THE PAPER CHROMATOGRAPHY OF SOME ISOMERIC MONOSUBSTITUTED PHENOLS. II.

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INTRODUCTION

The paper chromatography of phenols has been the subject of a number of recent studies[1-4]. The first part of this paper reported the use of water, toluene saturated with water, and mineral spirits saturated with water as mobile solvent systems. The use of ceric ammonium nitrate as a spot-locating agent for phenols was also reported[4]. The effect of the orientation of substituent groups on the R_F' value in the various solvent systems was also studied. The types of phenols considered were limited to monosubstituted isomers. For purposes of general information, however, a few single phenols were considered.

The work presented in this paper is a continuation of the previous work. A number of additional isomeric phenols are considered in the same three solvent systems and ceric ammonium nitrate is used as the spot-locating agent whenever possible. The effect of orientation on the R_F' value is considered along with some generalizations correlating R_F' value and structure.

EXPERIMENTAL

Reagents

The mobile solvents used were water, toluene saturated by shaking with distilled water and mineral spirits (Kauri-butanol value 37–38, aniline point 56–59°) saturated with distilled water. The spot-locating reagents used were: (1) ceric ammonium nitrate reagent[4], (2) p-nitrobenzenediazonium fluoborate solution in acetone and 0.1 N alcoholic potasssium hydroxide[5], and (3) alkaline potassium permanganate prepared by mixing equal volumes of 1 % potassium permanganate and 2 % sodium carbonate[6].

Procedure

The toluene and mineral spirits were kept saturated with water by the presence of a lower water layer in the tanks. The tanks were lined with paper sheets extending into the water layer. All chromatograms were run at 25° with Whatman No. 1 paper using the ascending development method. The papers were allowed to equilibrate 20 min in the tank before immersion. The solvents were allowed to travel 10 cm requiring 30–45 min. In a few cases in which the phenols were relatively volatile no equilibration was used and solvent travel was limited to 5 cm.

The paper sheets were sprayed with the reagent as soon as they were removed from the tank and then washed thoroughly with water to remove excess reagent. In cases where the ceric ammonium nitrate reagent was ineffective, *p*-nitrobenzenediazonium fluoborate was used followed by 0.1 *N* alcoholic potassium hydroxide. The papers were not washed when using this method. In any cases where *p*-nitrobenzenediazonium fluoborate was ineffective, alkaline potassium permanganate was used. All papers were air dried. The R_F' values reported are the distance traveled by the spot front divided by the distance traveled by the solvent front[7].

RESULTS AND DISCUSSION

Examination of the data obtained confirms the earlier findings that water, mineral spirits and toluene are quite suitable as mobile solvents for mono-substituted phenols. In general, water and mineral spirits are more satisfactory than toluene since toluene tends to carry too many phenols along with the solvent front. However, all three solvents are of value in separations involving mixtures of phenols where two dimensional paper chromatography is required[8]. It is interesting to note that of the seventy-eight phenols examined in both parts of this paper only one (*p,p'*-diphenol) had an R_F' value of zero in all three solvents.

The use of ceric ammonium nitrate as a spot locating agent was continued in this study. Some limitations were found in its use especially with *ortho* substituted phenols. Many of the *ortho* substituted phenols gave colors so light that the spots could not be detected. Of the fifteen *ortho* substituted phenols only seven gave spots having enough color to be determined. The only group of isomeric phenols that were completely unresponsive to ceric ammonium nitrate were the methoxy phenols. When ceric ammonium nitrate gave colors too weak to determine, *p*-nitrobenzenediazonium fluoborate was used as the spot-locating agent. In a few cases, this reagent gave poor results and an alkaline solution of potassium permanganate was used.

Of the three solvents considered, toluene normally gives the highest R_F' values within an isomeric group of phenols. There are some exceptions to this depending on the type of substituent. The exceptions are *o*-fluorophenol, *p*-hydroxyacetophenone, all isomers of hydroxybenzaldehydes, hydroxybenzylalcohols and hydroxyacetanilides. All of these exceptions have greater R_F' values in water. A similar effect was noted in the first part of this paper with the aminophenols, the hydroxyphenols and the hydroxybenzoic acids. None of the phenols examined had greater R_F' values in mineral spirits than in toluene, although some gave R_F' values of 1.0 with both solvents.

Previously it was found that the phenylphenols, the iodophenols, the *tert.*-butylphenols and the naphthols have greater R_F' values in mineral spirits than in water. To this list can now be added *o*-hydroxyacetophenone, *o*-hydroxypropiophenone, *o*-hydroxy-*n*-butyrophenone, *o*-methoxyphenol, *o*-ethoxyphenol, *m-tert.*-butylphenol, *ortho*- and *para* benzylphenols, *ortho* and *para* *n*-propylphenols, *ortho* and *para* *sec.*-butylphenols, *ortho* and *para* cyclohexylphenols, and all isomeric ethylphenols. These phenols appear to be the least readily ionized, thus enhancing their organic structure and minimizing their ionic nature. This tends to affect the partition of these phenols in favor of the organic solvent. This is supported by the fact that these phenols without exception, have greater R_F' values in toluene than in water. The large number of *ortho* substituted phenols in this group containing

TABLE I

R_F' VALUES OF ISOMERIC MONOSUBSTITUTED PHENOLS

Phenol	R_F' value at 25° Water	Mineral spirits	Toluene	Spot color	Reagent
o-Hydroxyacetophenone[a]	0.82	1.00	1.00	Brown	Alkaline KMnO$_4$
m-Hydroxyacetophenone[a]	0.73	0.07[b]	0.73	Tan-yellow	Ceric ammonium nitrate
p-Hydroxyacetophenone[a]	0.73	0.00	0.39	Gray-green	Ceric ammonium nitrate
o-Hydroxypropiophenone	0.86	1.00	1.00	Brown	Alkaline KMnO$_4$
m-Hydroxypropiophenone	0.66	0.22[b]	1.00	Very light tan	Ceric ammonium nitrate
p-Hydroxypropiophenone	0.64[b]	0.00	0.65[b]	Very light gray	Ceric ammonium nitrate
o-Hydroxy-n-butyrophenone	0.00	1.00	1.00	Brown	Alkaline KMnO$_4$
p-Hydroxy-n-butyrophenone	0.66[b]	0.17	1.00	Tan-yellow	Ceric ammonium nitrate
o-Hydroxybenzaldehyde	0.87	0.12	0.76	Red to purple	p-Nitrobenzenediazonium fluoborate
m-Hydroxybenzaldehyde	0.74	0.07	0.61	Tan.	Ceric ammonium nitrate
p-Hydroxybenzaldehyde	0.73	0.00	0.39	Light gray-green	Ceric ammonium nitrate
o-Hydroxybenzyl alcohol	0.85	0.07	0.41	Dark gray-green	Ceric ammonium nitrate
m-Hydroxybenzyl alcohol	0.81	0.00	0.07[b]	Light tan	Ceric ammonium nitrate
p-Hydroxybenzyl alcohol	0.84	0.00	0.06[b]	Light tan	Ceric ammonium nitrate
o-Benzylphenol	0.64[b]	0.97	1.00	Light brown	Ceric ammonium nitrate
p-Benzylphenol	0.00	0.86	1.00	Tan	Ceric ammonium nitrate
o-Methoxyphenol	0.69	0.74	1.00	Tan to gray	p-Nitrobenzenediazonium fluoborate
m-Methoxyphenol	0.74	0.26	0.96	Maroon	p-Nitrobenzenediazonium fluoborate
p-Methoxyphenol	0.79	0.22	0.92	Purple	p-Nitrobenzenediazonium fluoborate
o-Ethoxyphenol	0.20	0.55	1.00	Tan-gray	p-Nitrobenzenediazonium fluoborate
m-Ethoxyphenol	0.73	0.45	1.00	Brown	Ceric ammonium nitrate
p-Ethoxyphenol	0.67[c]	0.34[c]	1.00	Tan	Ceric ammonium nitrate
o-Ethylphenol	0.76	0.81	1.00	Purple	p-Nitrobenzenediazonium fluoborate
m-Ethylphenol	0.67[b]	0.74	1.00	Light tan	Ceric ammonium nitrate
p-Ethylphenol	0.58[b]	0.74	1.00	Very light yellow	Ceric ammonium nitrate
o-n-Propylphenol	0.64	0.93	1.0	Tan	Ceric ammonium nitrate
p-n-Propylphenol	0.00	0.85	1.0	Bleaches spot white	Ceric ammonium nitrate
o-sec.-Butylphenol[a]	0.00	0.92	1.00	Light yellow	Ceric ammonium nitrate
p-sec.-Butylphenol[a]	0.00	0.92	1.00	Gray to tan	Ceric ammonium nitrate
m-tert.-Butylphenol	0.00	0.96	1.00	Maroon	Ceric ammonium nitrate
o-Cyclohexylphenol	0.48[b]	0.99	1.00	Yellow-green	p-Nitrobenzenediazonium fluoborate
p-Cyclohexylphenol	0.00	0.92[b]	1.00	Light gray	Ceric ammonium nitrate
o-Fluorophenol	0.89	0.00	0.87	Light yellow	Ceric ammonium nitrate
m-Fluorophenol[a]	0.81	0.43	1.00	Light brown	Ceric ammonium nitrate
p-Fluorophenol[a]	0.79	0.33	0.96	Very light tan	Ceric ammonium nitrate
o-Hydroxyacetanilide	0.80[c]	0.00	0.00	Purple	Ceric ammonium nitrate
m-Hydroxyacetanilide	0.77	0.00	0.00	Tan	Ceric ammonium nitrate
p-Hydroxyacetanilide	0.83	0.00	0.00	Pink to purple	Ceric ammonium nitrate
p,p'-Isopropylidine diphenol (Bisphenol-A)	0.61[b]	0.10	0.89	Light yellow	Ceric ammonium nitrate

either methylene or oxygen in the side chain indicates that these products are less ionic in nature than the corresponding *meta* and *para* isomers. This is probably caused by intramolecular hydrogen bonding with the resulting effect of reducing the overall ionic nature of the molecule. The effect of this hydrogen bonding would not only reduce the ionic nature but would also explain the fact that many of these phenols did not give any detectable spots with ceric ammonium nitrate. The phenones were apparently bonded so strongly that they did not even react with the *p*-nitro-benzenediazonium fluoborate.

Phenols such as the cresols, hydroxyphenols, hydroxybenzoic acids, aminophenols, and diphenols were previously found to have greater R_F' values in water than in mineral spirits. To this group can be added, *p*-hydroxy-*n*-butyrophenone, *p,p'*-isopropylidene diphenol (Bisphenol-A), *meta* and *para* hydroxyacetophenone, *meta* and *para* hydroxypropiophenone, *meta* and *para* methoxyphenol, *meta* and *para* ethoxyphenol, and all isomers of hydroxybenzaldehyde, hydroxybenzyl alcohol, fluorophenol and hydroxyacetanilide. These phenols can be subdivided into two groups relative to their R_F' values in toluene. Those that contain ionizable substituents have higher R_F' values with water than with toluene. This group includes substituents such as benzyl alcohol, aldehyde, carboxyl and amino. The second group contains less ionizable substituents and consequently the phenols in this group have greater R_F' values with toluene than with water. The substituents in this group include methyl, fluoro, *meta* and *para* methoxy and *meta* and *para* ethoxy.

The so called "*ortho* effect" appears consistently throughout the data observed. Very minor deviations in which an *ortho* isomer has a smaller R_F' value than the *meta* or *para* isomer may be due only to experimental error. However, a few significant exceptions to the "*ortho* effect" are resorcinol with toluene, *p*-hydroxy-*n*-butyrophenone with water, all isomeric methoxyphenols with water, all isomeric ethoxyphenols with water and all isomeric fluorophenols with toluene and mineral spirits. The R_F' values in the three solvents, the spot-locating reagents and the spot colors are all shown in Table I.

The effect of the orientation of the substituent groups on the R_F' value of the phenols with water as the mobile solvent is shown in Fig. 1. When water is used as the mobile solvent, the separation mechanism involved is adsorption. When toluene and mineral spirits are the mobile solvents, the mechanism is partition.

For phenols in which all three isomers were available, Fig. 1 shows that the substituents of the *meta* and *para* isomers are practically all in the same order as the R_F' values decrease. The exceptions are all isomers of fluoro- and ethylphenols. The order of decreasing R_F' values is altered considerably in the *ortho* substituted phenols where other factors such as intramolecular hydrogen bonding influence the R_F' value. These factors are minimized with the *meta* and *para* isomers resulting in more uniformity in the order.

Figs. 2 and 3 show the effect of orientation when the mobile solvents are mineral spirits and toluene. With both solvents the decreasing order of R_F' values is the same for both *meta* and *para* substitution. In addition, the decreasing order of R_F' values is very nearly the same in either toluene or mineral spirits, although the order in water is very different and tends to be in a reverse order. This shows the similarity of the two partition systems and their difference from an adsorption system. The same effect was observed in the first part of this paper.
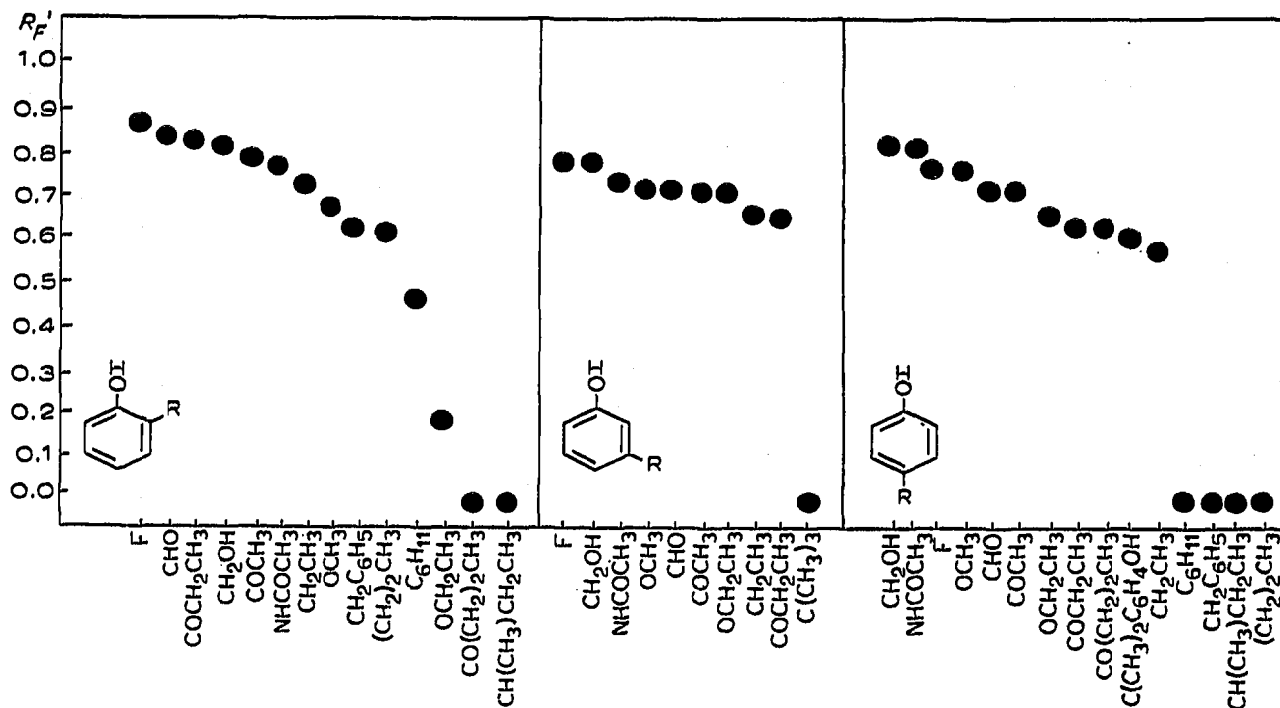
Fig. 1. Effect of the orientation of substituent groups on the R_F' value of phenols with water.
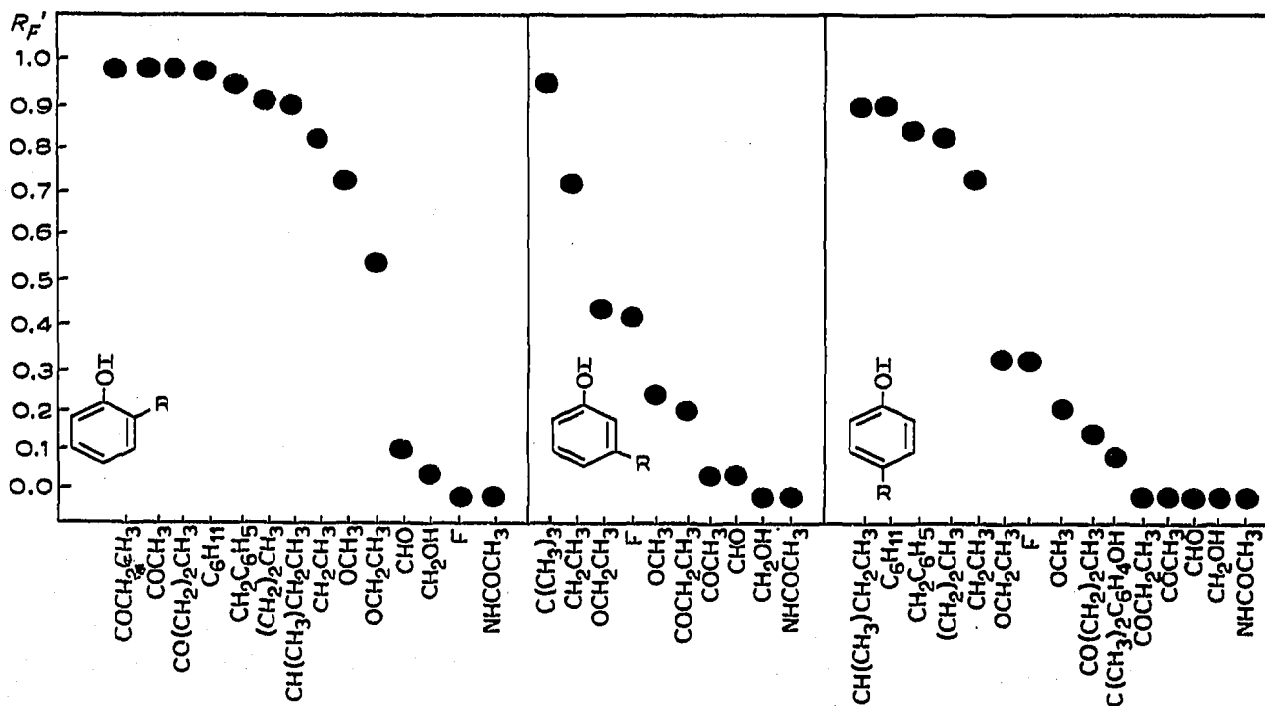

Fig. 2. Effect of the orientation of substituent groups on the R_F' value of phenols with mineral spirits.
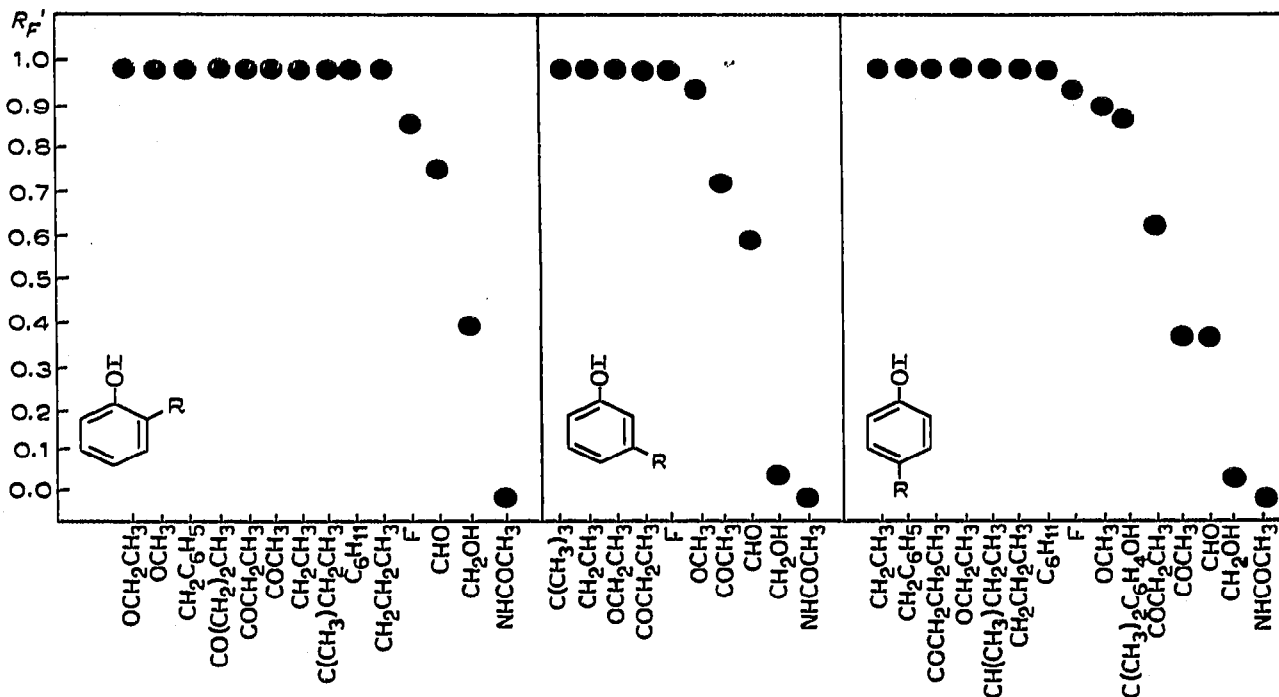
Fig. 3. Effect of the orientation of substituent groups on the R_F' value of phenols with toluene.

A comparison of the R_F' values of the halogenated phenols in all three solvents has been made. The results indicate that as the molecular weight of the side chain increases the R_F' values vary depending on the solvent. Fig. 4 shows that with water as the mobile solvent a slight decrease is noted in the R_F' values as the molecular weight increases. Fig. 5 shows that with mineral spirits a slight increase in R_F' values is noted for the *meta* and *para* isomers as the molecular weight increases. The *ortho* isomers do not follow this pattern, particularly in the case of *o*-fluorophenol. When toluene is used as the mobile solvent, the same type of curves are obtained as when mineral spirits is the solvent although the differences are less pronounced.
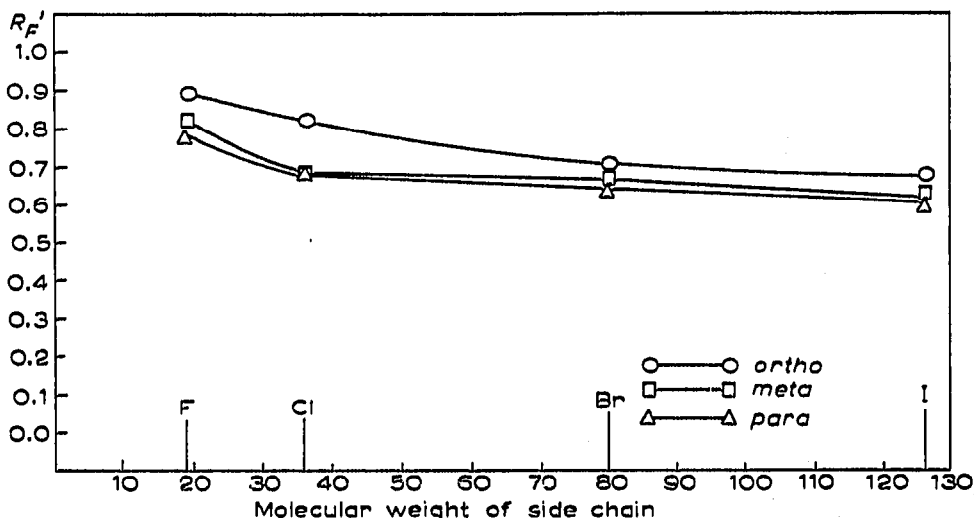

Fig. 4. R_F' value in water *vs.* mol.wt. of the halogen substituent.
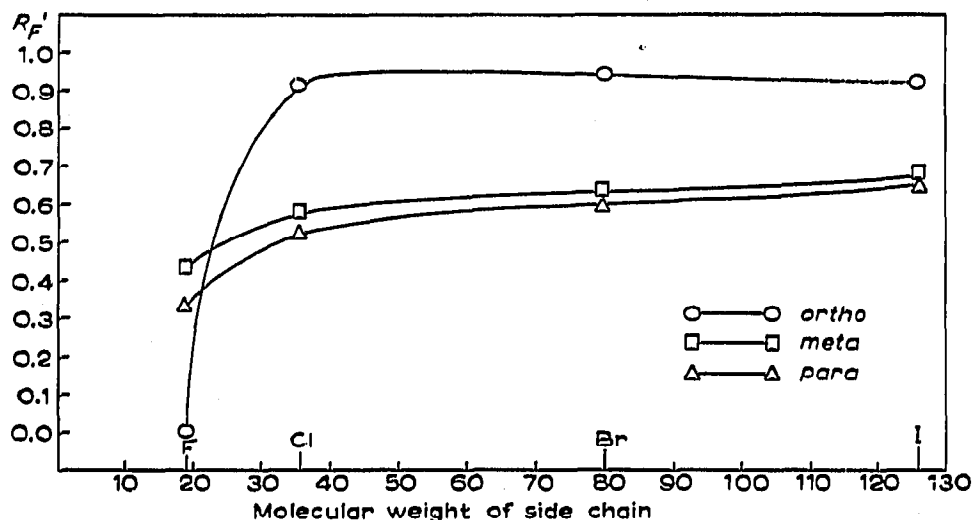
Fig. 5. R_F' value in mineral spirits *vs.* mol.wt. of the halogen substituent.

This demonstrates again the similarity of the two partition systems and their differ-ence to the adsorption system. The figure for the data with toluene is not included since all the R_F' values are above 0.95 with the exception of *o*-fluorophenol.

The R_F' values for the homologous series of substituted phenols from the cresols to the *n*-propyl phenols have been compared. Fig. 6 shows the variation in R_F' values of the *ortho* and *para* isomers as the molecular weight of the substituent in-creases when water is the mobile solvent. In this case, the R_F' values show a decrease as molecular weight increases. This should be expected since the compounds tend to become less ionic in nature as the molecular weight of the side chain increases. Fig. 7 shows the increase in R_F' values as the molecular weight increases when the mobile solvent is mineral spirits. The *meta* isomers have not been included in these figures since not all of them were available. However, the values for *meta*-cresol and *meta*-ethylphenol are intermediate between the two curves obtained and it should be
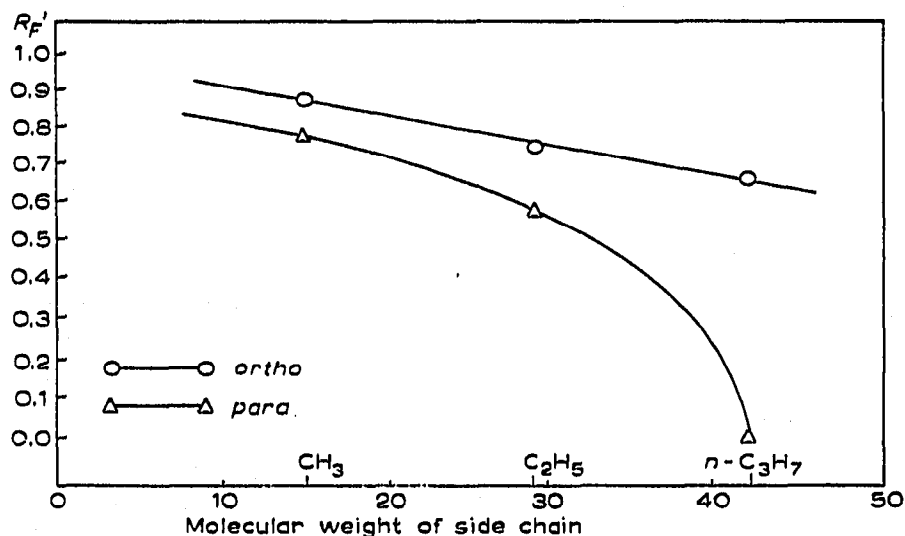

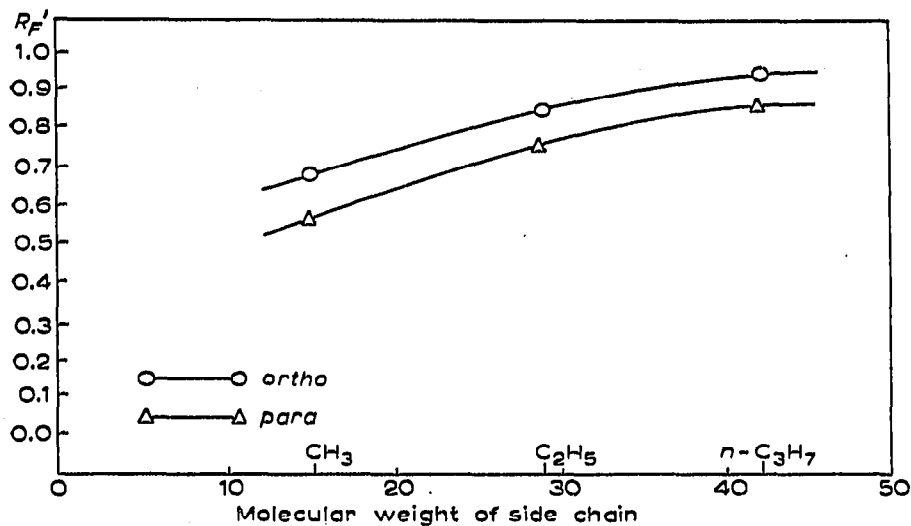Fig. 6. R_F' value in water *vs.* mol.wt. of non-branched hydrocarbon.

Fig. 7. R_F' value in mineral spirits *vs.* mol.wt. of non-branched hydrocarbon.

safe to assume that the values for *meta-n*-propylphenol would also be intermediate.

An attempt to correlate the R_F' values and the molecular weight of the substituents of the series from acetophenone to *n*-butyrophenone with the various solvents did not give conclusive results. Apparently, the nature of the substituent has a varying effect on the degree of change of the R_F' value in a given solvent.

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SUMMARY

The R_F' values of a number of isomeric monosubstituted phenols have been determined for three solvent systems. This is a continuation of our previous data. The results confirm the earlier work showing that most of the phenols have significant variations in R_F' value between these three solvents. Some limited correlations between R_F' values and the molecular weight of the side chain were found for members of homologous series. The use of ceric ammonium nitrate as a spot locating agent for phenols was found to have certain limitations, particularly for *ortho* substituted phenols. In general, however, this reagent is quite suitable for most phenols.

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