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## STUDIES IN THE RELATIONSHIP BETWEEN MOLECULAR STRUCTURE AND CHROMATOGRAPHIC BEHAVIOUR

## XIX. AN INVESTIGATION OF THE VALIDITY OF THE ADDITIVITY PRINCIPLE AS APPLIED TO THE GAS CHROMATOGRAPHIC BEHAVIOUR OF ALKYLPHENOLS

L. S. BARK

*Analytical Chemistry Research Laboratory, University of Salford, Salford, Lancs. (Great Britain)*

AND

K. F. CLARKE

*Analytical Chemistry Research Laboratory, Coalite and Chemical Products Ltd., Chesterfield, Derbyshire (Great Britain)*

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## SUMMARY

The additivity concept, inherent in the equations of MARTIN and KOVATS, is examined for some series of mono-substituted alkylphenols, chromatographed under a series of rigorously controlled conditions. It is concluded that for a chain length of up to four carbon atoms, the retention index changes by less than 100 units for each methylene group added, since the dominant factor controlling the chromatographic behaviour is the phenolic hydroxyl group. For a chain length larger than four carbon atoms, further substitution is sufficiently far removed from the hydroxyl group that the side chain behaves as an alkane, and the value for  $\Delta I$  (terminal  $-\text{CH}_2$ ) approximates closely to 100 units of retention index.

## INTRODUCTION

The role of chromatography in structural analysis is based simply on the idea that the chromatographic behaviour of a molecule in a particular chromatographic system is the result of a thermodynamically fundamental property of the molecule, and that if the molecule is slightly altered in constitution or the system is slightly modified, then the resulting changes in the chromatographic behaviour are caused and determined by the structure of the molecules concerned.

The theoretical basis for the study of the relationship between the molecular structure of molecules and their chromatographic behaviour is that initiated by MARTIN *et al.*<sup>1-3</sup>, who proposed a theoretical relationship between the chemical potential and the partition coefficient of a substance when the substance was chromatographed by partition chromatography. The partition coefficient is related to the  $R_F$

value of the substance and consequently to the  $R_M$  value of the substance (as defined by BATE-SMITH AND WESTALL<sup>4</sup>).

It can be shown that if the free energy of the whole molecule is considered to be the sum of the partial free energies of the single functional groups constituting the molecule, then the  $R_M$  value of the whole molecule is the sum of the  $\Delta R_M$  values for the constituent functional groups. This is the basic relationship for the structural analysis of organic compounds by measurement of their chromatographic parameters. The use of this relationship and the subsequent ideas have been reviewed by many workers. Amongst the latest reviews is that of BARK<sup>5</sup>, who reviews the application of both PC and TLC in the structural analysis of organic compounds. Separation of compounds by GLC depends on the partition of the compounds between an inert gas phase chosen as the mobile phase and the liquid stationary phase. Hence there should be a similar relationship between the retention of a substance in a particular system and the chemical constitution and structure of the substance.

An internationally accepted retention index system proposed by KOVATS<sup>6</sup> serves as the basic system for the application of the additivity principle to gas chromatography. From the work of KOVATS and other workers<sup>7-11</sup> have arisen six empirical rules governing the retention index ( $I$ ) (ref. 6) of a compound and its chemical constitution. The first four rules summarise regularities in retention indices of a group of substances as determined in one stationary phase; the two additional rules are required for a comparison of the retention indices of some substances on different stationary phases.

It is the intention of the present authors to investigate the applicability of these rules and the related ideas to the interpretation of the gas chromatographic behaviour of phenols chromatographed under conditions such that variations in behaviour of related compounds can be attributed either to changes in the molecular constitution of the species being chromatographed or to recognised changes in the chromatographic systems.

During the last decade there has been a considerable amount of work concerned with the chromatography of phenols in PC, TLC and GLC. An extensive review of the progress in the gas chromatographic analysis of phenols was made in 1966 (ref. 12). However, hitherto, little attempt has been made to investigate the validity of the KOVATS-MARTIN type relationship for phenols. This paper reports the investigation of a series of phenols chromatographed on several stationary phases and the subsequent application of the results to the testing of the validity of these relationships, with special reference to the first of the above empirical rules, *i.e.* in any homologous series the retention index of higher members increases by 100 units per methylene group introduced. (This has been previously demonstrated for the series of primary acids, methyl esters of fatty acids, *n*-aldehydes and methyl ketones (above a chain length of five carbon atoms).)

## EXPERIMENTAL

The phenols were chromatographed on a Perkin-Elmer F-11 gas chromatograph fitted with a flame ionisation detector. The experimental conditions under which the chromatograph was operated are tabulated in Table I. In all cases the gas supplies to the chromatograph and the detector were monitored through a series of control valves to control and maintain the flows and pressures.

TABLE I

LIST OF EXPERIMENTAL CONDITIONS UNDER WHICH THE CHROMATOGRAPH WAS OPERATED

Columns: (A) 50 m  $\times$  0.25 mm I.D. stainless-steel capillary column coated with stationary phase; (B) 2 m  $\times$  3 mm I.D. stainless-steel packed column. Stationary phases: (C) Apiezon L; (D) 2½% OV-1 silicone on HMDS-treated Chromosorb W (80–100 mesh). A1 and A2 refer to two different capillary columns coated with Apiezon L. In all cases the carrier gas was nitrogen at 15 lb./sq.in. and the detector supply was air at 20 lb./sq.in. and hydrogen at 20 lb./sq.in.

|                  | System No. |     |     |     |     |     |     |
|------------------|------------|-----|-----|-----|-----|-----|-----|
|                  | 1          | 2   | 3   | 4   | 5   | 6   | 7   |
| Column           | A1         | A1  | A2  | A2  | B   | B   | B   |
| Support          | C          | C   | C   | C   | D   | D   | D   |
| Temperature (°C) | 125        | 150 | 130 | 150 | 110 | 130 | 150 |

### Calibration of the chromatograph

The chromatograph was calibrated by the chromatography of a homologous series of *n*-alkanes under the same set of experimental conditions used for the phenols.

### RESULTS

The retention data and the chromatographic parameters calculated from them are given in Tables II, III and IV (for phenols) and V (for *n*-alkanes).

### DISCUSSION OF THE RESULTS

#### Chromatography of the alkylphenols

In order that a correlation between the chromatographic behaviour of phenols and their chemical structure may be useful, the chromatographic behaviour of any compound must be consistent in a given set of experimental conditions. Also, as well as the chromatographic behaviour of complete molecules, the effect of unit structures or chromatographically functional groups on the chromatographic behaviour of the phenols should be consistent in a given set of experimental conditions. It would not be expected that the chromatographic behaviour of a functional group will be constant in all environments, since mutual interaction between the functional group and the nucleus will be dependent on the physico-chemical characteristics associated with the functional group and the nucleus, and will vary as the strength and type of interaction vary.

Those experimental conditions, in which solute/stationary phase interactions were minimal, were chosen. Apiezon L, a paraffin grease, was chosen as one stationary phase and OV-1, a methyl silicone, was chosen as an alternative stationary phase. The temperature of the column and the carrier gas pressure remained constant throughout each run. Retention times are the average of three runs under conditions of constant temperature and pressure, in which the mean deviation was less than 3%. Under such rigorous standardisation of conditions, the results obtained on any one occasion are comparable with those obtained from other chromatograms.

The retention times of all of the alkylphenols chromatographed were measured directly from the chromatograms and corrected for dead volume by deduction of the

TABLE II

RETENTION DATA FOR THE HOMOLOGOUS SERIES OF *n*-ALKYLPHENOLS CHROMATOGRAPHED UNDER CONDITIONS DESCRIBED IN SYSTEMS I-7

*t*<sub>R</sub>' values are quoted to nearest 0.05 units.

| Phenol               | System 1                |      | System 2                |      | System 3                |      | System 4                |      | System 5                |      | System 6                |      | System 7                |      |
|----------------------|-------------------------|------|-------------------------|------|-------------------------|------|-------------------------|------|-------------------------|------|-------------------------|------|-------------------------|------|
|                      | <i>t</i> <sub>R</sub> ' | I    | <i>t</i> <sub>R</sub> ' | I    | <i>t</i> <sub>R</sub> ' | I    | <i>t</i> <sub>R</sub> ' | I    | <i>t</i> <sub>R</sub> ' | I    | <i>t</i> <sub>R</sub> ' | I    | <i>t</i> <sub>R</sub> ' | I    |
| Phenol               | 5.00                    | 1087 | 2.15                    | 1112 | 3.40                    | 1042 | 1.25                    | 1014 | 2.95                    | 989  | 1.80                    | 982  | 1.30                    | 1000 |
| 2-Methyl-            | 6.80                    | 1141 | 2.65                    | 1155 | 4.90                    | 1092 | 1.80                    | 1081 | 3.95                    | 1042 | 2.35                    | 1034 | 1.60                    | 1049 |
| 4-Methyl-            | 8.20                    | 1173 | 3.30                    | 1199 | 6.20                    | 1124 | 1.90                    | 1092 | 4.65                    | 1072 | 2.65                    | 1001 | 1.75                    | 1070 |
| 2-Ethyl-             | 10.25                   | 1211 | 3.75                    | 1223 | 8.10                    | 1160 | 2.85                    | 1142 | 6.25                    | 1134 | 3.40                    | 1112 | 2.20                    | 1127 |
| 4-Ethyl-             | 13.50                   | 1260 | 5.10                    | 1285 | 11.10                   | 1206 | 2.80                    | 1178 | 7.75                    | 1164 | 4.25                    | 1147 | 2.50                    | 1155 |
| 2- <i>n</i> -Propyl- | 15.70                   | 1286 | 5.45                    | 1298 | 13.60                   | 1232 | 3.50                    | 1216 | 9.85                    | 1216 | 4.95                    | 1187 | 3.10                    | 1214 |
| 4- <i>n</i> -Propyl- | 22.55                   | 1348 | 7.90                    | 1372 | 20.70                   | 1289 | 5.35                    | 1263 | 12.85                   | 1256 | 6.55                    | 1234 | 3.65                    | 1155 |

TABLE III

RETENTION DATA FOR THE HOMOLOGOUS SERIES OF 2-*sec*-ALKYLPHENOLS CHROMATOGRAPHED UNDER CONDITIONS DESCRIBED IN SYSTEMS I-7

*t*<sub>R</sub>' values are quoted to nearest 0.05 units.

| Phenol              | System 1                |      | System 2                |      | System 3                |      | System 4                |      | System 5                |      | System 6                |      | System 7                |      |
|---------------------|-------------------------|------|-------------------------|------|-------------------------|------|-------------------------|------|-------------------------|------|-------------------------|------|-------------------------|------|
|                     | <i>t</i> <sub>R</sub> ' | I    | <i>t</i> <sub>R</sub> ' | I    | <i>t</i> <sub>R</sub> ' | I    | <i>t</i> <sub>R</sub> ' | I    | <i>t</i> <sub>R</sub> ' | I    | <i>t</i> <sub>R</sub> ' | I    | <i>t</i> <sub>R</sub> ' | I    |
| Isopropyl-          | 13.40                   | 1259 | 4.70                    | 1272 | 11.30                   | 1203 | 3.05                    | 1189 | 8.60                    | 1183 | 4.65                    | 1175 | 2.80                    | 1181 |
| <i>sec</i> -Butyl-  | 19.30                   | 1322 | 6.20                    | 1324 | 17.40                   | 1265 | 4.40                    | 1262 | 13.95                   | 1283 | 6.65                    | 1248 | 3.85                    | 1256 |
| 2-(1-Methylbutyl)-  | 28.90                   | 1396 | 8.90                    | 1395 | 29.05                   | 1335 | 6.50                    | 1343 | 25.15                   | 1377 | 10.36                   | 1339 | 5.60                    | 1346 |
| 2-(1-Methylpentyl)- | 49.55                   | 1486 | 11.30                   | 1488 | 53.40                   | 1418 | 10.55                   | 1438 | 42.85                   | 1473 | 16.64                   | 1436 | 8.45                    | 1442 |
| 2-(1-Methylhexyl)-  | 85.80                   | 1583 | 23.05                   | 1584 | 99.90                   | 1503 | 17.20                   | 1538 | 72.75                   | 1570 | 26.75                   | 1533 | 12.80                   | 1540 |
| 2-(1-Methylheptyl)- | 153.60                  | 1683 | 37.95                   | 1681 | 187.65                  | 1591 | 27.90                   | 1636 | —                       | —    | 43.21                   | 1633 | 18.95                   | 1633 |

TABLE IV

RETENTION DATA FOR THE HOMOLOGOUS SERIES OF 4-*sec*-ALKYLPHENOLS CHROMATOGRAPHED UNDER CONDITIONS DESCRIBED IN SYSTEMS 1-7  
 $t_R'$  values are reported to the nearest 0.05 units.

| Phenol               | System 1 |      | System 2 |      | System 3 |      | System 4 |      | System 5 |      | System 6 |      | System 7 |      |
|----------------------|----------|------|----------|------|----------|------|----------|------|----------|------|----------|------|----------|------|
|                      | $t_R'$   | $I$  | $t_R'$   | $I$  | $t_R'$   | $I$  | $t_R'$   | $I$  | $t_R'$   | $I$  | $t_R'$   | $I$  | $t_R'$   | $I$  |
| 4-Isopropyl-         | 17.50    | 1305 | 6.45     | 1331 | 16.10    | 1255 | 3.85     | 1236 | 11.75    | 1240 | 5.75     | 1218 | 3.30     | 1220 |
| 4- <i>sec</i> -Butyl | 27.80    | 1385 | 9.25     | 1493 | 26.15    | 1310 | 5.75     | 1317 | 20.10    | 1337 | 9.05     | 1311 | 4.75     | 1306 |
| 4-(1-Methylbutyl)-   | 47.95    | 1480 | 14.50    | 1485 | 45.00    | 1389 | 9.20     | 1411 | 34.50    | 1435 | 14.55    | 1499 | 7.15     | 1495 |
| 4-(1-Methylpentyl)-  | 85.20    | 1580 | 22.70    | 1580 | 80.80    | 1475 | 15.05    | 1511 | 60.20    | 1535 | 22.80    | 1501 | 10.10    | 1507 |
| 4-(1-Methylhexyl)-   | 150.80   | 1680 | 37.40    | 1679 | 161.45   | 1570 | 24.70    | 1610 | 105.50   | 1637 | 36.35    | 1596 | 17.05    | 1608 |
| 4-(1-Methylheptyl)-  | 269.00   | 1780 | 62.35    | 1779 | 327.65   | 1665 | 40.35    | 1710 | —        | —    | 57.50    | 1690 | 26.20    | 1709 |

TABLE V

RETENTION DATA OF THE HOMOLOGOUS SERIES OF *n*-ALKANES CHROMATOGRAPHED UNDER CONDITIONS DESCRIBED IN SYSTEMS 1-7  
 $t_R'$  values are reported to the nearest 0.03 units.

| <i>n</i> -Alkane | System 1 |                    | System 2 |                    | System 3 |                    | System 4 |                    | System 5 |                    | System 6 |                    | System 7 |                    |
|------------------|----------|--------------------|----------|--------------------|----------|--------------------|----------|--------------------|----------|--------------------|----------|--------------------|----------|--------------------|
|                  | $t_R'$   | $\text{Log } t_R'$ | $t_R'$   | $\text{Log } t_R'$ | $t_R'$   | $\text{Log } t_R'$ | $t_R'$   | $\text{Log } t_R'$ | $t_R'$   | $\text{Log } t_R'$ | $t_R'$   | $\text{Log } t_R'$ | $t_R'$   | $\text{Log } t_R'$ |
| Octane           | 1.70     | 0.2304             | 0.75     | 1.8751             | 1.20     | 0.0792             | 0.75     | 1.8751             | 1.80     | 0.2553             | 1.20     | 0.0792             | 0.85     | 1.9294             |
| Nonane           | 1.70     | 0.2304             | 0.75     | 1.8751             | 1.20     | 0.0792             | 1.17     | 0.0670             | 3.15     | 0.4983             | 1.90     | 0.2788             | 1.25     | 0.1055             |
| Decane           | 3.10     | 0.4914             | 1.20     | 0.0792             | 2.50     | 0.3979             | 3.05     | 0.4843             | 9.60     | 0.9823             | 4.95     | 0.6947             | 2.88     | 0.4661             |
| Dodecane         | 9.80     | 0.9912             | 3.20     | 0.5051             | 10.70    | 1.0294             | 8.35     | 0.9217             | 29.25    | 1.4662             | 13.30    | 1.1239             | 6.88     | 0.8372             |
| Tetradecane      | 30.60    | 1.4857             | 8.85     | 0.9469             | 46.10    | 1.6637             | —        | —                  | 89.20    | 1.9502             | 32.15    | 1.5503             | 16.4     | 1.2161             |
| Hexadecane       | 99.30    | 1.9969             | 24.90    | 1.3970             | —        | —                  | 23.35    | 1.3681             | —        | —                  | —        | —                  | —        | —                  |

air peak time calculated by the method of PETERSON AND HIRSCH<sup>13</sup>. The unit of retention time can be any value. It would probably be best if it were measured in absolute units of time, *viz.* seconds, however, in practical chromatography one measures the distance of the peak apex from the start, on a chart driven by a synchronous motor, which is self-consistent. Thus, whilst precision can be ascertained, the accuracy is not proven. In such practical circumstances it is best to use the time of the chart motor and assume it to be absolute. Since all results are taken from the charts obtained at the same constant speed for each chromatogram, no error is caused if the values of the retention time,  $t_R'$ , are compared directly. Thus, the unit of retention time used here was that for 0.1 in. to be traversed on the chart. (This is nominally 24 sec.)

Retention indices were calculated by the VAN DEN DOOL AND KRATZ modification<sup>14</sup> of the KOVATS equation<sup>8</sup>, in which  $t_R'$ , the adjusted retention time, was substituted for the retention volume,  $V_R$ .

$$I_T^{\text{St.Ph.}}(\mathbf{X}) = 100i \cdot \frac{[\log t_R'(\mathbf{X}) - \log t_R'(P_z)]}{[\log t_R'(P_{z+i}) - \log t_R'(P_z)]} + 100z$$

where

- $z$  = carbon number of reference hydrocarbon  $P_z$ ;
- $(z + i)$  = carbon number of reference hydrocarbon  $P_{z+i}$ ;
- $t_R'$  = adjusted retention time.

$$t_R'(P_{z+i}) \geq t_R'(\mathbf{X}) \geq t_R'(P_z)$$

The chromatograph and indirectly the chromatographic conditions were calibrated by chromatography of the homologous series of  $n$ -alkanes. A graphical representation of the chromatographic behaviour of the homologous series of  $n$ -alkanes in which  $\log t_R'$  was plotted against carbon number of the  $n$ -alkanes, was prepared for each series of experimental conditions used. In all cases a linear plot was obtained showing that there is a linear increase in  $\log t_R'$  for every methylene group added to the carbon chain in the experimental conditions used.

The linearity and its reproducibility have been taken as indicating that our experimental conditions and techniques are sufficiently standardised to ensure that meaningful comparisons of chromatographic results, obtained under these conditions, are valid. Not only can the results from  $n$ -alkanes be accepted but so can results from other types of molecules. We thus propose that the chromatographic behaviour of the alkylphenols may be discussed in terms of the change in retention index for changes in structure of the phenols being chromatographed and also for changes in the chromatographic systems.

#### $\Delta I$ (group)

This is the change in retention index ( $I$ ) produced by the substitution of a group into the parent nucleus. In the present series of alkylphenols, the change in chromatographic behaviour produced by the addition of methylene groups to the side chain of the parent alkylphenol is discussed.

In a chromatographic system, in which chromatography is a true partition process,  $\Delta I(-\text{CH}_2)$ , the increase in retention index, would be expected to remain

TABLE VI  
THE INCREASE ( $\Delta I$ ) AND RETENTION INDEX ( $I$ ) FOR EACH METHYLENE GROUP ADDED FOR THE HOMOLOGOUS SERIES OF *n*-ALKYLPHENOLS

| Phenol               | System 1 |            | System 2 |            | System 3 |            | System 4 |            | System 5 |            | System 6 |            | System 7 |            |
|----------------------|----------|------------|----------|------------|----------|------------|----------|------------|----------|------------|----------|------------|----------|------------|
|                      | $I$      | $\Delta I$ | $I$      | $\Delta I$ | $I$      | $\Delta I$ | $I$      | $\Delta I$ | $I$      | $\Delta I$ | $I$      | $\Delta I$ | $I$      | $\Delta I$ |
| Phenol               | 1087     | —          | 1112     | —          | 1042     | —          | 1014     | —          | 989      | —          | 982      | —          | 1000     | —          |
| 2-Methyl-            | 1141     | 54         | 1156     | 44         | 1092     | 50         | 1081     | 67         | 1042     | 54         | 1035     | 53         | 1049     | 49         |
| 2-Ethyl-             | 1211     | 70         | 1224     | 68         | 1161     | 78         | 1142     | 61         | 1134     | 82         | 1112     | 77         | 1127     | 78         |
| 2- <i>n</i> -Propyl- | 1286     | 75         | 1298     | 75         | 1232     | 71         | 1216     | 75         | 1216     | 82         | 1187     | 75         | 1214     | 87         |
| 4-Methyl-            | 1173     | 87         | 1199     | 87         | 1124     | 82         | 1092     | 78         | 1072     | 83         | 1061     | 79         | 1070     | 70         |
| 4-Ethyl-             | 1260     | 87         | 1285     | 86         | 1206     | 82         | 1178     | 86         | 1164     | 92         | 1147     | 86         | 1155     | 85         |
| 4- <i>n</i> -Propyl- | 1348     | 86         | 1372     | 87         | 1289     | 83         | 1263     | 85         | 1256     | 92         | 1234     | 87         | 1245     | 90         |

constant for each methylene group added to a nucleus. Table II contains the retention data for the series of 2- and 4-alkylphenols.

The 4-*n*-alkylphenols show a linear increase in the retention index for each methylene group added when chromatographed on Apiezon L, but show a non-linear increase in retention index for each methylene group added when chromatographed on OV-1. When chromatographed on OV-1, the increase in retention index for the addition of a methylene group to position 4 of the phenol nucleus is less than the increase in the retention index for subsequent additions of methyl groups to the alkyl chain.

A non-linear increase in the retention index was observed in the 2-*n*-alkylphenol series when chromatographed on both Apiezon L and OV-1.

That the addition of a methylene group to the nucleus does not produce the same change in the chromatographic behaviour as the addition of a second group to a side chain has been recognised by several workers. MARCINKIEWICZ *et al.*<sup>15</sup> indicated that in calculating  $\Delta R_M(-CH_2)$  they could not use the values obtained from 4-methylphenol since the methylene group here is attached directly to the ring and it is thus under the electronic influence of that ring. They regarded this methylene group as being constitutively different from a homologous methylene group.

The increase in retention index for each methylene group added for the series of *n*-alkylphenols is shown in Table VI.

The non-linearity of the increase in the retention index in the first three members of the 2- and 4-*n*-alkylphenols may be explained by the electronic effects induced by the first substitution. The hyper-conjugative release of electrons by the methyl group in the first substitution will have the effect of reducing the overall polarity of the hydroxyl group. Therefore the increase in retention index expected from the addition of the methylene group will be affected by the relative increase in volatility of the phenol, caused by the decrease in the polarity of the hydroxyl group and the consequent decrease in the intermolecular hydrogen bonding.

The electronic effects on the hydroxyl group due to the addition of subsequent methylene groups to the side chain will be minimised since the second methylene group no longer forms part of a conjugate double bond system and the electronic effects cannot, therefore, be transmitted to the hydroxyl group. The increase in the retention index for subsequent additions of methylene groups can be correlated with this addition of a methylene group without any consideration of the remainder of the molecule.

The first two members of the 2-*n*-alkylphenol series show greater deviation from linearity in the increase of retention index for each methylene group added than do any subsequent members. In addition to the electronic effects caused by substitution into the ring, the approach of the hydroxyl group of the phenol molecules to the phase interface is sterically hindered by the methyl group in the *ortho* position. A relatively shorter increase in retention time, and hence in the retention index, would thus be expected for the addition of the first methylene group at the *ortho* position than would be expected for any subsequent additions to the side chain. This effect due to steric hindrance has been termed the '*ortho* effect' and has been demonstrated for phenols and other compounds in TLC.

In the 4-substituted phenols the electronic effects of substitution are greater than the steric effects caused by substitution of groups into this position 4 and prob-



TABLE VIIa  
THE CHANGE IN THE RETENTION INDEX FOR EACH METHYLENE GROUP ADDED FOR THE HOMOLOGOUS SERIES OF 2-*sec.*-ALKYLPHENOLS

| Phenol                 | System 1 |            | System 2 |            | System 3 |            | System 4 |            | System 5 |            | System 6 |            | System 7 |            |
|------------------------|----------|------------|----------|------------|----------|------------|----------|------------|----------|------------|----------|------------|----------|------------|
|                        | I        | $\Delta I$ | I        | $\Delta I$ | I        | $\Delta I$ | I        | $\Delta I$ | I        | $\Delta I$ | I        | $\Delta I$ | I        | $\Delta I$ |
| 2-Ethyl-               | 1212     | —          | 1223     | —          | 1161     | —          | 1142     | —          | 1134     | —          | 1112     | —          | 1127     | —          |
| 2-Isopropyl-           | 1259     | 47         | 1272     | 49         | 1203     | 42         | 1189     | 47         | 1183     | 49         | 1165     | 53         | 1182     | 55         |
| 2- <i>sec.</i> -Butyl- | 1322     | 63         | 1324     | 52         | 1265     | 62         | 1262     | 73         | 1283     | 100        | 1248     | 73         | 1257     | 55         |
| 2-(1-Methylbutyl)-     | 1396     | 74         | 1395     | 71         | 1335     | 70         | 1343     | 81         | 1377     | 94         | 1339     | 91         | 1346     | 89         |
| 2-(1-Methylpentyl)-    | 1485     | 89         | 1488     | 93         | 1418     | 83         | 1439     | 96         | 1474     | 97         | 1436     | 97         | 1442     | 96         |
| 2-(1-Methylhexyl)-     | 1583     | 98         | 1584     | 96         | 1503     | 85         | 1538     | 99         | 1570     | 96         | 1533     | 97         | 1540     | 98         |
| 2-(1-Methylheptyl)-    | 1683     | 100        | 1681     | 97         | 1591     | 89         | 1636     | 98         | —        | —          | 1633     | 100        | 1633     | 93         |

TABLE VIIb  
THE CHANGE IN THE RETENTION INDEX FOR EACH METHYLENE GROUP ADDED FOR THE HOMOLOGOUS SERIES OF 4-*sec.*-ALKYLPHENOLS

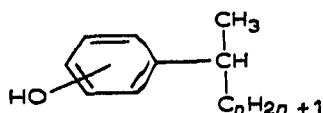
| Phenol                 | System 1 |            | System 2 |            | System 3 |            | System 4 |            | System 5 |            | System 6 |            | System 7 |            |
|------------------------|----------|------------|----------|------------|----------|------------|----------|------------|----------|------------|----------|------------|----------|------------|
|                        | I        | $\Delta I$ | I        | $\Delta I$ | I        | $\Delta I$ | I        | $\Delta I$ | I        | $\Delta I$ | I        | $\Delta I$ | I        | $\Delta I$ |
| 4-Ethyl-               | 1260     | —          | 1285     | —          | 1206     | —          | 1178     | —          | 1164     | —          | 1148     | —          | 1155     | —          |
| 4-Isopropyl-           | 1305     | 45         | 1331     | 46         | 1255     | 49         | 1236     | 58         | 1240     | 76         | 1218     | 70         | 1220     | 65         |
| 4- <i>sec.</i> -Butyl- | 1386     | 81         | 1403     | 72         | 1310     | 55         | 1317     | 81         | 1337     | 97         | 1311     | 97         | 1306     | 86         |
| 4-(1-Methylbutyl)-     | 1480     | 94         | 1485     | 82         | 1389     | 79         | 1411     | 94         | 1435     | 98         | 1409     | 98         | 1405     | 99         |
| 4-(1-Methylpentyl)-    | 1580     | 100        | 1580     | 95         | 1475     | 86         | 1511     | 100        | 1535     | 100        | 1501     | 92         | 1507     | 102        |
| 4-(1-Methylhexyl)-     | 1680     | 100        | 1679     | 99         | 1570     | 95         | 1611     | 100        | 1637     | 102        | 1596     | 95         | 1608     | 101        |
| 4-(1-Methylheptyl)-    | 1780     | 100        | 1780     | 101        | 1665     | 95         | 1710     | 99         | —        | —          | 1690     | 94         | 1709     | 101        |

ably outweigh the steric effects. However, in the case of 2-substituted phenols both electronic effects and steric effects are important.

The increase in retention index for each methylene group added does not, however, reach the value of 100 in any of the systems used.

The dominant factor affecting the chromatographic behaviour of phenols in general is undoubtedly the polar hydroxyl group, and the modification of the chromatographic behaviour due to the addition of methylene groups is overshadowed by the effect of this hydroxyl group. It is concluded that a minimum chain length is required before the increase in retention index for each methylene group added to the side chain has a value of 100 units of retention index.

No *n*-alkylphenol with a chain length larger than three carbon atoms was available for this investigation and consequently the homologous series of *sec.*-alkylphenols of general formulæ,



of which compounds were available for  $n = 0$  to 6, was examined.

The increase in retention index for each methylene group added for the homologous series of *sec.*-alkylphenols is shown in Tables VIIa and b (Table VIIa refers to phenols derived from 2-ethylphenol, Table VIIb refers to phenols derived from 4-ethylphenol).

Examination of the retention data for the series of 2- and 4-alkylphenols indicates that the effect of chain branching is of paramount importance. In all examples quoted in Tables VIIa and b the increase in retention index for the addition of a methylene group to position 1 of the side chain,  $\Delta I(1-\text{CH}_2)$ , is considerably less than the increase in the retention index for the addition of a methylene group to the terminal position of the side chain,  $\Delta I(\text{terminal } -\text{CH}_2)$ .

It is suggested that the addition of a methyl group to position 1 of an alkyl chain produces no effective increase in chain length, whereas the addition of a methylene group to the terminal position does produce an increase in chain length equivalent to one step along the homologous series of *n*-alkanes. It is considered that the energy required to detach the molecules from the surface of the stationary phase will be proportional to the chain length. Since the addition of a methylene group to position 1 of an alkyl chain does not effectively increase the chain length, it would be expected that a secondary alkylphenol would elute before the isomeric *n*-alkylphenol and that  $\Delta I(1-\text{CH}_2)$  would be less than  $\Delta I(\text{terminal } -\text{CH}_2)$ . These hypotheses are consistent with the structures of the molecules concerned, and with the chromatographic values obtained.

A regular increase in the retention index was observed for each methylene group added along the series from 4-*sec.*-butylphenol to 4-(1-methylheptyl)phenol. This increase approximates closely to 100 in the examples quoted.

In the series of 2-alkylphenols the value for  $\Delta I(1-\text{CH}_2)$  is again considerably less than for  $\Delta I(\text{terminal } -\text{CH}_2)$ . The increase in the retention index for each methylene group added does not approach 100 units of retention index until higher along the series. This again is undoubtedly due to the 'ortho effect', *i.e.* the effect of steric

hindrance of the hydroxyl group by the *ortho*-substituted group. From 2-(1-methylbutyl)phenol the additional methylene groups are sufficiently far removed in space as to have no effect on the chromatographic properties of the hydroxyl group. Thus the addition of the methylene group to the terminal position of the alkyl side chain produces the same chromatographic behaviour as the addition of a methylene group to the *n*-alkanes.

## CONCLUSION

It is concluded that for a chain length of up to four carbon atoms the increase in retention for each methylene group added to the alkyl side chain of 2- and 4-alkylphenols is less than 100 units of retention index, since the dominant factor controlling the chromatographic behaviour is the phenolic hydroxyl group.

For a chain length larger than four carbon atoms, further substitution is sufficiently far removed from the hydroxyl group, and the chain length is sufficiently long for the alkylphenol to assume some of the properties of a *n*-alkane, and for the value of  $\Delta I$  (terminal  $-\text{CH}_2$ ) to approximate clearly to 100 units of retention index.

It would also be expected that the substitution of more than one methyl group into the nucleus would result in "non-additive" properties to be shown by the second and subsequent methylene groups, since only the first group would be entering a simple  $\pi$  bond system with only one functional group.

The difference between the addition of the first methyl group to the aromatic nucleus and subsequent addition of methylene groups to this methyl group in their effect on the chromatographic behaviour has also been recognised by MARCINKIEWICZ *et al.*<sup>15</sup>, who worked on paper chromatography and some reversed-phase chromatographic systems. They regarded the methylene group (ring attached) as being constitutively different from alkyl groups not directly attached to the aromatic nucleus. They calculated  $\Delta R_M$  (ring attached) by comparing phenol with its mono-, di- and trimethylated derivatives but restricted their calculations to those phenols which did not contain substituents *ortho* to the hydroxyl group.

The effect of substitution of more than one methylene unit directly into the ring is currently being investigated by chromatographing a series of mono-, di- and trimethylphenols, under a selection of chromatographic conditions.

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