STUDIES IN THE RELATIONSHIP BETWEEN MOLECULAR STRUCTURE AND CHROMATOGRAPHIC BEHAVIOUR

VII. THE BEHAVIOUR OF HALOGENATED PHENOLS AND SOME HALOGENO-; ALKYL-SUBSTITUTED PHENOLS ON ALUMINA-IMPREGNATED PAPERS, AND ON THIN LAYERS OF ALUMINA*

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INTRODUCTION

While a number of workers[1–10] have attempted to separate simple halogenated phenols and/or halogeno-; alkyl-substituted phenols by paper partition chromatography, few attempts[11–12] have been made to use adsorption chromatography, either on impregnated papers or on thin layers for the resolution of these compounds.

SEEBOTH[11] has considered the separation of one halogenated phenol only, *p*-chlorophenol, from a number of other phenols containing diverse substituents, on a silica gel substrate.

Silica gel thin layers were also used by WUSTEMAN and coworkers[12] for the separation of a number of phenols as their sulphate esters. Neither the isomeric monochloro compounds, nor the isomeric 2,3- and 2,4-dichloro compounds could be resolved.

On polyamide thin layers, in five simple solvents of increasing polarity, WANG[13] found little difference in R_F values of the "3" or "4" substituted isomers of the monohalogenated chloro-, bromo- and iodo-phenols. In all cases, however, the halogenated phenols had lower R_F values than the parent phenol.

HUSAIN has recently attempted the separation of chlorinated cresols and chlorinated xylenols by paper chromatography[8] and by thin-layer chromatography on silica gel[14]. The same three solvent systems were used in each case, *viz.*:

(a) petroleum ether (80–100°) saturated with formic acid;

(b) xylene saturated with formamide;

(c) the organic layer from a mixture of benzene–acetic acid–water (2:2:1, v/v).

In each technique it was found that an increase in the number of substituent groups in the molecule caused an increase in R_F values, that 6-chloro-2-cresol could not be separated from 4,6-dichloro-2,4-cresol, and that evidence for an *ortho* effect existed. For the thin-layer system, the chlorocresols could not be resolved from the parent cresols.

Recently, we have chromatographed a number of nitrophenols, including halogenated nitrophenols and halogeno-; alkyl-substituted nitrophenols, on alumina-

* For Parts I, II and V of this series, see refs. 15, 20 and 16.

impregnated surfaces[15]. We have stated[15] that the hydroxylated alumina surface acted as a proton donor to the phenolic oxygen atom, and to other proton acceptor groups in the phenolic molecule, and the resultant hydrogen bonds are of importance in the chromatographic process. We have also considered the role of hydrogen bonding in the chromatography of alkylphenols on alumina surfaces[16]. We have previously shown for both alkyl[17] and halogeno[18] substituted phenoxyacetic acids, chromatographed on paper using polar eluents, that the number of alkyl or halogeno substituents, their positions relative to one another and to the phenoxyacetic acid group, were factors influencing the chromatographic behaviour of the compounds. We showed that the electronic effects of the substituents, on the carboxylic acid group, are somewhat "softened" by the ether oxygen atom, which tends to act as an electron buffer preventing large variations in the electron density of the chromatographically functional group, *viz.* the acid group. In studies of the alkyl phenols chromatographed by partition chromatography[19] we have indicated that the transfer of electron density effects to the phenolic group, the chromatographically functional group, is relatively easy, and hence the relative position of the chromatographically functional group and the substituents is of importance.

Those alkylphenols, however, contain only one functional group—the phenolic—that takes part in the actual formation of bonds during the chromatographic process, but this group may be affected both sterically and electronically by the presence of alkyl substituents. In the halogenophenols as in the nitrophenols there are two functional groups. The halogeno groups are capable of forming hydrogen bonds not only with the phenolic hydroxyl group, but with any other hydroxyl groups in the chromatographic system, as well as electronically affecting the phenolic group. In phenols containing both halogeno and alkyl substituents, the electronic effects of either type of substituent may be readily transferred throughout the molecule and the overall effect may well be dependent on the relative positions of all the substituents. To investigate this we have chromatographed a series of halogeno- and halogeno-; alkyl-substituted phenols under rigorously standardised conditions. A variety of eluant systems have been used to study the effects of both non-polar solvents and systems containing polar solvents capable of competing with the polar surface for formation of hydrogen bonds with the phenols.

EXPERIMENTAL

Chromatography on alumina-impregnated papers

Four grades of alumina-impregnated papers were used:

(a) cellulose paper (Whatman No. 1) impregnated with 2 % of alumina;

(b) cellulose paper (Whatman No. 1) impregnated with 7.5 % of alumina;

(c) glass fibre "paper" (Whatman No. 1) impregnated with 7.5 % of alumina;

(d) cellulose paper (Schleicher and Schüll No. 288) impregnated with 25 % of alumina.

The pretreatment of the papers, the application of the phenols and the development conditions were as previously described[15].

Thin-layer chromatography

Column grade alumina (Hopkin & Williams M.F.C. (Camag) grade, neutral,

Brockmann activity, I–II, 100–200 mesh) was crushed and the 200–230 mesh fraction was used to prepare the layers as previously described. The activation conditions were also those used before.

Application of the phenols and development conditions

The multiple-spotting device previously described[20] was used to apply the phenols (1 μl of 0.25 % v/v solutions in suitable solvents) to the cooled activated plates.

The chromatograms were eluted by an ascending technique, at a constant temperature of 25° ± 0.5° in our double saturation chamber[20].

The length of run, standardised by time (90 min), was 14.5 ± 0.5 cm.

Eluent systems

The following eluents were used:

(I) Cyclohexane
(II) Dioxane
(III) Cyclohexane–dioxane (75:25, v/v)
(IV) Cyclohexane–dioxane (1:1, v/v)
(V) Benzene–methanol (95:5, v/v)
(VI) Benzene–ethanol (95:5, v/v)
(VII) Benzene–ethyl acetate (3:7, v/v)

These were purified as previously indicated[15,16].

Detection of the phenols

These were detected as yellow spots on a purple background by spraying the eluted chromatograms with alkaline potassium permanganate[16].

RESULTS

These are shown in Tables I–IV. Each result is the mean of at least four determinations obtained from papers or plates carrying an internal standard, the R_F values of which agreed within ± 0.01 R_F units with the predetermined mean value for that standard when run under the chosen conditions. The results obtained for the individual phenols also agreed within ± 0.01 R_F units with the average values quoted. In addition to the systems indicated in Tables I–IV, the following systems were investigated:

No. 5. Cyclohexane-dioxane (75:25, v/v)/cellulose paper + 2 % of alumina;
No. 6. Cyclohexane–dioxane (75:25, v/v)/cellulose paper + 7.5 % of alumina;
No. 7. Cyclohexane–dioxane (75:25, v/v)/glass fibre paper + 7.5 % of alumina.

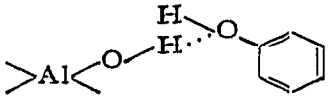
In all these systems the R_F value of all compounds was 1.00.

DISCUSSION OF RESULTS

For simplification, the phenols are subdivided into small groups, with more closely defined limits than solely halogenated phenols. When solvent systems failed to provide reasonable separations of the phenols, by causing the phenols to

move with the solvent front, the results are not included in the discussion. This is because these cases and solvents are regarded as extremes of the systems.

As previously discussed[15] the hydrogen bonding between the phenols and the polar surface is probably between polar groups on the phenol and the hydroxylic groups adsorbed on the alumina surface. Thus the bonds are probably



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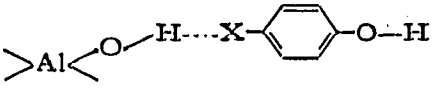

Dissolution into the eluent occurs by normal processes. Considering the homologous series of chlorinated phenols (Table I) it is seen that an increase in the number of chloro groups in the molecule results in a decrease in the R_F value of the compound. It is therefore evident that in addition to the primary hydrogen bonding between the phenolic oxygen atom and the hydrogen atoms of the hydroxylated alumina surface, there is a contribution from hydrogen bonding between these hydrogen atoms and the chlorine atoms. For the monochloro-substituted phenols, the 2-compound has a slightly higher R_F value than the 3- and 4-compounds. This suggests that some internal hydrogen bonding occurs in the former compound. However, such an effect is not apparent in the disubstituted compounds. This is probably because the hydrogen bonds with the surface are strong ones, and overshadow the fine effect of internal hydrogen bonding. Considering the values for the other monohalogeno-substituted phenols, the monobromo- and monoiodophenols show evidence of the *ortho* effect. When the monofluoro compounds have made any appreciable movement, *e.g.* in systems containing dioxan or other surface to phenol hydrogen bond breakers, such as ethanol or methanol, the *ortho* effect is not noticeably apparent. It is suggested that the relatively smaller size of the fluorosubstituent in the position *ortho* to the phenolic hydroxyl, makes the probability of internal hydrogen bonding less than when chloro or bromo substituents are present[21]. Thus the hydrogen bonding between the phenolic group and the surface may play a relatively more pronounced role. The relative position of the halogeno substituent to the chromatographically functional group is still however noticeable in the fluoro-substituted phenols. The electron-withdrawing effect of the fluoro group causes an increase in the polarity of the phenolic hydroxyl group; the further away from the phenolic group is the fluoro, then the lesser is the increase; as shown by a consideration of the R_F values for phenol and the 3-monofluorophenols chromatographed in systems where the introduction of a fluoro group has a marked effect (*viz.* solvent/support systems 12, 13, 14).

Since substitution of one halogeno substituent into phenol causes a decrease in the R_F value, it is expected that substitution of more than one group should cause a greater decrease. The behaviour of the polychlorinated phenols indicates that such an additive effect[22] does exist. The behaviour of other polyhalogenated phenols is in accordance with that expected by comparison with the polychlorinated phenols.

Mixed halogeno-alkylphenols

The results in Table II show that the methylated 4-chlorophenols can be divided into 3 groups according to the number of *ortho*-methyl groups in the molecule. In this, these compounds behave in the expected manner, the R_F values increasing with the number of *ortho*-methyl groups, as did the simple methylated phenols[16]. The results

TABLE I

PHENOLS CONTAINING ONLY HALOGENO SUBSTITUENTS

Key to solvent/support system Nos.:

1 = Cyclohexane/cellulose paper + 2 % of alumina.
2 = Cyclohexane/cellulose paper + 7.5 % of alumina.
3 = Cyclohexane/glass fibre paper + 7.5 % of alumina.
4 = Cyclohexane/cellulose paper + 25 % of alumina.
8 = Cyclohexane–dioxane (75:25, v/v)/ cellulose paper + 25 % of alumina.
9 = Cyclohexane/alumina thin layers.
10 = Cyclohexane–dioxane (1:1, v/v)/alumina thin layers.
11 = Dioxane/alumina thin layers.
12 = Benzene–methanol (95:5, v/v)/alumina thin layers.
13 = Benzene–ethanol (95:5, v/v)/ alumina thin layers.
14 = Benzene–ethyl acetate (3:7, v/v)/alumina thin layers.

Key	*Phenol*	*R_F values for solvent/support system No.*										
		1	*2*	*3*	*4*	*8*	*9*	*10*	*11*	*12*	*13*	*14*
0	Phenol	0.10	0.05	0.06	0.00	0.25	0.00	0.48	0.95	0.26	0.29	0.50
1	2-Chloro	0.08	0.05	0.06	0.00	0.16	0.00	0.22	0.30	0.24	0.24	0.16
2	3-Chloro	0.08	0.02	0.03	0.00	0.13	0.00	0.18	0.28	0.19	0.22	0.10
3	4-Chloro	0.08	0.02	0.03	0.00	0.13	0.00	0.20	0.29	0.19	0.22	0.10
4	2,3-Dichloro	0.05	0.00	0.00	0.00	0.07	0.00	0.06	0.10	0.11	0.10	0.06
5	2,4-Dichloro	0.05	0.00	0.00	0.00	0.09	0.00	0.06	0.09	0.12	0.11	0.05
6	2,5-Dichloro	0.05	0.00	0.00	0.00	0.06	0.00	0.07	0.09	0.11	0.10	0.06
7	2,6-Dichloro	0.06	0.00	0.00	0.00	0.10	0.00	0.06	0.09	0.11	0.10	0.06
8	3,4-Dichloro	0.05	0.00	0.00	0.00	0.09	0.00	0.06	0.12	0.13	0.13	0.05
9	3,5-Dichloro	0.05	0.00	0.00	0.00	0.09	0.00	0.06	0.12	0.13	0.13	0.05
10	2,4,5-Trichloro	0.00	0.00	0.00	0.00	0.03	0.00	0.03	0.05	0.07	0.04	0.02
11	2,4,6-Trichloro	0.00	0.00	0.00	0.00	0.03	0.00	0.03	0.05	0.06	0.03	0.00
12	2,3,4,6-Tetrachloro	0.00	0.00	0.00	0.00	0.02	0.00	0.02	0.02	0.03	0.03	0.00
13	2,3,4,5,6-Pentachloro	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
14	2-Fluoro	0.06	0.04	0.06	0.00	0.18	0.00	0.32	0.35	0.16	0.18	0.13
15	3-Fluoro	0.08	0.02	0.05	0.00	0.20	0.00	0.32	0.35	0.21	0.21	0.18
16	4-Fluoro	0.08	0.03	0.05	0.00	0.27	0.00	0.32	0.35	0.24	0.25	0.24
17	2-Bromo	0.13	0.08	0.08	0.00	0.18	0.00	0.32	0.32	0.26	0.26	0.16
18	3-Bromo	0.08	0.03	0.00	0.00	0.14	0.00	0.21	0.28	0.21	0.22	0.14
19	4-Bromo	0.08	0.03	0.00	0.00	0.15	0.00	0.21	0.28	0.21	0.22	0.14
20	2-Iodo	0.14	0.08	0.08	0.00	0.21	0.00	0.32	0.36	0.29	0.28	0.16
21	3-Iodo	0.11	0.03	0.05	0.00	0.20	0.00	0.31	0.35	0.24	0.20	0.14
22	4-Iodo	0.11	0.03	0.06	0.00	0.18	0.00	0.31	0.35	0.21	0.20	0.14
23	2,4-Dibromo	0.06	0.00	0.00	0.00	0.07	0.00	0.06	0.09	0.12	0.10	0.05
24	3,5-Dibromo	0.05	0.00	0.00	0.00	0.06	0.00	0.06	0.09	0.12	0.10	0.06
25	2,4,6-Tribromo	0.00	0.00	0.00	0.00	0.04	0.00	0.05	0.05	0.07	0.03	0.00
26	2,4,6-Triiodo	0.00	0.00	0.00	0.00	0.03	0.00	0.05	0.05	0.09	0.03	0.00
27	2,4-Diiodo-6-chloro	0.00	0.00	0.00	0.00	0.06	0.00	0.04	0.05	0.09	0.05	0.00
28	2,6-Diiodo-4-chloro	0.00	0.00	0.00	0.00	0.05	0.00	0.04	0.05	0.04	0.03	0.00
29	2,6-Diiodo-4-bromo	0.00	0.00	0.00	0.00	0.05	0.00	0.04	0.05	0.10	0.05	0.00

TABLE II

MIXED CHLORO-ALKYLPHENOLS NOT CONTAINING CHLORO GROUPS *ortho* TO THE PHENOL

Key	*Phenol*	R_F *values for solvent/support system No.**										
		1	*2*	*3*	*4*	*8*	*9*	*10*	*11*	*12*	*13*	*14*
3	4-Chloro	0.08	0.02	0.03	0.00	0.13	0.00	0.18	0.28	0.19	0.22	0.10
30	4-Chloro-3-methyl	0.14	0.06	0.09	0.00	0.29	0.00	0.55	0.76	0.24	0.24	0.37
31	4-Chloro-2,3-dimethyl	0.35	0.09	0.10	0.02	0.61	0.00	0.77	1.00	0.38	0.36	0.74
32	4-Chloro-2,5-dimethyl	0.34	0.08	0.12	0.02	0.62	0.00	0.74	1.00	0.37	0.42	0.73
33	4-Chloro-2,6-dimethyl	0.70	0.29	0.27	0.00	0.80	0.00	0.89	1.00	0.43	0.44	0.85
34	4-Chloro-3,5-dimethyl	0.16	0.07	0.10	0.00	0.38	0.00	0.60	1.00	0.24	0.26	0.38
35	4-Chloro-2,3,5-trimethyl	0.38	0.09	0.12	0.02	0.64	0.02	0.76	1.00	0.36	0.34	0.75
36	4-Chloro-3-methyl-5-ethyl	0.18	0.08	0.11	0.00	0.47	0.00	0.67	1.00	0.28	0.28	0.42

* For solvent/support systems, see Table I.

also show that the presence of an additional methyl or other alkyl group in a position other than an *ortho* position has only a small effect on the R_F values. This small effect is probably due to the increased solubility of the substituted compound compared with the parent compound 4-chlorophenol. The electron-donating properties of the methyl group, although small, are probably significant in decreasing the polarity of the phenolic bond and hence lowering the amount of hydrogen bonding between the phenolic group and the surface.

The methyl substituted 2-chlorophenols (Table III) show an unexpectedly large increase in R_F values, compared with the parent compound 2-chlorophenol. Though the independent effects of ring-substituted methyl and chloro groups are small, the above results may be explained by considering the electron-delocalising effects of the substituents as a whole. The electron donation by the methyl groups coupled with the electron withdrawing effect of the 2-chlorine atom would appear to strengthen the internal hydrogen bond between the chlorine atom and the phenolic group. The

TABLE III

MIXED HALOGENO-ALKYLPHENOLS CONTAINING HALOGENO GROUPS *ortho* TO THE PHENOLS

Key	*Phenol*	R_F *values for solvent/support system No.**										
		1	*2*	*3*	*4*	*8*	*9*	*10*	*11*	*12*	*13*	*14*
1	2-Chloro-	0.08	0.05	0.06	0.00	0.16	0.00	0.22	0.30	0.24	0.24	0.16
37	2-Chloro-4,5-dimethyl	0.71	0.22	0.19	0.03	0.27	0.00	0.57	1.00	0.46	0.52	0.31
38	2,4-Dichloro-6-methyl	0.89	0.62	0.54	0.04	0.52	0.00	0.73	1.00	0.39	0.39	0.43
39	2,4-Dichloro-3,5-dimethyl	0.66	0.20	0.17	0.10	0.18	0.02	0.34	0.90	0.21	0.21	0.20
40	2,4-Dichloro-3,6-dimethyl	0.92	0.72	0.60	0.02	0.60	0.00	0.83	1.00	0.40	0.40	0.46
41	2,6-Dichloro-4-methyl	0.74	0.27	0.25	0.00	0.13	0.00	0.22	0.30	0.18	0.11	0.08
42	2,6-Dichloro-3,4-dimethyl	0.83	0.32	0.30	0.02	0.19	0.00	0.35	0.90	0.21	0.22	0.20
43	2,4,6-Trichloro-3-methyl	0.72	0.20	0.20	0.00	0.06	0.00	0.25	0.64	0.12	0.10	0.02
44	2,4,6-Trichloro-3,5-dimethyl	0.78	0.27	0.22	0.02	0.10	0.00	0.30	0.78	0.15	0.14	0.03
45	2,4,6-Trichloro-3-methyl-5-ethyl	0.81	0.38	0.32	0.00	0.15	0.00	0.40	0.83	0.16	0.14	0.06

* For solvent/support systems, see Table I.

effect of the presence of a methyl group in the 6-position is to cause the expected increase in R_F values relative to isomeric compounds in which the methyl group is situated elsewhere in the ring. As with the chloro substituents, the effects of more than one methyl group are additive. The analogous but contrasting effects of the substituents of a methyl or a chloro group in a compound already so substituted may be seen by considering the values obtained for the phenols listed in Table III.

A comparison of the values obtained by substituting an ethyl rather than a methyl group (phenol 43, 44, 45, Table III) indicates that the ethyl group has a larger effect than does the methyl group in the same position relative to the other groups.

The relative effects of various hydrocarbon groups in various positions can well be seen by considering the values in Table IV. The presence of methyl, cyclohexyl or phenyl groups in the 4-position of 2-bromophenols increases the R_F values of these compounds relative to those of the unsubstituted compounds. The presence in the 6-position of an electron-donating group such as an alkyl or cyclo-alkyl group has the expected result of increasing the R_F values.

However electronic effects are not the only effects which play a part. The steric effect of such groups as 6-*tert.*-butyl, 6-cyclohexyl, and 6-phenyl play a part in causing a decrease in the amount of hydrogen bonding between the phenolic group and the solid substrate. It is probable that the difference in effect of cyclohexyl and phenyl is due to both steric and electronic effects. The ease of delocatisation of the π-orbital systems in the 2,4-dibromo-6-phenylphenol has a greater effect than does the relatively minor change in size, and hence there is a greater tendency for the electrons to be withdrawn from the phenolic group, resulting in stronger attachment of the phenol to the solid substrate.

The relatively large effect of the *tert.*-butyl group is seen by comparing the

TABLE IV

2-BROMO-ALKYLPHENOLS

Key	*Phenol*	*R_F values for solvent/support system No.**										
		1	*2*	*3*	*4*	*8*	*9*	*10*	*11*	*12*	*13*	*14*
17	2-Bromo	0.13	0.08	0.08	0.00	0.18	0.00	0.32	0.32	0.26	0.26	0.16
46	2-Bromo-4-methyl	0.56	0.14	0.10	0.02	0.21	0.00	0.35	0.90	0.28	0.29	0.21
47	2-Bromo-4-cyclohexyl	0.78	0.25	0.24	0.02	0.23	0.00	0.64	1.00	0.31	0.30	0.34
48	2-Bromo-4-phenyl	0.36	0.08	0.05	0.00	0.08	0.00	0.56	1.00	0.28	0.28	0.34
49	2-Bromo-3,4,6-trimethyl	0.90	0.53	0.50	0.07	0.87	0.04	0.76	1.00	0.46	0.54	0.39
50	2-Bromo-3-methyl-4,6-di-*tert.*-butyl	0.98	0.94	0.79	1.00	0.95	0.52	1.00	1.00	1.00	1.00	1.00
51	2,4-Dibromo-5-methyl	0.94	0.64	0.64	0.05	0.37	0.02	0.66	1.00	0.44	0.40	0.22
52	2,4-Dibromo-6-methyl	0.93	0.62	0.62	0.04	0.52	0.00	0.66	1.00	0.41	0.37	0.28
53	2,4-Dibromo-6-*tert.*-butyl	0.97	0.90	0.90	0.39	0.93	0.21	0.96	1.00	0.83	0.65	0.94
54	2,4-Dibromo-6-cyclohexyl	0.92	0.67	0.67	0.06	0.87	0.02	0.74	1.00	0.57	0.62	0.78
55	2,4-Dibromo-6-phenyl	0.62	0.33	0.30	0.00	0.48	0.00	0.77	1.00	0.42	0.53	0.74
56	2,4-Dibromo-3,6-dimethyl	0.91	0.61	0.61	0.05	0.56	0.03	0.77	1.00	0.49	0.53	0.45
57	2,4-Dibromo-5,6-dimethyl	0.90	0.62	0.60	0.04	0.56	0.02	0.83	1.00	0.46	0.53	0.41
58	2,4-Dibromo-3,5,6-trimethyl	0.93	0.64	0.67	0.05	0.87	0.04	0.92	1.00	0.53	0.64	0.63
59	2,6-Dibromo-4-methyl	0.83	0.36	0.35	0.00	0.24	0.00	0.37	1.00	0.31	0.32	0.25
60	2,6-Dibromo-4-*tert.*-butyl	0.85	0.38	0.38	0.00	0.34	0.00	0.44	1.00	0.32	0.35	0.30

* For solvent/support systems, see Table I.

TABLE V

THE EFFECT OF THE ADDITION OF A "4"-CHLORO GROUP

Compound	*Solvent system*	R_F *values*		
		Parent phenol	*4-Chloro substituted phenol*	*Difference*
Phenol	I2	0.26	0.19	—0.07
	I3	0.29	0.22	—0.07
	I4	0.50	0.10	—0.40
2,3-Dimethyl*	I2	0.43	0.38	—0.05
	I3	0.41	0.36	—0.05
	I4	0.70	0.74	+0.04
2,5-Dimethyl*	I2	0.43	0.37	—0.06
	I3	0.41	0.42	+0.01
	I4	0.70	0.73	+0.03
2,6-Dimethyl*	I2	0.52	0.43	—0.09
	I3	0.54	0.44	—0.10
	I4	0.80	0.85	+0.05
3,5-Dimethyl	I2	0.32	0.24	—0.08
	I3	0.32	0.26	—0.06
	I4	0.60	0.38	—0.28

* Values for the alkylphenol from Part V of the series[16].

behaviour of 2-bromo-3,4,6-trimethylphenol with that of 2-bromo-3,4-dimethyl-6-*tert.*-butylphenol, and that of 2,4-dibromo-6-methylphenol with that of 2,4-dibromo-6-*tert.*-butylphenol, especially in systems containing polar solvents such as methanol, ethanol and ethyl acetate. We have previously shown in paper chromatography[17,18,23] that the addition of a group to a given molecule is not only dependent upon its nature but also on the natures of the groups already present in the molecule; PATAKI[24] has given confirmation of this. The electronic interaction of groups on the benzene nucleus, will be dependent upon the relative positions of groups having electrophilic or electrophobic characters. The effect on R_F values of substituting an electrophilic group in a particular position, *e.g.* a chloro group in a position *para* to the phenol

TABLE VI

THE EFFECT OF THE ADDITION OF A "3"-METHYL GROUP

Compound	*Solvent system*	R_F *values*		
		Parent phenol	*3-Substituted phenol*	*Difference*
Phenol	I2	0.26	0.34	+0.08
	I3	0.29	0.32	+0.03
	I4	0.50	0.56	+0.06
2,4,6-Trichloro	I2	0.06	0.12	+0.06
	I3	0.03	0.10	+0.09
	I4	0.00	0.02	+0.02
2,4,6-Trichloro-3-methyl	I2	0.12	0.15	+0.03
	I3	0.10	0.14	+0.04
	I4	0.02	0.03	+0.01

(*viz.* a "4"-chlorophenol) is shown in Table V. Similarly for the inclusion of an electron donor group such as methyl: considering the "3"-methyl substituted phenols we have the values given in Table VI.

We may thus conclude that since all results are reproducible to $\pm$ 0.01 R_F units, the above comparisons show that the position of the chloro group relative to the other substituents, is important. The fact that there is not as significant a difference for the methyl group is probably due to its relatively weaker electronic influence.

The importance of positional effects can be seen by comparing the values obtained for isomeric pairs: 2,4-dibromo-6-methyl- with 2,6-dibromo-4-methylphenol and 2,4-dibromo-6-*tert.*-butyl- with 2,6-dibromo-4-*tert.*-butylphenol. The bromine atom in the 6-position has a smaller effect than either the methyl or *tert.*-butyl groups. The slight differences in the values for the last 2 of these 4, is probably caused by the bulk of the 4-*tert.*-butyl group, as it is to be expected from the behaviour of these two groups when substituted in phenol[16].

CONCLUSION

The primary mechanism in the chromatographic separation of phenol on alumina surfaces has been shown to be the hydrogen bonding between the oxygen atom of the phenolic group and hydrogen atoms on the surface of the hydroxylated alumina. In halogenated phenols the alumina surface probably acts as a proton donor to the halogeno group, resulting in the formation of a hydrogen bond. Variations in the strengths and amount of hydrogen bonding in a series of compounds chromatographed under a particular solvent/stationary phase system, is shown in the consequent variation in the R_F values of the compounds. Thus the R_F values of analogous halogenophenols, increase with an increase in the size and a decrease in the electronegativities of the halogen atoms.

Where it is possible to have internal hydrogen bonding between the phenolic and halogeno groups, an "*ortho*" effect is seen. In polyhalogenated phenol, this effect, whilst probably present, is not particularly obvious.

In the chromatography of these phenols, it can be seen that not only the nature of the substituents is important but also the number and relative positions of the various substituents are very important. Since there is a ready delocalisation of electronic effects in a π-bonded system, it is not possible to introduce a group *into the nucleus* without having an effect on all other groups in the nucleus.

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SUMMARY

Sixty halogenated and halogeno-; alkyl-substituted phenols have been chromatographed on alumina surfaces (alumina-impregnated papers and alumina thin layers) in eight eluent systems. The R_F values of the phenols decrease with an increase in the number of halogen atoms in the molecule thus indicating that the alumina surface acts as a proton donor towards the halogen atom as well as towards the phenolic group. Some evidence of an *ortho* effect involving the halogen atoms in the 2-position is seen. Alkyl groups substituted into the 2-position have a marked effect on the R_F values but the effect of these groups in the 3- or 4-positions is smaller. The positions of the halogen atoms relative to the phenolic group and their positions relative to other substituents is of significance in governing the chromatographic behaviour of these phenols.

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