

CHROMATOGRAPHIC SEPARATION OF PHENOLS ON
ION-EXCHANGE PAPER

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INTRODUCTION

Impregnated papers have been reported to provide improved chromatographic separation of phenols. In addition to partitioning, steric, and other effects by which separations are accomplished on ordinary chromatographic paper, separations on impregnated paper are effected by differences in polarity of individual phenols with respect to the stationary phase, or because of the properties of some phenols to form chelates with the stationary phase that affect the partitioning.

Among the reagents that have been used for these chromatographic separations are sodium tetraborate¹⁻⁴, sodium molybdate⁵⁻⁷, sodium tungstate or vanadate⁷, polyamide⁸, formamide⁹ and dimethylformamide¹⁰.

The separation of some dihydric phenols cannot be conveniently accomplished by the use of some of these inorganic stationary phases, because of the streaking that occurs. A disadvantage of others is the time required to obtain a separation (15-45 h). The method of SUNDT¹⁰, which uses dimethylformamide-impregnated paper with a cyclohexane-ethyl acetate (5:1) solvent, was found to be convenient and useful. However, conditioning of sheets prior to development resulted in "blooming" of some phenols that have low vapor pressures. This prevented the clean separation of guaiacol and alkylguaiacols.

These separation of phenols by a column of cation-exchange resins has been reported¹¹. In the present work, paper loaded with ion-exchange resin was used to separate phenols that were studied in connection with those derived from pulping or lignin sources.

EXPERIMENTAL

Reeve Angel Grade SB-2 Amberlite ion-exchange resin-loaded paper was used for this work. The resin, Amberlite IRA-400, a strong base type in the Cl⁻ form, was used in this form. The use of two solvents (A and B) was studied. Solvent A, which consisted of cyclohexane-ethyl acetate-acetic acid (5:1:1, v/v), provided good separation of monohydric and dihydric phenols, but was less effective for phenolic aldehydes and for moving hydroxybenzoic acids. Solvent B, which consisted of butanol-water-acetic acid (6:2:1), gave better results for the latter two groups, but most simple phenols were not well separated.

* Maintained at Madison, Wisc., in cooperation with the University of Wisconsin.

All chromatographic runs were made at 25° with descending solvent flow in the machine direction of 22-in. strips of the resin-loaded paper. For the separation of monohydric and dihydric phenols with solvent A, the paper strips were preconditioned for several hours in a jar of saturated water vapor before applying the phenols. The moisture content of the paper was found to reduce the rate of solvent front movement and to avoid elongated spots that resulted from rapid solvent travel. No preconditioning was necessary for chromatographic separations that used solvent B. Chromatography jars were well saturated with vapors of the solvent to be used. With solvent A, solvent travel was 40 cm in 2¹/₂ h. With solvent B, the front moved 38 cm in 4 h.

Sheets were dried in a circulating air oven at 50° for 5 or 10 min. Spots were detected by a light spray of diazotized sulfanilic acid followed by 20% sodium carbonate¹².

RESULTS AND DISCUSSION

R_F values that were determined are given in Table I through IV. These values show slight variations in different runs, apparently depending upon humidity of the paper and flow rate of the solvent. A difference of R_F value of about 0.05 was necessary to obtain resolution of mixtures of compounds with solvent A. In general, *ortho*-isomers could be separated from either *meta* or *para* forms, such as *o*-, *m*- and *p*-cresols, but a mixture of *meta*- and *para*-isomers was not resolved. Excellent separation of a mixture of the four catechols and four guaiacols listed was possible with solvent A. Of the dimethylphenols, the 2,3-, 2,4- and 2,5-isomers could not be separated, and the 3,4-isomer was only partially separated from the 3,5-isomer with solvent A.

The chief advantage of solvent B, butanol-water-acetic acid (6:2:1), was the

TABLE I
MONOHYDRIC PHENOLS

Compound	R_F value	
	Solvent A	Solvent B
Phenol	0.28	0.73
<i>o</i> -Cresol	0.48	0.81
<i>m</i> -Cresol	0.40	0.81
<i>p</i> -Cresol	0.41	0.81
<i>o</i> -Ethylphenol	0.67	0.87
<i>m</i> -Ethylphenol	0.52	0.87
<i>p</i> -Ethylphenol	0.55	0.86
<i>p</i> -Propylphenol	0.69	0.92
<i>o</i> -Phenylphenol	0.54	0.75
<i>m</i> -Phenylphenol	0.35	0.73
<i>p</i> -Phenylphenol	0.32	0.70
<i>p</i> -Benzylphenol	0.51	0.83
2,3-Dimethylphenol	0.56	0.82
2,4-Dimethylphenol	0.58	0.82
2,5-Dimethylphenol	0.57	0.86
2,6-Dimethylphenol	0.72	0.89
3,4-Dimethylphenol	0.45	0.82
3,5-Dimethylphenol	0.48	0.82
Biphenol	0.02	0.24
2,2'-Dihydroxybiphenyl	0.14	0.53

TABLE II
DIHYDRIC AND TRIHYDRIC PHENOLS

Compound	R_F value	
	Solvent A	Solvent B
Catechol	0.08	0.51
4-Methylcatechol	0.12	0.57
4-Ethylcatechol	0.20	0.69
4-Propylcatechol	0.24	0.73
Guaiacol	0.59	0.79
Creosol	0.70	0.82
4-Ethylguaiacol	0.81	0.87
4- <i>n</i> -Propylguaiacol	0.88	0.93
Eugenol	0.08	0.93
Isoeugenol	0.19	0.85
Coniferyl alcohol	0.10	0.65
Resorcinol	0.02	0.31
Orcinol	0.02	0.39
Pyrogallol	0.00	0.18
Pyrogallol 1,3-dimethyl ether	0.10	0.76

greater mobility it afforded the highly polar hydroxybenzoic acids. As with solvent A, solvent B required an R_F difference of about 0.05 to permit separation of individual compounds. It was again impossible to resolve completely a mixture of 2,4-, 2,5- and 3,4-dihydroxy-isomers, but good separations of monohydroxy from dihydroxy types and their derivatives were possible.

SUNDT¹⁰ has pointed out the relationship of pK_a values of some phenols and their R_F values obtained with this chromatographic system. He also suggests that acidity is not the only factor affecting migration of compounds, based upon poor

TABLE III
HYDROXY AROMATIC ACIDS

Compound	R_F value	
	Solvent A	Solvent B
<i>p</i> -Hydroxybenzoic acid	0.04	0.50
<i>m</i> -Hydroxybenzoic acid	0.09	0.47
2,4-Dihydroxybenzoic acid (β -resorcylic)	0.02	0.28
2,5-Dihydroxybenzoic acid (gentisic)	0.02	0.24
3,4-Dihydroxybenzoic acid (protocatechuic)	0.00	0.24
3-Methoxy-4-hydroxybenzoic acid (vanillic)	0.08	0.58
3,5-Dimethoxy-4-hydroxybenzoic acid (syringic)	0.06	0.65
<i>o</i> -Hydroxycinnamic acid	0.11	0.44
<i>p</i> -Hydroxycinnamic acid	0.03	0.46
3,4-Dihydroxycinnamic acid (caffeic)	0.00	0.21
3-Methoxy-4-hydroxycinnamic acid (ferulic)	0.10	0.52
3,4-Dimethoxycinnamic acid	0.08	—
3,5-Dimethoxy-4-hydroxycinnamic acid (sinapic)	0.07	0.53
<i>p</i> -Hydroxyphenylacetic acid	0.02	0.46
3,4-Dihydroxyphenylacetic acid	0.00	0.20
3-(<i>p</i> -Hydroxyphenyl)-propionic acid	0.08	0.57
3-(3,4-Dihydroxyphenyl)-propionic acid	0.01	0.29

TABLE IV
AROMATIC ALDEHYDES AND KETONES

Compound	R_F value	
	Solvent A	Solvent B
<i>p</i> -Hydroxybenzaldehyde	0.07	0.71
2,4-Dihydroxybenzaldehyde	0.08	0.61
2,5-Dihydroxybenzaldehyde	0.07	0.57
3,4-Dihydroxybenzaldehyde	0.02	0.42
2-Hydroxy-3-methoxybenzaldehyde (<i>o</i> -vanillin)	0.64	0.84
Vanillin	0.20	0.75
Veratraldehyde	0.45	0.87
Syringaldehyde	0.10	0.74
Coniferyl aldehyde	0.08	0.71
Cinnamaldehyde	—	0.92
Hydroxymethylfurfural	0.08	0.68
5-Formylvanillin	0.16	0.40
5-Carboxylvanilin	0.03	0.26
2,4-Dihydroxyacetophenone	0.18	0.68
Acetovanillone	0.20	0.78
Acetosyringone	0.34	0.78
2,4-Dihydroxypropiofenone	0.30	0.73
3,4-Dihydroxypropiofenone	0.06	0.55
Maltol	0.42	0.81

correlation between pK_a and R_F values of 2,5- and 2,3-dimethylphenols. R_F values obtained for several phenols in the present work with solvent A are very similar to those of SUNDT. The same relationship of R_F and pK_a values exists, including the non-resolution of 2,5- and 2,3-dimethylphenols, despite their pronounced difference in pK_a values. A comparison of some of the present results with those of SUNDT is given in Table V.

TABLE V
RELATIONSHIP BETWEEN ACID STRENGTH (pK_a) AND R_F VALUES

Compound	pK_a	Reference	R_F^*	R_F^{**}
<i>m</i> -Cresol	10.08	13	0.41	0.40
<i>p</i> -Cresol	10.10	14	0.42	0.41
<i>o</i> -Cresol	10.19	14	0.49	0.48
3,5-Dimethylphenol	10.23	15	0.50	0.48
3,4-Dimethylphenol	10.43	15	0.45	0.45
2,5-Dimethylphenol	10.46	15	0.57	0.57
2,3-Dimethylphenol	10.57	15	0.56	0.56
2,4-Dimethylphenol	10.63	15	0.59	0.58
2,5-Dimethylphenol	10.66	15	0.65	0.72

* Dimethylformamide-impregnated paper, SUNDT¹⁰.

** This work: Reeve Angel SB-2 paper, solvent A: cyclohexane-ethyl acetate-acetic acid (5:1:1).

SUMMARY

Paper loaded with strong base ion-exchange resin in Cl^- form was used to accomplish the chromatographic separation of a number of monohydric and dihydric

phenols and their derivatives by the use of two solvent systems. Data obtained confirmed the results of others who found that there is good correlation between pK_a values of some phenols and their R_F values for separation on paper that contains a highly polar stationary phase. This is not true for other phenols, suggesting that several factors may affect these chromatographic separations.

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