, 2,3-DiMePh, 2,3,4-TriMePh, 2,3,4,5-TetraMePh	0.9984	10.4	1.0000	0.9	1.0000	0.3
4	2,6-DiMePh, 2-Et-6-MePh, 2-Me-6-*n*-PrPh	0.9746	15.3	1.0000	0.3	1.0000	0.6
5	3,4-DiMePh, 4-Et-3-MePh, 3,4-DiEtPh	0.8939	34.1	0.9999	1.1	1.0000	0.7
6	2-*n*-PrPh, 2-*n*-BuPh, 2-*n*-PePh, 2-*n*-HexPh	0.9980	8.0	1.0000	0.6	1.0000	0.8
7	2,6-DiMePh, 2,3,6-TriMePh, 2,3,5,6-TetraMePh	0.9747	29.8	1.0000	0.9	1.0000	1.0
8	4-EtPh, 4-Et-2-MePh, 2,4-DiEtPh	0.9956	5.9	0.9999	0.7	0.9999	1.0
9	2,6-DiMePh, 2-Et-6-MePh, 2,6-DiEtPh	0.9761	14.5	0.9998	1.3	0.9999	1.1
10	2,6-DiMePh, 2,3,6-TriMePh, 2,3,4,6-TetraMePh	0.9782	28.4	1.0000	0.9	1.0000	1.3
11	Ph, 2-MePh, 2-EtPh, 2-*n*-PrPh	0.9945	10.0	0.9997	2.4	0.9996	1.5
12	4-MePh, 2,4-DiMePh, 2-Et-4-MePh, 4-Me-2-*n*-PrPh	0.9859	14.9	0.9999	1.5	0.9996	2.6
13	3,4-DiMePh, 2,4,5-TriMePh, 2-Et-4,5-DiMePh	–	–	0.9997	1.6	0.9991	2.7
14	Ph, 4-MePh, 4-EtPh, 4-*n*-PrPh, 4-*n*-BuPh	0.9988	7.1	0.9998	2.6	0.9997	3.3
15	3-MePh, 2,5-DiMePh, 2-Et-5-MePh, 3-Me-6-*n*-PrPh	0.9986	3.8	0.9989	4.3	0.9993	3.3
16	Ph, 2,5-DiMePh, 2,5-DiEtPh	0.9999	2.7	0.9997	4.0	0.9998	3.5
17	4-EtPh, 4-*n*-PrPh, 4-*n*-BuPh, 4-*n*-PePh, 4-*n*-HexPh	0.9994	5.6	0.9995	5.2	0.9997	3.6
18	Ph, 3-MePh, 3-EtPh, 3-Et-5-MePh	0.9991	5.6	0.9998	2.3	0.9996	3.6
19	4-iso-PrPh, 4-*sec.*-BuPh, 4-*tert.*-PePh	0.9920	11.1	0.9998	1.7	0.9992	3.6
20	Ph, 3-MePh, 3-EtPh, 3-*n*-PrPh, 3-*n*-BuPh	0.9993	6.4	0.9996	4.5	0.9997	3.9
21	2-EtPh, 2-Et-5-MePh, 2,5-DiEtPh, 2-Et-5-*n*-PrPh, 2-Et-5-*n*-BuPh	0.9999	1.7	0.9997	3.9	0.9996	4.2
22	4-MePh, 3,4-DiMePh, 3,4,5-TriMePh	0.9998	2.9	0.9999	2.4	0.9995	4.4

Correlation dependences were considered for homologous series which were formed by the one-type characteristic of the successive introduction of the methylene group into the side-chain or ring of C_6–C_8 phenols. Application of eqn. 4 to such series permitted linear-regression equations of the dependence of retention indices on the molecular characteristics of alkylphenols to be obtained (Table III). The results showed that all the parameters studied correlate with the retention indices, the equations with structural characteristics V_W and $^{1-4}\chi_p$ being of greater significance and having lower standard deviations of the calculated retention indices. Thus, the correlation coefficient of equations $I = at_b + b$ is 0.8939–0.9999, whereas that of equations with V_W and $^{1-4}\chi_p$ is 0.999–1.000.

Table IV presents data on the predictive capacity of the equations obtained. Two equations producing minimum standard deviations were used to calculate the retention indices of each compound. Thus, the retention index of phenol was determined by eqns. 11 and 14, that of 2,6-dimethylphenol by eqns. 4 and 7, that of 2-ethylphenol by eqns. 11 and 21, etc. (see Table III). The results show that both structure parameters may be used for the preliminary calculation of the retention indices of alkylphenols. The error in the determination of the retention indices by $^{1-4}\chi_p$ does not exceed 4 i.u. and that of V_W 5 i.u. The use of connectivity indices is more preferable. In contrast to V_W, they differentiate isomeric compounds well.

TABLE IV

COMPARISON OF EXPERIMENTAL AND PREDICTED *I* VALUES OF ALKYLPHENOLS

Compound	I_{exp}	*Predicted from* $^{1-4}\chi_p$		*Predicted from* V_W	
		I_m	ΔI	I_m	ΔI
Ph	1281	1280.8	0.2	1280.4	0.6
2-MePh	1354	1355.7	−1.7	1355.3	−1.3
4-MePh	1385	1385.1	−0.1	1385.5	−0.5
3-MePh	1386	1384.5	1.5	1384.0	2.0
2,6-DiMePh	1416	1415.9	0.1	1416.3	−0.3
2,5-DiMePh	1453	1457.1	−4.1	1458.2	−5.2
2,4-DiMePh	1456	1457.8	−1.8	1456.4	−0.4
3,4-DiMePh	1530	1529.5	0.5	1530.0	0
2-EtPh	1430	1430.3	−0.3	1429.6	0.4
4-EtPh	1473	1473.2	−0.2	1473.4	−0.4
2-Et-6-MePh	1485	1485.2	−0.2	1484.0	1.0
2-Et-5-MePh	1529	1530.5	−1.5	1529.5	−0.4
4-Et-2-MePh	1539	1539.2	−0.2	1539.5	−0.5
2,3,6-TriMePh	1551	1550.9	0.1	1551.1	−0.1
2-*n*-PrPh	1502	1501.7	0.3	1501.3	0.7
4-*n*-PrPh	1563	1566.9	−3.9	1566.6	−3.6
2,5-DiEtPh	1624	1620.8	3.2	1621.3	2.7
4-*n*-BuPh	1661	1661.2	−0.2	1662.5	−1.5

The characteristics presented in Table V were used for studies of their influence on correlation indices according to eqn. 3.

Table VI represents multiple correlation coefficients, standard deviations and

TABLE V

PHYSICO-CHEMICAL AND STRUCTURAL CHARACTERISTICS OF ALKYLPHENOLS

Compound	R_M	*Ionization constant* (pK_a)		*Connectivity index*			
		In methanol, pK_a^m	*In water,* pK_a^w	$^1\chi$	$^2\chi$	$^3\chi_p$	$^4\chi_p$
Ph	27.992	14.20	10.02	2.1343	1.3356	0.7562	0.4280
2-MePh	32.838	14.80	10.33	2.5510	1.7865	1.1155	0.5634
4-MePh	32.874	14.55	10.27	2.5450	1.8356	1.0340	0.5448
3-MePh	32.921	14.38	10.10	2.5450	1.8613	1.0017	0.6280
2,6-DiMePh	37.797	15.27	10.63	2.9676	2.2404	1.4395	0.8057
2,5-DiMePh	38.089	14.90	10.40	2.9616	2.2899	1.3646	0.7194
2,4-DiMePh	39.843	15.05	10.60	2.9616	2.2899	1.3523	0.8054
3,5-DiMePh	38.229	14.51	10.19	2.9557	2.3459	1.2065	0.9500
2,3-DiMePh	37.885	15.09	10.53	2.9676	2.2190	1.5760	0.7443
3,4-DiMePh	38.274	14.62	10.36	2.9616	2.2686	1.4905	0.7256
2-PrPh	41.986	15.07	10.55	3.6116	2.3787	1.5110	0.9916
3-iso-PrPh	42.120	14.42	10.14	3.4877	2.7497	1.5369	0.8839
4-*n*-PrPh	42.213	14.55	10.32	3.6056	2.4165	1.4750	0.9513
2-BuPh	46.688	15.09	10.55	4.1116	2.7323	1.7913	1.0895
4-PePh	52.616	14.76	10.57	4.6056	3.1236	2.0053	1.2417

TABLE VI

REGRESSION COEFFICIENTS FOR EQNS. 3 FOR ALKYLPHENOLS

Eqn. No.	*Form of function*	*Coefficients of equations*						*r*	*s*
		a_1	a_2	a_3	a_4	a_5	b		
1	$I = f(t_b, V_W)$	4.3	2.3				383.8	0.997	8.9
2	$I = f(t_b, R_M)$	4.2	5.0				380.6	0.997	8.8
3	$I = f(t_b, pK_a^m)$	5.5	35.9				−234.0	0.998	7.4
4	$I = f(t_b, {}^3\chi_p)$	4.5	80.2				402.6	0.999	6.1
5	$I = f(t_b, V_W, {}^3\chi_p)$	4.3	0.5	68.2			409.2	0.999	5.9
6	$I = f(t_b, R_M, {}^3\chi_p)$	4.3	1.4	65.7			409.8	0.999	5.7
7	$I = f(t_b, pK_a^w, {}^3\chi_p)$	4.7	22.8	57.7			149.5	0.999	5.6
8	$I = f(t_b, pK_a^w, {}^1\chi, {}^3\chi_p)$	4.5	22.7	10.9	47.0		167.9	0.999	5.1
9	$I = f(t_b, {}^1\chi, {}^2\chi, {}^3\chi_p)$	4.5	14.3	−22.4	82.3		406.2	0.999	4.9
10	$I = f(t_b, R_M, {}^2\chi, {}^3\chi_p)$	4.4	3.4	−37.9	73.6		386.8	0.999	4.2
11	$I = f(t_b, R_M, {}^1\chi, {}^2\chi, {}^3\chi_p)$	4.4	4.5	− 7.8	−41.8	72.9	376.5	0.999	4.1
12	$I = f(t_b, R_M, V_W, {}^2\chi, {}^3\chi_p)$	4.4	4.7	− 0.7	−38.2	75.5	384.9	0.999	4.1

coefficients of multi-factor dependence equations of alkylphenol retention indices on different parameters providing the highest level of correlation with successive increases in their number.

Although specific interaction forces of alkylphenols with the stationary phase are manifested on the polar HPE, the boiling temperature reflects the greater part of such interactions and the correlation coefficient for the equation $I = at_b + b$ is 0.993.

As seen from Table VI, the simultaneous use with t_b of other characteristics (eqns. 1–4) permits the studied dependence to be improved, the introduction of the connectivity index ${}^3\chi_p$ providing the highest correlation coefficient. Further increases in the number of variables makes it possible only to decrease the standard deviation at the same correlation level of 0.999.

A positive influence of connectivity indices on the correlation level is also confirmed by the fact that all four- and five-factor equations providing minimum standard deviations in the calculation of I (e.g., eqns. 10 and 11), contain connectivity indices of different orders. At the same time, the absence of reference values for t_b, R_M, pK_a for a wide range of alkylphenols impedes considerably the prediction of their

TABLE VII

CORRELATION COEFFICIENTS AND STANDARD DEVIATIONS (i.u.) FOR EQUATION $I = f(V_W, {}^1\chi, {}^2\chi, {}^4\chi_{p+pc}, {}^5\chi_{p+pc})$ FOR DIFFERENT GROUPS OF ALKYLPHENOLS

Group of alkylphenols	*No. of compounds*	*r*	*s*
All alkylphenols	52	0.948	39.0
Group 1	20	0.997	9.8
Group 2	24	0.991	15.8
Group 3	8	0.999	3.8

TABLE VIII

REGRESSION COEFFICIENTS FOR EQNS. 3 FOR DIFFERENT GROUPS OF ALKYLPHENOLS

Group	*Eqn. No.*	*Form of function*	*Coefficients of equations*	
			a_1	a_2
Group 1	1	$I = f(V_W, {}^4\chi_p)$	7.1	115.7
	2	$I = f({}^3\chi_p, {}^5\chi_p)$	203.4	333.1
	3	$I = f(V_W, {}^1\chi, {}^3\chi_c)$	27.1	−361.7
	4	$I = f({}^3\chi_p, {}^4\chi_p, {}^5\chi_p)$	160.8	127.7
	5	$I = f(V_W, {}^1\chi, {}^2\chi, {}^5\chi_{pc})$	45.0	−585.1
	6	$I = f({}^1\chi, {}^2\chi, {}^3\chi_c, {}^4\chi_{p+pc})$	17.1	179.3
	7	$I = f(V_W, {}^1\chi, {}^2\chi, {}^4\chi_{p+pc}, {}^5\chi_{p+pc})$	50.7	−598.6
	8	$I = f({}^1\chi, {}^2\chi, {}^3\chi_c, {}^4\chi_{p+pc}, {}^5\chi_p)$	−55.3	210.4
	9	$I = f(V_W, {}^1\chi, {}^2\chi, {}^4\chi_{p+pc}, {}^5\chi_p, {}^5\chi_{pc})$	49.5	616.8
	10	$I = f({}^1\chi, {}^2\chi, {}^3\chi_p, {}^3\chi_c, {}^4\chi_{p+pc}, {}^5\chi_p)$	−65.5	208.2
	11	$I = f(V_W, {}^1\chi, {}^2\chi, {}^4\chi_p, {}^4\chi_{pc}, {}^5\chi_p, {}^5\chi_{pc})$	49.4	−616.6
	12	$I = f({}^1\chi, {}^2\chi, {}^3\chi_p, {}^3\chi_c, {}^4\chi_{p+pc}, {}^5\chi_p, {}^5\chi_{pc})$	−64.5	204.5
	13	$I = f(V_W, {}^1\chi, {}^2\chi, {}^3\chi_p, {}^4\chi_p, {}^4\chi_{pc}, {}^5\chi_p, {}^5\chi_{pc})$	45.8	−616.8
	14	$I = f({}^1\chi, {}^2\chi, {}^3\chi_p, {}^3\chi_c, {}^4\chi_p, {}^4\chi_{pc}, {}^5\chi_p, {}^5\chi_{pc})$	−118.4	200.8
Group 2	15	$I = f(V_W, {}^4\chi_p)$	3.1	234.6
	16	$I = f({}^2\chi, {}^3\chi_p)$	127.9	198.1
	17	$I = f(V_W, {}^1\chi, {}^3\chi_p)$	9.5	−99.4
	18	$I = f({}^2\chi, {}^3\chi_p, {}^5\chi_{p+pc})$	122.5	227.7
	19	$I = f(V_W, {}^2\chi, {}^3\chi_p, {}^5\chi_p)$	3.2	134.3
	20	$I = f({}^2\chi, {}^3\chi_p, {}^4\chi_{pc}, {}^5\chi_p)$	183.2	232.7
	21	$I = f(V_W, {}^2\chi, {}^3\chi_p, {}^4\chi_{pc}, {}^5\chi_p)$	−1.1	196.3
	22	$I = f({}^1\chi, {}^2\chi, {}^3\chi_p, {}^4\chi_{p+pc}, {}^5\chi_p)$	18.9	187.8
	23	$I = f(V_W, {}^1\chi, {}^2\chi, {}^3\chi_p, {}^3\chi_c, {}^5\chi_p)$	−10.0	164.8
	24	$I = f({}^2\chi, {}^3\chi_p, {}^4\chi_p, {}^4\chi_{pc}, {}^5\chi_p, {}^5\chi_{pc})$	201.3	248.6
	25	$I = f(V_W, {}^1\chi, {}^2\chi, {}^3\chi_p, {}^4\chi_p, {}^4\chi_{pc}, {}^5\chi_p)$	−9.3	175.8
	26	$I = f({}^1\chi, {}^2\chi, {}^3\chi_p, {}^4\chi_p, {}^4\chi_{pc}, {}^5\chi_p, {}^5\chi_{pc})$	22.7	198.7
	27	$I = f(V_W, {}^1\chi, {}^2\chi, {}^3\chi_p, {}^3\chi_c, {}^4\chi_p, {}^5\chi_p, {}^5\chi_{pc})$	−14.7	282.8
	28	$I = f({}^1\chi, {}^2\chi, {}^3\chi_p, {}^3\chi_c, {}^4\chi_p, {}^4\chi_{pc}, {}^5\chi_p, {}^5\chi_{pc})$	28.9	201.3
Group 3	29	$I = f(V_W, {}^4\chi_{p+pc})$	2.7	182.8
	30	$I = f({}^1\chi, {}^4\chi_{p+pc})$	37.4	204.3
	31	$I = f(V_W, {}^3\chi_{p+c}, {}^4\chi_{p+pc})$	3.3	67.3
	32	$I = f({}^1\chi, {}^3\chi_{p+c}, {}^4\chi_{p+pc})$	51.0	71.1
	33	$I = f(V_W, {}^1\chi, {}^2\chi, {}^3\chi_c)$	69.5	−1138.0
	34	$I = f({}^1\chi, {}^2\chi, {}^3\chi_p, {}^4\chi_{p+pc})$	26.9	56.3

retention indices with the use of correlation equations. Therefore, the use in the correlation schemes of structural parameters (V_W, χ) which are determined easily from the structural formulae of the compounds, is preferred.

In order to establish correlations of retention indices with the mentioned structural parameters of alkylphenols, an attempt was made to consider all possible multi-factor regression equations of the form $I = (V_W, {}^1\chi \ldots {}^5\chi_{p+pc})$. However, the three- to five-factor equations obtained are characterized by a low correlation coefficient of 0.946–0.948 and the standard deviation reaches 39–42 i.u. The low correlation may be explained by the effect of alkyl substituents on the degree of shielding of the OH group, which in turn influences the alkylphenol retention indices.

a_3	a_4	a_5	a_6	a_7	a_8	b	r	s
						859.1	0.979	28.0
						1070.6	0.978	29.3
−178.3						588.1	0.992	17.6
250.5						1061.2	0.982	26.6
−201.3	−109.4					354.1	0.995	14.4
−369.7	137.9					977.2	0.989	20.4
−305.7	137.6	−308.1				240.1	0.997	9.8
−370.3	138.7	220.1				1034.2	0.991	18.2
−283.9	137.5	−186.2	−301.7			287.4	0.998	8.5
23.5	−360.0	128.5	236.2			1041.6	0.991	18.1
−282.4	142.8	138.3	188.0	−304.0		289.6	0.998	8.5
27.3	−362.1	144.2	216.2	−23.7		1042.2	0.992	18.1
−244.9	57.3	198.9	138.7	−167.8	−336.5	369.2	0.998	8.0
92.1	−305.5	265.3	145.3	175.5	−117.3	1075.4	0.992	17.5
						886.4	0.991	15.6
						893.3	0.995	11.0
176.2						783.7	0.993	13.7
−27.6						890.3	0.996	10.2
152.5	−187.7					787.1	0.997	9.0
−58.5	−201.3					845.6	0.998	7.7
255.6	72.0	−187.4				869.6	0.998	7.6
218.8	−45.6	−190.8				826.4	0.998	7.6
244.9	213.0	7.1	−179.9			961.0	0.998	7.3
−76.0	−105.1	−180.3	37.5			839.5	0.998	7.4
242.9	185.1	−36.0	21.7	−185.7		931.5	0.998	7.2
222.1	−97.4	−85.4	−188.6	40.0		822.1	0.998	7.4
289.7	165.7	3.9	−120.6	−160.7	64.7	979.5	0.998	6.8
207.3	−12.5	−100.0	−72.3	−190.2	40.5	817.9	0.998	7.3
						964.5	0.999	4.9
						1021.0	0.998	6.0
107.7						893.7	1.000	2.7
127.3						958.1	0.999	4.0
−182.3	−694.2					146.2	1.000	1.9
49.1	134.6					949.6	1.000	2.1

In order to determine the correlation dependence, it is expedient to divide the set of the alkylphenols studied into three groups differing in the degree of shielding of the hydroxyl group: group 1, phenol and alkylphenols with substituents in positions 3, 4 and 5 (unshielded alkylphenols); group 2, alkylphenols in which the shielding group is only in position 2 or 6 (partially shielded alkylphenols); and group 3, alkylphenols containing substituents in positions 2 and 6 (completely shielded alkylphenols).

In spite of the known inaccuracy of such a classification (in particular, the value of alkyl substituents is not taken into account), the manifestation of steric effects inside the enumerated groups is of the same character, which permits a higher level of correlation between the retention and structural factors. Table VII presents the results

of processing of the five-factor equation in the form $I = (V_W, {}^1\chi, {}^2\chi, {}^4\chi_{p+pc}, {}^5\chi_{p+pc})$. They show that a higher level of correlation compared with the whole set of alkylphenols is provided for each group of alkylphenols.

The path and cluster connectivity indices and also the total path and cluster indices of the first five orders and the descriptor V_W were used for the formation of the structural models of alkylphenols.

The results of statistical processing of multi-factor equations, which have the highest level of correlation in each group of alkylphenols with subsequent increase in the number of factors, are given in Table VIII. The data obtained show that an increase in the degree of shielding of the hydroxyl group of alkylphenols results in an increase in the correlation coefficient in the sequence group 1 < group 2 < group 3. In this instance the number of parameters that are required to reach approximately the same level of correlation decreases in the sequence group 1 < group 2 < group 3. Thus, if for alkylphenols of group 1 a value of $r = 0.998$ is reached with the use of the six-factor polynomial of the first power (eqn. 9) and for alkylphenols of group 2 the same value of r is obtained with the help of the four-factor equation (eqn. 20), then with group 3 compounds the analogous value of r is provided by two-factor equation (eqn. 30).

When analysing the composition and nature of the factors that constitute the equations obtained, the role of cluster indices and total path and cluster indices, which increases with the degree of shielding of hydroxyl groups, ought to be noted. Thus, for example, the fact that the total path and cluster index ${}^4\chi_{p+pc}$ is present all the equations for group 3 indicate a prevailing role of this index in models of phenol connectivity which describe the peculiarities of the retention of alkylphenols with substituents in positions 2 and 6. An analogous effect is produced by the cluster index ${}^3\chi_c$, the contribution of which to the models of molecular connectivity of group 1 is rather noticeably. In models of molecular connectivity of group 2 the contribution of the path index ${}^3\chi_p$ is rather essential.

The descriptor V_W (Table VIII) has a noticeable influence on the correlation coefficient. The additional introduction of V_W permits an increase in r (eqns. 12 and 13)

TABLE IX

INFLUENCE OF V_W AND ${}^1\chi$ ON CORRELATION COEFFICIENT OF REGRESSION EQUATIONS

Form of function	*Group of alkylphenols*		
	1	*2*	*3*
$I = f({}^1\chi, {}^2\chi)$	0.963	0.966	0.961
$I = f(V_W, {}^2\chi)$	0.978	0.967	0.963
$I = f({}^1\chi, {}^2\chi, {}^3\chi_p)$	0.973	0.996	0.980
$I = f(V_W, {}^2\chi, {}^3\chi_p)$	0.980	0.996	0.982
$I = f({}^1\chi, {}^2\chi, {}^3\chi_p, {}^4\chi_p)$	0.978	0.996	0.988
$I = f(V_W, {}^2\chi, {}^3\chi_p, {}^4\chi_p)$	0.982	0.996	0.991
$I = f({}^1\chi, {}^3\chi_{p+c})$	0.966	0.988	0.996
$I = f(V_W, {}^3\chi_{p+c})$	0.976	0.989	0.999
$I = f({}^1\chi, {}^3\chi_{p+c}, {}^4\chi_{p+pc}, {}^5\chi_{p+pc})$	0.978	0.990	0.999
$I = f(V_W, {}^3\chi_{p+c}, {}^4\chi_{p+pc}, {}^5\chi_{p+pc})$	0.984	0.990	1.000

TABLE X

EXPERIMENTAL AND PREDICTED I VALUES OF ALKYLPHENOLS

Group of alkylphenols	*Compound*	I_{exp}	I_{pred}	ΔI
Group 1	3-MePh	1386.0	1386.1	−0.1
	3-EtPh	1483.0	1479.2	3.8
	3,4-DiMePh	1530.0	1525.2	4.8
	4-*n*-PrPh	1563.0	1563.9	−0.9
	3-*n*-PrPh	1565.0	1571.4	−6.4
	4-*n*-BuPh	1661.0	1656.6	4.4
	4-*n*-PePh	1765.0	1769.9	−4.9
Group 2	2-MePh	1354.0	1347.6	−6.4
	2,5-DiMePh	1453.0	1450.5	2.5
	2,4-DiMePh	1456.0	1459.3	−3.3
	2-*n*-PrPh	1502.0	1499.1	2.9
	2-Et-4-MePh	1523.0	1520.0	3.0
	2-Et-5-MePh	1529.0	1534.4	−5.4
	2-Et-4,5-DiMePh	1656.0	1661.7	−5.7
	2-Et-5-*n*-PrPh	1706.0	1699.8	6.2
Group 3	2,6-DiMePh	1416.0	1415.8	0.2
	2-Et-6-MePh	1485.0	1485.8	−0.8
	2,6-DiEtPh	1549.0	1546.8	2.2
	2,3,6-TriMePh	1551.0	1546.4	4.6
	2,3,4,6-TetraMePh	1690.0	1683.4	6.6

or a decrease in s (eqns. 20, 21, 26 and 27). Comparative data on the influence of V_W and the connectivity index $^1\chi$ on the correlation coefficient of the corresponding equations are given in Table IX. The introduction of V_W into the molecular connectivity models instead of $^1\chi$ for all alkylphenol groups increases the correlation coefficient. In this instance, V_W and $^1\chi$ have opposite effects on the retention indices. There are analogous data in Table VIII (eqns. 29–32). The use of V_W instead of $^2\chi$ and $^3\chi$ also increases the correlation level of the corresponding equations.

A check of the practical applicability of the equations in Table VIII was made by successive exclusion of certain values of the retention indices from the total bulk of groups, by determining the coefficients of new equations using the models obtained and by the subsequent calculation of retention indices for these alkylphenols. The data obtained (Table X) indicate sufficient reliability of the proposed equations and their suitability for the prediction of retention indices and the identification of alkylphenols in different mixtures without the use of standards.

CONCLUSION

The combination of molecular connectivity indices of the first five orders with Van der Waals volumes permits structural models of alkylphenols to be obtained. These models describe adequately the peculiarities of their chromatographic behaviour.

The descriptor V_W contributes considerably to the molecular connectivity

models, and increases substantially the level of correlation of the corresponding equations. Among the connectivity indices, the influence of the order indices $^3\chi_p$ and $^3\chi_c$ and the total path and cluster index $^4\chi_{p+pc}$, which make important contributions to the retention indices, should be noted.

REFERENCES

1 A. N. Korol, *Usp. Khim.*, 51 (1982) 1225.
2 T. Görnerová, *Petrochémia*, 23 (1983) 172.
3 W. Ecknig, *Z. Chem.*, 25 (1985) 240.
4 D. N. Grigorjeva and R. V. Golovnya, *Zh. Anal. Khim.*, 40 (1985) 1733.
5 R. Kaliszan, *CRC Crit. Rev. Anal. Chem.*, 16 (1986) 323.
6 M. Šingliar, *Petrochémia*, 27 (1987) 4.
7 E. Kováts and P. Weisz, *Ber. Bunsenges. Phys. Chem.*, 69 (1965) 812.
8 V. G. Berezkin, *Neftekhimiya*, 1 (1961) 169.
9 M. S. Vigderhaus, *Usp. Khim.*, 36 (1967) 1810.
10 J. Franc, *Collect. Czech. Chem. Commun.*, 25 (1960) 1573.
11 B. L. Karger, Y. Elmehrik and R. L. Stern, *Anal. Chem.*, 40 (1968) 1227.
12 B. L. Karger, Y. Elmehrik and W. Andrade, *J. Chromatogr. Sci.*, 7 (1969) 209.
13 M. Kremser, M. Jernejčič and L. Premru, *J. Chromatogr.*, 65 (1972) 129.
14 G. H. E. Nieuwdorp, C. L. de Ligny and N. G. van der Veen, *J. Chromatogr.*, 154 (1978) 133.
15 Yu. E. Lille, *Tr. Nauchno-Issled. Inst. Slantsev*, 21 (1976) 67.
16 A. Radecki and J. Grzybowski, *J. Chromatogr.*, 152 (1978) 211.
17 A. Radecki, J. Grzybowski, H. Lamparczyk and A. Nasal, *J. High Resolut. Chromatogr. Chromatogr. Commun.*, 2 (1979) 581.
18 P. Buryan and J. Macák, *J. Chromatogr.*, 237 (1982) 381.
19 L. H. Hall and L. B. Kier, *Bull. Environ. Contam. Toxicol.*, 32 (1984) 354.
20 V. P. Dmitrikov and V. M. Nabivach, *Zh. Anal. Khim.*, 42 (1987) 1110.
21 V. M. Nabivach, V. P. Dmitrikov and T. A. Zhigunova, *Vopr. Khim. Khim. Tekhnol.*, 88 (1988) 100.
22 P. Buryan and J. Macák, *J. Chromatogr.*, 139 (1977) 69.
23 A. Bondi, *J. Phys. Chem.*, 68 (1964) 441.
24 L. B. Kier and L. H. Hall, *Molecular Connectivity in Chemistry and Drug Research*, Academic Press, New York, 1976.