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RELATIONSHIP BETWEEN THE RETENTION INDICES OF PHENOLS ON POLAR AND NON-POLAR STATIONARY PHASES

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SUMMARY

Phenolic compounds with one hydroxyl group and one or more substituents in the benzene ring were investigated on two polar and one non-polar stationary phases. The Kováts retention indices were determined for 44 phenols on electron-donor (NGA) and electron-withdrawing (OV-225) stationary phases.

High correlation coefficients indicate that the retention index of a phenol on a polar stationary phase consists of the retention index of the phenol on a non-polar stationary phase and the molar refractivity of the whole molecule.

INTRODUCTION

The mechanism of the chromatographic separation of various compounds on non-polar stationary phases has been satisfactorily elucidated. Appropriate relationships indicate that the separation on these phases is affected mostly by the vapour pressure of the compounds being separated, this in turn being related to parameters such as molecular weight and polarity. Recently, some workers have considered the problem of the elucidation of the mechanism of the separation of polar compounds on polar stationary phases. This problem is more complex, as the compounds can also interact directly with the stationary phase through functional groups or substituents. The interactions are of the dipole-dipole, dipole-ion or hydrogen bonding type and can result in charge displacement or charge transfer. Further, polar stationary phases provide favourable conditions for separation even with identical polarities owing to the availability of electron-donating or electron-withdrawing substituents in their structure.

We have previously considered the separation of phenols on non-polar and polar stationary phases^{1,2}. Significant correlations were obtained between the Kováts retention indices on these stationary phases and the chemical structures of compounds being separated.

Relationships between retention indices and chemical structure have been derived by many workers. Cook and Raushel³, for instance, reported retention indices for more than 30 benzene derivatives on three non-polar stationary phases. They found that the retention index of each compound was the sum of the retention

indices of the benzene ring and the substituents. This enabled Kováts retention indices to be predicted for multi-substituted benzene derivatives for a particular temperature and stationary phase. West and Hall⁴ employed ten stationary phases with different McReynolds polarities to determine increments of retention indices for 70 mono- and multi-substituted benzene derivatives. On this basis they were able to predict the retention index of any derivative. Qualitative gas-liquid chromatographic (GLC) analysis of phenols was reported by Hřivnák and Macák⁵, who determined relative retention times for ten alkylphenols on four stationary phases. Landault and Guiochon⁶ determined Kováts retention indices for 20 mono- and multi-substituted methylphenols in a capillary column.

In this work, more than 40 phenols which carried one hydroxyl group and one or more substituents in the benzene ring were studied. The substituents differed markedly in their electron acceptor-donor strengths. Typical electron-donating substituents were $-\text{NH}_2$, $-\text{CH}_3$, $-\text{C}_2\text{H}_5$, $-\text{C}(\text{CH}_3)_3$ and $-\text{OCH}_3$, and electron-withdrawing substituents $-\text{NO}_2$, $-\text{Cl}$, $-\text{Br}$ and $-\text{I}$.

The phenols were separated on three stationary phases: non-polar SE-30 and polar OV-225 (3-cyanopropyl methylpolysiloxane) and NGA (polyneopentyl glycol adipate).

EXPERIMENTAL

Reagents

The phenols were of spectroscopic, GLC or analytical-reagent grade from various manufacturers. Spectroscopic-grade *n*-alkanes, manufactured by Applied Science Labs. (State College, PA, U.S.A.), were used.

Instrumentation

A Pye-Unicam Series 104 gas chromatograph with a flame-ionization detector was used. Microsyringes (5 and 10 μl) were supplied by Scientific Glass Engineering (North Melbourne, Australia). Glass columns (2.9 m \times 2.0 mm I.D.) were packed with 3% SE-30, OV-225 or NGA coated on Chromosorb W HMDS (80-100 mesh).

Samples (0.1 g) of the phenols were dissolved in 5 ml of methanol and 0.6- μl volumes were injected into the column. The solutions were injected successively in order of increasing boiling points of the phenols. Each solution was injected three times.

RESULTS AND DISCUSSION

NGA and OV-225 have almost identical McReynolds polarities⁷. The total values of the McReynolds constants of these stationary phases are 1849 and 1813, respectively. Their chemical structures suggest, however, that they should differ considerably in their electron acceptor-donor properties. These properties were measured by the Brown method⁸. Ethanol was used as an electron acceptor and 2-butanone as an electron donor, with *n*-hexane as a non-polar standard. Another group of test compounds included 1-propanol, 3-pentanone and *n*-nonane. OV-225 was found to exhibit electron-withdrawing properties, whereas NGA was an electron-donor at equal polarity.

The Kováts retention indices of the compounds on SE-30, NGA and OV-225 are given in Table I.

TABLE I

KOVÁTS RETENTION INDICES FOR PHENOLIC COMPOUNDS ON SE-30, NGA AND OV-225 STATIONARY PHASES

Me = Methyl; *i* = iso; Pr = propyl; BHT = butylated hydroxytoluene.

No.	Phenol	Kováts retention indices		
		SE-30	OV-225	NGA
1	2-Me	1035	1587	1742
2	4-Me	1059	1654	1813
3	3-Me	1065	1648	1782
4	2,6-Me ₂	1098	1593	1716
5	2,4-Me ₂	1134	1660	1825
6	3-C ₂ H ₅	1160	1742	1898
7	4-C ₂ H ₅	1162	1746	1890
8	3,5-Me ₂	1163	1706	1877
9	2,3-Me ₂	1169	1693	1857
10	2,4-Cl ₂	1183	1708	1877
11	4-Cl	1192	1922	2058
12	3-Cl	1194	1911	2061
13	2,4,6-Me ₃	1204	1612	1778
14	2,6-Cl ₂	1206	1727	1871
15	4-OCH ₃	1210	1930	2050
16	3-OCH ₃	1211	1940	2083
17	2,3,5-Me ₃	1260	1823	1960
18	4-Br	1274	2054	2191
19	3-Me-4-Cl	1283	2025	2135
20	4-NH ₂	1314	2154	2277
21	4-OH	1334	2330	2515
22	3-NH ₂	1335	2219	2352
23	2,4,6-Cl ₃	1349	1928	2067
24	2,4,5-Cl ₃	1362	2039	2158
25	3-OH	1368	2371	2576
26	3,5-Cl ₂	1391	2217	2343
27	4-I	1398	2230	2348
28	4-CO ₂ CH ₃	1500	2376	2461
29	2-NH ₂	1242	2039	2196
30	3-Br	1270	2069	2214
31	2- <i>i</i> -Pr-5-CH ₃	1271	1776	1932
32	BHT	1494	1782	1830
33	2-OCH ₃	1095	1544	1627
34	2-NO ₂	1149	1556	1703
35	2,6-(OCH ₃) ₂	1347	1936	2014
36	2-OCH ₃ -4-Pr	1392	1810	1884
37	2-OCH ₃ -4-CHO	1447	2199	2235
38	2,6-(OCH ₃) ₂ -4-CH ₃	1473	2076	2106
39	2-OCH ₃ -4-COCH ₃	1531	2283	2326
40	4-COCH ₃	1578	2478	2529
41	2,6-(OCH ₃) ₂ -4-Pr	1624	2254	2256
42	2,6-(OCH ₃) ₂ -4-COCH ₃	1849	2685	2683
43	2-OCH ₃ -4-CH ₂ -CH=CH ₂	1367	1848	1923

Table II gives the molar refractivities of particular substituents and the whole molecules, taken from a paper by Hansch *et al.*⁹

The retention index of a compound on a polar stationary phase was found to

TABLE II

MOLAR REFRACTIVITIES FOR PARTICULAR SUBSTITUENTS AND THE WHOLE MOLECULES

No.	MR_o^*	MR_m^*	MR_p^*	ΣMR^*
1	5.65	0	0	32.83
2	0	0	5.65	32.83
3	0	5.65	0	32.83
4	11.30	0	0	37.45
5	5.65	0	5.65	37.45
6	0	10.30	0	37.48
7	0	0	10.30	37.48
8	0	11.30	0	37.45
9	5.65	5.65	0	37.45
10	6.03	0	6.03	38.21
11	0	0	6.03	33.21
12	0	6.03	0	33.21
13	11.30	0	5.65	42.07
14	12.06	0	0	38.21
15	0	0	7.87	35.05
16	0	7.87	0	35.05
17	5.65	11.30	0	38.21
18	0	0	8.88	36.06
19	0	5.65	6.03	37.84
20	0	0	5.42	32.60
21	0	0	2.85	28.03
22	0	5.42	0	32.60
23	12.06	0	6.03	43.21
24	6.03	6.03	6.03	43.21
25	0	2.85	0	28.03
26	0	12.06	0	38.21
27	0	0	13.94	41.02
28	0	0	12.87	40.05
29	5.42	0	0	32.60
30	0	8.88	0	36.06
31	14.98	5.65	0	45.75
32	39.24	0	5.65	70.01
33	7.87	0	0	35.05
34	7.36	0	0	34.54
35	15.74	0	0	41.89
36	0	0	14.96	48.98
37	7.87	0	6.88	40.90
38	15.74	0	5.65	46.51
39	7.87	0	11.18	38.36
40	0	0	11.18	38.36
41	15.74	0	14.96	55.82
42	15.74	0	11.18	52.04
43	7.87	0	14.49	48.51

* MR_o , MR_m , MR_p = values of the molar refractivity for the substituents in *ortho*, *meta* and *para* positions, respectively; ΣMR = values of the molar refractivity for the whole molecule.

consist of the retention index of the compound on a non-polar phase, which accounts for its volatility, and the molar refractivity, which accounts for electrostatic interactions of the compound with the stationary phase.

The regression analysis of all of the phenols revealed that they could be divided into two groups. One group includes compounds 1-32, carrying inactive *ortho*-substituents, and compounds 33-43, carrying $-\text{OCH}_3$ and $-\text{NO}_2$ substituents in the *ortho*-position, which are capable of hydrogen bond formation.

Eqs. 1 and 2 describe relationships between retention indices on NGA and OV-225, respectively, and retention indices on non-polar SE-30 and molar refractivities of substituents of the first group of phenols.

$$I_{\text{NGA}} = 2.15(\pm 0.18) I_{\text{SE-30}} - 23(\pm 3) MR_o - 20(\pm 6) MR_m - 24(\pm 6) MR_p - 367(\pm 209) \quad (1)$$

$$n = 32 \quad s = 48.3 \quad R = 0.9830$$

$$I_{\text{OV-225}} = 2.20(\pm 0.15) I_{\text{SE-30}} - 22(\pm 2) MR_o - 20(\pm 5) MR_m - 21(\pm 5) MR_p - 599(\pm 174) \quad (2)$$

$$n = 32 \quad s = 40.2 \quad R = 0.9883$$

where n is the number of phenols, s is the standard deviation and R is the correlation coefficient. The values in parentheses indicate standard errors in the regression coefficients.

Analogous relationships for the second group of phenols are given by eqns. 3 and 4.

$$I_{\text{NGA}} = 1.97(\pm 0.46) I_{\text{SE-30}} - 15.2(\pm 13.1) MR_o - 20.8(\pm 16.1) MR_p - 406(\pm 529) \quad (3)$$

$$n = 11 \quad s = 85.3 \quad R = 0.9796$$

$$I_{\text{OV-225}} = 2.10(\pm 0.55) I_{\text{SE-30}} - 13.5(\pm 15) MR_o - 19.7(\pm 19) MR_p - 680(\pm 620) \quad (4)$$

$$n = 11 \quad s = 93.9 \quad R = 0.9796$$

It is remarkable that in eqns. 1 and 2, where the population of the compounds is relatively large, the regression coefficients for the molar refractivity terms are identical, irrespective of the position of the substituents in the ring. Hence, it seemed worthwhile to replace the molar refractivities of the substituents in eqns. 1-4 by the molar refractivities of the whole molecules. These modified relationships are given by eqns. 5-8.

To demonstrate the presence or absence of co-linearity between the variables in eqns. 5-8 and Tables III-VI, squared correlation matrices were included, which represent squared correlation coefficients between all variables occurring in a particular regression equation. The data in Tables III and IV suggest that with reasonably high numbers of data points (n) the molar refractivity is virtually independent of the retention index on non-polar SE-30. In this way, the possibility of fortuitous correlations in eqns. 5 and 6 has been eliminated. Another conclusion is that there are no relationships in this instance between MR and molecular size, because if there were, the relationship between MR and $I_{\text{SE-30}}$ would have been much sounder.

$$I_{\text{NGA}} = 2.12(\pm 0.16) I_{\text{SE-30}} - 24.7(\pm 2.6) MR + 339.9(\pm 182) \quad (5)$$

$$n = 32 \quad s = 46.1 \quad R = 0.9831$$

TABLE III
SQUARED CORRELATION MATRIX FOR EQN. 5

	I_{NGA}	I_{SE-30}	MR
I_{NGA}	1	0.5086	0.0911
I_{SE-30}		1	0.0037
MR			1

TABLE IV
SQUARED CORRELATION MATRIX FOR EQN. 6

	I_{OV-225}	I_{SE-30}	MR
I_{OV-225}	1	0.5918	0.0490
I_{SE-30}		1	0.0037
MR			1

TABLE V
SQUARED CORRELATION MATRIX FOR EQN. 7

	I_{NGA}	I_{SE-30}	MR
I_{NGA}	1	0.8904	0.1964
I_{SE-30}		1	0.4948
MR			1

TABLE VI
SQUARED CORRELATION MATRIX FOR EQN. 8

	I_{OV-225}	I_{SE-30}	MR
I_{OV-225}	1	0.9105	0.2312
I_{SE-30}		1	0.4948
MR			1

$$I_{OV-225} = 2.18(\pm 0.17)I_{SE-30} - 22.5(\pm 2.9)MR + 39.8(\pm 19.7) \quad (6)$$

$$n = 32 \quad s = 50.1 \quad R = 0.9803$$

$$I_{NGA} = 1.94(\pm 0.22)I_{SE-30} - 20.9(\pm 6.9)MR + 247.7(\pm 243) \quad (7)$$

$$n = 11 \quad s = 45.9 \quad R = 0.9931$$

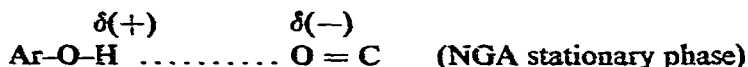
$$I_{OV-225} = 2.08(\pm 0.28)I_{SE-30} - 19.8(\pm 9)MR - 61.4(\pm 30.8) \quad (8)$$

$$n = 11 \quad s = 58.1 \quad R = 0.9909$$

High correlation coefficients in eqns. 1-8 indicate that the retention index of a phenol on a polar stationary phase consists of the retention index of the phenol on a non-polar stationary phase and the molar refractivity of the whole molecule. Further, the regression equations imply that the retention index on a polar stationary

phases is equally affected by the molar refractivity of particular substituents at the *ortho*, *meta* and *para* positions (eqns. 1-4) and by that of the whole molecule (eqns. 5-8). Hence, in this instance the molar refractivity should be regarded as a measure of the polarizability of a molecule (eqns. 5-8) rather than as a measure of the steric hindrance of the substituent in its interaction with the stationary phase (eqns. 1-4).

The regression equations suggest that the larger the *MR* value of a compound (*i.e.*, the larger its polarizability), the lower is the retention index. This can be explained in terms of the influence of the molecular polarizability on the strength of hydrogen bonding between the phenolic hydroxyl group and a polar stationary phase



To polarize the hydrogen-bonded phenol molecule, energy is required. This polarization will always be opposed by the hydrogen bond strength. Hence, the hydrogen bonding of the phenolic hydroxyl group with the stationary phase will be weaker and, consequently, the relative retention index of the compound will be smaller. Accordingly, the differences in the retention times of phenols on polar stationary phases compared with those on non-polar stationary phases should be interpreted in terms of the differences in the magnitude of the stationary phase-induced dipole moment.

REFERENCES

- 1 A. Radecki and J. Grzybowski, *J. Chromatogr.*, 152 (1978) 211.
- 2 A. Radecki, J. Grzybowski, H. Lamparczyk and A. Nasal, *J. High Resolut. Chromatogr. Chromatogr. Commun.*, 2 (1979) 581.
- 3 L. E. Cook and F. M. Raushel, *J. Chromatogr.*, 65 (1972) 556.
- 4 S. D. West and R. C. Hall, *J. Chromatogr. Sci.*, 13 (1975) 5.
- 5 J. Hřivnák and J. Macák, *Anal. Chem.*, 43 (1971) 1039.
- 6 C. Landault and G. Guiochon, *Anal. Chem.*, 39 (1967) 713.
- 7 *Chromatography Product Catalogue*, No. 21, Applied Science Labs., State College, PA, U.S.A., 1978.
- 8 I. Brown, *J. Chromatogr.*, 10 (1963) 284.
- 9 C. Hansch, A. Leo, S. H. Unger, Ki Huam Kin, D. Nikaitani and E. J. Lien, *J. Med. Chem.*, 16 (1973) 1207.