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THE USE OF R_C VALUES FOR STRUCTURAL STUDIES IN THE PAPER CHROMATOGRAPHY OF PHENOLS

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SUMMARY

An investigation was carried out of the chromatographic behaviour of some alkyl derivatives of phenol, pyrocatechol, hydroquinone, and 4,4'-isopropylidene-bisphenol using papers impregnated with formamide or monomethylformamide. The R_F values of the compounds were related to a homologous series of standards; pyrocatechol and 4-alkylpyrocatechols containing C_1 - C_{12} alkyls were used for this purpose and were assigned to R_C values. The ΔR_C contributions of the individual groups were established, and their additivity was verified.

INTRODUCTION

The chromatographic behaviour of the alkyl derivatives of phenols has already aroused much interest. From the point of view of chromatography, the above compounds represent very simple systems, which along with their easy detectability makes them suited for investigations of the relationships between the structure and chromatographic behaviour. These investigations are in most cases based on the well-known MARTIN's relationship, which can be written as follows:

$$R_M = \Sigma \Delta R_M + K \quad (1)$$

where $R_M = \log (1/R_F - 1)$; the ΔR_M are the contributions of the individual parts of the molecule of the chromatographed compound, and K is a constant which in the first place includes the ratio of the cross section of the stationary to the mobile phase. Several authors¹⁻⁶ have succeeded in verifying the above relationship for the alkyl derivatives of phenols. In so far as other relationships⁷ which have been found are concerned, the deviations were mainly due to experimental difficulties¹.

Attempts have been made to reduce the experimental errors, on the one hand, by improving the techniques used, *e.g.*, by preventing the evaporation of the phases in the course of chromatography between aluminium foils⁸, and on the other, by correcting the R_F or R_M values obtained in the measurements by means of one or

two standards⁹. However, even if the reproducibility is satisfactory, an important complication may arise, namely, that the term K in eqn. 1 is not constant, since both phases exhibit a concentration gradient along the paper strip^{10,11}. For instance, COPIUS PEEREBOOM¹¹ found that the ratio of the cross-sections of both phases on a paper impregnated with paraffin oil decreased from 14.6 (start) to 2.0 (front). These complications can be avoided by using a procedure suggested by DECKER¹². The compound being analysed is run together with a homologous series of standards chosen in advance. Integers are assigned to the individual members of this series; DECKER suggests the symbol R_C for these values (analogous to the Kováts' indices in GC). The R_C value of the compound being analyzed is determined by interpolation on an experimental curve obtained by plotting the R_F values of the standards against their R_C values. Thus, a value of a hypothetical member of the homologous series is assigned to the compound being analysed, this member having the same position on the chromatogram as the compound. Since the R_M values of both the above compounds are equal, and if relationship (1) is valid, it then follows:

$$\Sigma \Delta R_M + K = n \cdot \Delta R_M(\text{CH}_2) + \Delta R_M(\text{basic compound}) + K$$

where n is the number of the carbon atoms in the chain of the hypothetical standard. Since $R_C = n$, the following holds

$$R_C = \sum \frac{\Delta R_M}{\Delta R_M(\text{CH}_2)} - \frac{\Delta R_M(\text{basic compound})}{\Delta R_M(\text{CH}_2)}$$

By introducing ΔR_C for the ratio $\Delta R_M/\Delta R_M(\text{CH}_2)$, we obtain the relationship

$$R_C = \Sigma \Delta R_C - \Delta R_C(\text{basic compound}) \quad (2)$$

At constant temperature, the R_C value is independent of the degree of impregnation, any gradient of the phases and their evaporation, as long as their chemical composition remains unchanged.

EXPERIMENTAL

The materials used were prepared according to the literature data or by re-purifying commercial products.

4-Alkylpyrocatechols having C_6 to C_{12} alkyls were prepared by acylation of pyrocatechol (1 mole) with the corresponding carboxylic acid (1 mole) and using boron fluoride etherate (1.2 mole) at 80° for 3 h (yield 20–30% of the theoretical); this was followed by reduction of the isolated 4-acylpyrocatechol according to CLEMENSEN (see ref. 13): 4-hexylpyrocatechol (b.p. $150\text{--}160^\circ/1$ Torr), 4-heptylpyrocatechol (m.p. $65.5\text{--}66.5^\circ$, ref. 13, $65\text{--}67^\circ$), 4-octylpyrocatechol (m.p. $60.5\text{--}61.5^\circ$, ref. 13, $57\text{--}58^\circ$), 4-nonylpyrocatechol ($72.5\text{--}73.5^\circ$, ref. 13, 68°), 4-decylpyrocatechol ($69\text{--}70.5^\circ$), 4-undecylpyrocatechol (m.p. $81\text{--}82^\circ$), 4-dodecylpyrocatechol (m.p. $76\text{--}77^\circ$). 3-*tert.*-Butyl-5-ethylpyrocatechol and 3-*tert.*-butyl-5-propylpyrocatechol were prepared by alkylation of 4-ethylpyrocatechol or 4-propylpyrocatechol (0.01 mole) with *tert.*-butyl alcohol (0.01 mole) in acetic acid, catalysed by sulphuric acid (0.01 mole) at room temperature for 24 h; after the usual treatment of the reaction mixture, the raw alkylation product was used.

Chromatograms were run on Whatman No. 1 paper, impregnated with 20% formamide in ethyl acetate or with 20% monomethylformamide in benzene (dried for 10 min), employing the techniques without removal of the excess of the phase by filtration through the filter paper. In the formamide-chloroform system the descending technique was used; in the other cases, ascending chromatography was employed. The chromatograms were detected by spraying them with a freshly prepared mixture of a 15% solution of ferric chloride and 1% solution of potassium ferricyanide. The R_C values listed in Tables II and IV were obtained as the mean from at least three measurements. The maximum differences between the individual measurements of R_C and the mean value were ± 0.25 in the formamide systems, and ± 0.5 in the system with stationary phase of monomethylformamide.

RESULTS AND DISCUSSION

In the present work, alkyl derivatives of the following compounds were chromatographed, and their R_C values determined: phenol, pyrocatechol, hydroquinone, 4,4'-isopropylidenebisphenol (subsequently referred to as bisphenol A). The alkyl groups studied were: methyl, ethyl, isopropyl, *tert.*-butyl, 1,1,3,3-tetramethylbutyl groups (subsequently referred to as *tert.*-octyl) and 1,1,3,3,5,5-hexamethylhexyl (subsequently referred to as *tert.*-dodecyl) groups, as well as some other model compounds. Pyrocatechol and 4-alkylpyrocatechols containing C_1 to C_{12} alkyls were chosen as the homologous series of standards; their polar character covered the whole range of polarity of the compounds studied. The first member in this series, *i.e.* pyrocatechol, was assigned an R_C value equal to zero, 4-methylpyrocatechol was assigned $R_C = 1$ etc., *cf.* Table I.

Deviations from the validity of relationship (1) could be expected with the first and second member of the homologous series of standards^{1,12}. To evaluate the

TABLE I

 R_C AND R_F VALUES OF 4-ALKYLPYROCATECHOLS

Paper impregnated with 20% formamide (I_1) or monomethylformamide (I_2), developed with chloroform (S_1) or a mixture of isopropyl ether and heptane (1:2) (S_2).

Compound	R_C	R_F values in the chromatographic system		
		I_1S_1	I_1S_2	I_2S_2
Pyrocatechol	0	0.05	0.04	—
4-Methylpyrocatechol	1	0.10	0.07	—
4-Ethylpyrocatechol	2	0.18	0.13	—
4-Propylpyrocatechol	3	0.30	0.24	0.05
4-Butylpyrocatechol	4	0.45	0.40	0.08
4-Pentylpyrocatechol	5	0.60	0.55	0.13
4-Hexylpyrocatechol	6	0.71	0.68	0.21
4-Heptylpyrocatechol	7	0.78	0.78	0.31
4-Octylpyrocatechol	8	0.81	—	0.42
4-Nonylpyrocatechol	9	—	—	0.54
4-Decylpyrocatechol	10	—	—	0.64
4-Undecylpyrocatechol	11	—	—	0.71
4-Dodecylpyrocatechol	12	—	—	0.77

magnitude of these deviations the polarity of the first four members of the series of 4-alkylpyrocatechols investigated was lowered by introducing the *tert.*-butyl group into position 6; the derivatives thus obtained were chromatographed in a system with a stationary phase of monomethylformamide. The R_C values (Table V) of the neighbouring members of this new homologous series differ by approximately a unit, *i.e.* the increments are the same as in the case of the higher members of the original series; this means that no great deviations occur.

The pyrocatechol derivatives are extremely sensitive towards detection, which allows the use of small amounts of these compounds and thus chromatographic runs of several standards from one starting line without influencing their R_F values. Chromatographic runs were carried out on paper impregnated with formamide or monomethylformamide, and a mixture of diisopropyl ether-heptane (1:2) was used as the mobile phase; in the case of formamide, chloroform was also used. The R_F values of most of the phenols investigated are very close in both the formamide systems, but differ in compounds having varying abilities of hydrogen bond formation. This is of practical importance, *e.g.* in the analysis of reaction mixtures formed by the alkylation of phenols, when it is possible by chromatographing in both these systems to differentiate between the derivatives formed by alkylation on the oxygen atom and polyalkyl derivatives due to alkylation in the nucleus. The system where monomethyl-

TABLE II

R_C VALUES OF COMPOUNDS USED IN THE CALCULATIONS OF THE ΔR_C INCREMENTS

Paper impregnated with 20% formamide (I_1) or monomethylformamide (I_2), developed with chloroform (S_1) or a mixture of diisopropyl ether-heptane (1:2) (S_2).

Compound	Chromatographic system		
	I_1S_1	I_1S_2	I_2S_2
Phenol	3.7	3.7	4.8
2-Methylphenol	5.2	5.1	6.2
2-Ethylphenol	6.3	6.5	7.6
2-Isopropylphenol	—	—	8.7
2- <i>tert.</i> -Butylphenol	—	—	10.6
2-Methoxyphenol	—	—	5.3
4-Isopropylphenol	—	—	7.6
4-Benzylphenol	—	6.3	6.6
4-Methoxyphenol	—	—	3.4
2,6-Dimethylphenol	—	6.0	7.7
4-Isopropylpyrocatechol	3.0	3.0	—
4- <i>tert.</i> -Butylpyrocatechol	—	—	3.6
2- <i>tert.</i> -Butylhydroquinone	1.8	2.9	—
2- <i>tert.</i> -Octylhydroquinone	4.7	—	5.2
2- <i>tert.</i> -Dodecylhydroquinone	—	—	8.2
2,5-Diisopropylhydroquinone	4.1	5.1	—
2,5-Di- <i>tert.</i> -butylhydroquinone	6.3	—	—
2,6-Di- <i>tert.</i> -butylhydroquinone	—	—	8.1
4,4'-Methylenebis(2,6-xyleneol)	—	—	3.7
4,4'-Isopropylidene-bis(2-methylphenol)	—	4.5	—
2,6-Dimethyl-4,4'-isopropylidene-bisphenol	6.1	—	—
2,6-Diethyl-4,4'-isopropylidene-bisphenol	—	—	4.7
2,6-Diisopropyl-4,4'-isopropylidene-bisphenol	—	—	6.6
2- <i>tert.</i> -Butyl-4,4'-isopropylidene-bisphenol	6.8	—	—
2-Methyl-6- <i>tert.</i> -butyl-4,4'-isopropylidene-bisphenol	—	—	6.3

TABLE III

 ΔR_C INCREMENTS OF INDIVIDUAL GROUPS

Paper impregnated with 20% formamide (I_1) or 20% monomethylformamide (I_2), developed with chloroform (S_1) or a mixture of diisopropyl ether-heptane (1:2) (S_2).

Group	Chromatographic system		
	I_1S_1	I_1S_2	I_2S_2
ΔR_C (basic compound)	-8.1	-8.7	-12.7
Phenyl	2.0	1.6	0.8
Phenolic group	-6.4	-6.6	-8.7
<i>p</i> -Isopropyl ^a	3.0	3.0	2.8
<i>p</i> - <i>tert.</i> -Butyl	—	—	3.6
<i>p</i> -Methoxy	—	—	-1.4
<i>o</i> -Methyl	1.5	1.4	1.4
<i>o</i> -Ethyl	2.6	2.8	2.8
<i>o</i> -Isopropyl	3.4	4.0	3.9
<i>o</i> - <i>tert.</i> -Butyl	4.5	5.8	5.8
<i>o</i> - <i>tert.</i> -Octyl	7.4	—	9.1
<i>o</i> - <i>tert.</i> -Dodecyl	—	—	12.1
<i>o</i> -Methoxy	—	—	0.5
<i>o,o'</i> -Dimethyl	3.8	2.3	2.9
<i>o,o'</i> -Diethyl	—	—	5.0
<i>o,o'</i> -Diisopropyl	—	—	6.9
<i>o,o'</i> -Di- <i>tert.</i> -butyl	—	—	12.0
<i>o</i> -Methyl- <i>o'</i> - <i>tert.</i> -butyl	—	—	6.6

^a Isopropylidene group was calculated as isopropyl group.

formamide is used as the stationary phase is suitable for less polar phenols. The R_F values of standards are given in Table I, the R_C values of the compounds investigated are presented in Tables II and IV. It was found during this study that the R_C values of some of the compounds analysed were not completely reproducible, especially in the presence of monomethylformamide. The reproducibility observed in the preliminary experiments with dimethylformamide was even less. Such a fluctuation of values is probably due to changes in the water content of the stationary phase. This is also corroborated by a comparison between chromatograms run in winter and in summer, when there are considerable differences in the humidity of the air at the same temperature. In systems containing formamide a small fluctuation in the water content does not lead to any essential changes in the R_C values. The validity of relationship (2) was verified by comparing the measured and calculated values of R_C of the phenolic derivatives studied (Table IV), and the agreement was found to be satisfactory in most cases. The values of the increments ΔR_C (Table III) were calculated from the R_C values of compounds listed in Table II. The isopropylidene bridge in the alkylated bisphenol A's was calculated as an isopropyl group. The comparison of the bisphenols with the analogous mononuclear phenols allows the determination of the constant— ΔR_C (basic compound) in eqn. 2. The ΔR_C values for alkyls in the position *ortho* to the hydroxy group holds only if the other *ortho* position is free. If both the *ortho* positions are occupied with alkyls, the total value of both alkyls was determined. If the other *ortho* position is also occupied by a hydroxy group, *i.e.* in the case of *ortho* alkyl derivatives of pyrocatechol, it is not possible to employ the ΔR_C values from

TABLE IV

R_C VALUES OF PHENOLIC COMPOUNDS

Paper impregnated with 20% formamide (I₁) or monomethylformamide (I₂), developed with chloroform (S₁) or a mixture of diisopropyl ether—heptane (1:2) (S₂).

Compound	Chromatographic system					
	I ₁ S ₁		I ₁ S ₂		I ₂ S ₂	
	Found	Calc.	Found	Calc.	Found	Calc.
2-Methoxyphenol	6.5	—	3.8	—	5.3	—
4-Methoxyphenol	3.8	—	2.4	—	3.4	—
4-Isopropylphenol	6.9	6.7	6.6	6.7	7.6	—
2-Methoxy-4- <i>tert.</i> -butylphenol	—	—	—	—	10.3	9.8
4- <i>tert.</i> -Butylpyrocatechol	3.6	—	3.7	—	3.6	—
4- <i>tert.</i> -Octylpyrocatechol	6.6	—	6.9	—	6.8	—
4- <i>tert.</i> -Octyl-5-methylpyrocatechol	—	—	7.0	—	6.9	—
4- <i>tert.</i> -Dodecylpyrocatechol	—	—	—	—	9.9	—
2- <i>tert.</i> -Butyl-5-methylhydroquinone	3.3	3.3	4.2	4.3	—	—
2- <i>tert.</i> -Octyl-5-methylhydroquinone	6.2	6.2	—	—	7.1	6.6
2,5-Diisopropylhydroquinone	4.1	—	5.1	—	4.1	3.9
2,5-Di- <i>tert.</i> -butylhydroquinone	6.3	—	—	—	7.8	7.7
2-Methoxy-4- <i>tert.</i> -butylphenol	—	—	—	—	9.3	8.9
2- <i>tert.</i> -Butyl-4-methoxyphenol	—	—	—	—	9.1	9.2
4,4'-Isopropylidene-bisphenol	2.3	2.3	2.0	1.7	—	—
2-Methyl-4,4'-isopropylidene-bisphenol	3.9	3.8	3.0	3.1	—	—
2,6-Dimethyl-4,4'-isopropylidene-bisphenol	6.1	—	3.9	4.0	—	—
4,4'-Isopropylidene-bis(2-methylphenol)	5.4	5.3	4.5	—	—	—
6-Methyl-4,4'-isopropylidene-bis(2-methylphenol)	—	—	5.3	5.4	4.0	4.0
4,4'-Isopropylidene-bis(2,6-dimethylphenol)	—	—	6.2	6.3	5.3	5.5
2-Ethyl-4,4'-isopropylidene-bisphenol	5.0	4.9	4.4	4.5	—	—
4,4'-Isopropylidene-bis(2-ethylphenol)	7.5	7.5	6.7	7.3	5.2	5.3
6-Ethyl-4,4'-isopropylidene-bis(2-ethylphenol)	—	—	—	—	7.2	7.5
4,4'-Isopropylidene-bis(2,6-diethylphenol)	—	—	—	—	10.2	9.7
2-Isopropyl-4,4'-isopropylidene-bisphenol	5.6	5.7	5.8	5.7	4.0	3.6
4,4'-Isopropylidene-bis(2-isopropylphenol)	—	—	—	—	7.1	7.5
6-Isopropyl-4,4'-isopropylidene-bis(2-isopropylphenol)	—	—	—	—	10.5	10.5
2- <i>tert.</i> -Butyl-4,4'-isopropylidene-bisphenol	6.8	—	7.0	7.5	5.3	5.5
2,6-Di- <i>tert.</i> -butyl-4,4'-isopropylidene-bisphenol	—	—	—	—	11.5	11.7
4,4'-Isopropylidene-bis(2- <i>tert.</i> -butylphenol)	—	—	—	—	10.5	11.3
2- <i>tert.</i> -Octyl-4,4'-isopropylidene-bisphenol	—	—	—	—	8.8	8.8
2- <i>tert.</i> -Dodecyl-4,4'-isopropylidene-bisphenol	—	—	—	—	11.7	11.8
2-Methyl-2'- <i>tert.</i> -butyl-4,4'-isopropylidene-bisphenol	—	—	—	—	6.8	6.9
2,6-Dimethyl-2'- <i>tert.</i> -butyl-4,4'-isopropylidene-bisphenol	—	—	—	—	7.9	8.4
6-Methyl-2'- <i>tert.</i> -butyl-4,4'-isopropylidene-bis(2-methylphenol)	—	—	—	—	8.8	9.2
2-Methyl-6- <i>tert.</i> -octyl-4,4'-isopropylidene-bisphenol	—	—	—	—	9.8	—
2-Methyl-2'- <i>tert.</i> -octyl-4,4'-isopropylidene-bisphenol	—	—	—	—	10.4	10.2
4,4'-Methylene-bis(2,6-xyleneol)	—	—	4.7	4.3	3.7	—
4,4'-Methylene-bis(2-methyl-6- <i>tert.</i> -butylphenol)	—	—	—	—	11.1	11.1
3,3,3',3'-Tetramethyl-1,1'-spirobiindane-6,6'-diol	6.7	—	6.4	—	5.3	—
3,3,3',3'-Tetramethyl-1,1'-spirobiindane-6,6',7-triol	3.4	—	2.6	—	—	—

TABLE V

 R_C VALUES OF THE 3-ALKYL DERIVATIVES OF PYROCATECHOL

Paper impregnated with 20% monomethylformamide, developed with a mixture of diisopropyl ether-heptane (1:2).

Compound	R_C
3- <i>tert.</i> -Butylpyrocatechol	7.2
3- <i>tert.</i> -Butyl-5-methylpyrocatechol	8.1
3- <i>tert.</i> -Butyl-5-ethylpyrocatechol	9.2
3- <i>tert.</i> -Butyl-5-propylpyrocatechol	10.3
3,5-Di- <i>tert.</i> -butylpyrocatechol	11.0
3-Methyl-5- <i>tert.</i> -butylpyrocatechol	6.1
3-Isopropylpyrocatechol	4.7

Table III for the calculations. These compounds have higher R_C values than the calculated ones. Another example of the finding that the chromatographic behaviour of phenolic derivatives can be influenced by some other structural feature is illustrated by the behaviour of 4-*tert.*-octylpyrocatechol and 4-*tert.*-octyl-5-methylpyrocatechol, whose R_F values are virtually identical.

It can be concluded, therefore, that in order to determine ΔR_C values which would characterise all the structural features of a substituted phenol molecule, it would be necessary to investigate a much larger set of compounds than we had at our disposal.

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