

CHROM. 5711

AUTOMATIC LIQUID CHROMATOGRAPHY OF ORGANIC COMPOUNDS

III. THE RELATIONSHIP BETWEEN THE CHROMATOGRAPHIC BEHAVIOUR AND THE CHEMICAL STRUCTURE OF BENZENE DERIVATIVES*

MICHIKO YAMADA**, NOBORU NOMURA*** AND DEN-ITSU SHIHO**

Faculty of Pharmaceutical Sciences and Faculty of Education, University of Toyama, Gofuku, Toyama (Japan)

(First received July 28th, 1971; revised manuscript received September 15th, 1971)

SUMMARY

The relationship between the distribution coefficients (K_D) of benzene derivatives on the hydrogen and sodium forms of styrene-based strong cation-exchange resins, *e.g.* Bio-Rad AG 50W X8, and their chemical structures are discussed. A comparison of the K_D values of the hydrogen and sodium forms of the resin, the effect of the size of the halogen atom on the K_D values and of the additivities of the K_D values with respect to the number of carbon atoms in the alkyl groups in alkyl phenyl ethers and alkylphenols and to substituents in phenol derivatives are considered.

INTRODUCTION

To account for the relationship between the chemical structures of benzene derivatives and their chromatographic behaviour, the roles of many factors such as boiling point, molecular weight, carbon number, Hammett's σ value, polarity of substituent, polarizability, hydrogen bonding, steric hindrance and Van der Waals' force have been discussed in the case of gas¹⁻³, paper⁴⁻⁸, and thin-layer⁹⁻¹² chromatography. Furthermore, additivity of the R_M value⁸⁻¹², K_D value^{13,14}, retention index¹⁵, and group adsorption energy and area of adsorption group¹⁶ have been reported.

In liquid chromatography using styrene-based resin, ion-exchange, ion-exclusion, salting-out, distribution and adsorption have all been reported as the separation mechanisms. Also data on the affinity (or selective adsorption) of phenols, aniline and benzoic acids for strong cation-¹⁷⁻¹⁹, anion-exchange²⁰⁻²² and macro reticula strong anion-exchange resins²³ have been reported. But theoretical studies on the relation between column chromatographic behaviour on ion-exchange resins and

* Paper presented at the 32nd Meeting of Hokuriku Branch of the Pharmaceutical Society of Japan, Kanazawa, Japan, June 26th, 1971.

** Faculty of Pharmaceutical Sciences.

*** Faculty of Education.

chemical structure are few^{23,24}, because the formulation of the column conditions for the theoretical treatment is difficult.

It has been reported in a previous paper²⁵ that molecular adsorption plays a major role in the separation of benzene derivatives on ion-exchange resins under close column conditions. In this paper, the relationship between the chemical structure of the benzene derivatives and their molecular adsorption on the hydrogen and sodium forms of a styrene-based strong cation-exchange resin is discussed.

EXPERIMENTAL

Sample

The samples used as solutes were treated as described previously²⁵. In the case of samples having a low solubility in water 100 μ l of the aqueous solution were injected and complete solution was obtained by adding a little acetone. It was confirmed that their chromatographic behaviour was not influenced by addition of a little acetone.

Equipment

The UV detector used was the same as in a previous paper²⁵. But an automatic liquid chromatograph employing thermal reaction energy detection²⁰ was used for samples having small absorption coefficients. This equipment was placed in a room having a constant temperature of $25 \pm 1^\circ$.

Stationary phase

The hydrogen and sodium forms of Bio-Rad AG 50W X8 (mean particle diameter 30 μ m) treated as described previously²⁵ were used. The column had 0.8 cm I.D. and was 6.3 or 18.5 and 3.3 cm long in the case of the UV detection and thermal detection methods, respectively.

Measuring conditions

Deionized and redistilled water was used as eluent and run at a rate of 0.36 ml/min. The column temperature was controlled at 60° in the UV detection method, and at 50° , the highest temperature to which it was possible to set it, in the thermal detection method. The detection column was used only in thermal detection. The sensitivity in the thermal detection method was $\pm 1/1000^\circ$ or $\pm 3/10\ 000^\circ$ full scale. The interference filters used in the UV detection method were selected as described in a previous paper²⁵.

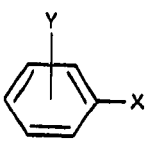
RESULTS AND DISCUSSION

The distribution coefficients (K_D values) of thirty-eight benzene derivatives on the hydrogen and sodium forms of Bio-Rad AG 50W X8 have been previously reported²⁵. In this report, the K_D values of some compounds which have not been reported before are given (Table I). The relative standard deviations of the retention volumes of most of the compounds were less than 1% ($n > 5$).

The dissociation of benzoic acids and nitrophenols is low due to the low pH inside the resin in the hydrogen form, and thus, molecular adsorption rather than

TABLE I

 K_D VALUES OF BENZENE DERIVATIVES ON THE H^+ AND Na^+ FORMS OF BIO-RAD AG 50W X8

Compound		Sample amount (μ mole)	K_D value H^+ form (ml/g)	Sample amount (μ mole)	K_D value Na^+ form (ml/g)
					
X	Y				
H	H^{**}	2.42	6.95 [‡]	3.20	5.57 [‡]
	CH_3^{**}		13.8 [‡]		12.7 [‡]
	OCH_3^{*a}	1.79	10.7	5.15	9.01
	$OC_2H_5^{*a}$	1.27	14.2	1.18	13.7
	$O-n-C_3H_7^{*a}$	2.61	24.0		22.6
	$O-i-C_3H_7^{*a}$	2.61	16.5	2.61	14.3
	F^{**}	2.87	7.38 [‡]	2.90	6.92 [‡]
	Cl^{**}		20.6 [‡]		21.1 [‡]
	Br^{**}		28.0 [‡]		28.7 [‡]
	I^{**}	2.65	46.5 [‡]	2.65	49.1 [‡]
HO	F^*	2 ^a 1.0	4.37	1.0	5.82
		3 ^a 1.0	4.86	1.0	7.68
		4 ^b 1.0	4.69	1.0	6.80
	I^*	2 ^b 1.0	18.3	1.0	31.3
		3 ^b 1.0	23.5	1.0	48.3
		4 ^b 1.0	24.0	1.0	51.6
	$C_2H_5^*$	2 ^a 1.53	8.73	1.56	11.4
		3 ^a 1.43	9.50	1.62	13.2
		4 ^a 1.56	10.4	1.64	15.0
	$n-C_3H_7^*$	2 ^a 1.73	12.6		
	$i-C_3H_7^*$	2 ^a		1.73	14.8
		3 ^a		1.75	17.1
		4 ^a		1.50	19.7
	$t-C_4H_9^*$	2 ^a	16.6		21.5
		3 ^a	14.4		18.6
		4 ^a	16.8		22.7

* UV detection system: Column 0.8×18.5 or 6.3 cm. Column temp., 60° . Flow rate, 0.36 ml/min. Interference filter: (a) 273 nm, (b) 280 nm.

** Thermal detection system: Column 0.8×8.3 cm. Column temp., 50° . Flow rate, 0.36 ml/min. Sensitivity, $\pm 1/1000^\circ$ or $\pm 3/10000^\circ$ full scale.

‡ Converted to the K_D values under the conditions of the UV detection system.

ion exclusion should be considered as the mechanism. They were however partially ion-exchanged on the sodium form*.

Monosubstituted benzene derivatives

The relationship between the logarithmic K_D values on the hydrogen and sodium forms of Bio-Rad AG 50W X8 ($\log K_{DH}$ and $\log K_{DNa}$) is shown in Fig. 1. The plots lie approximately on a straight line with a slope of 45° . As was done in Table I of this paper and Tables II and III of the previous paper²⁵, the ratio of the K_{DH} and

* Confirmed by UV spectroscopy as in a previous paper.

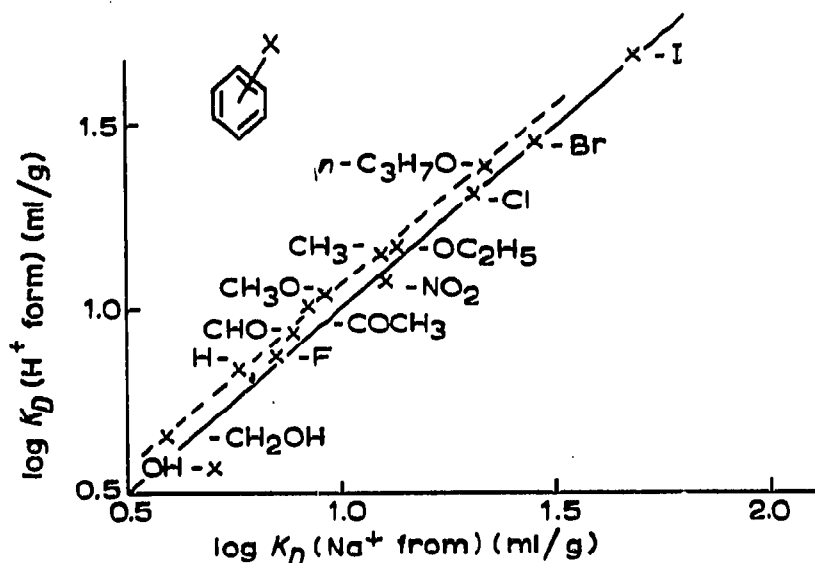


Fig. 1. Relation between $\log K_D$ values of monosubstituted benzene derivatives on the Na^+ and H^+ forms of Bio-Rad AG 50W X8. Column temp.: 60° . Flow rate: 0.36 ml/min. Eluent: water.

$K_{D\text{Na}}$ values of each compound was classified according to the following criteria: (1) $K_{D\text{H}} < K_{D\text{Na}}$, (2) $K_{D\text{H}} = K_{D\text{Na}}$, and (3) $K_{D\text{H}} > K_{D\text{Na}}$. The compounds in the first class contain a polar group (e.g. hydroxyl, nitro); the second class have very large K values (e.g. chloro-, bromo- and iodobenzene); and the third class contain a non-polar group (e.g. aldehyde, acetyl, methyl, alkoxy, hydroxymethyl, hydrogen). Non-polar compounds are hardly influenced by the form of the resin (H^+ or Na^+) and must therefore be adsorbed on the resin skeleton rather than on the ion-exchange group. This is due to the fact that the ratio of the weight that the styrene skeleton occupies in a unit weight of the hydrogen and sodium form of the resin is 1 to 0.9. Actually, the $K_{D\text{Na}}/K_{D\text{H}}$ ratio of non-polar compounds is nearly equal to 0.9. The line joining the

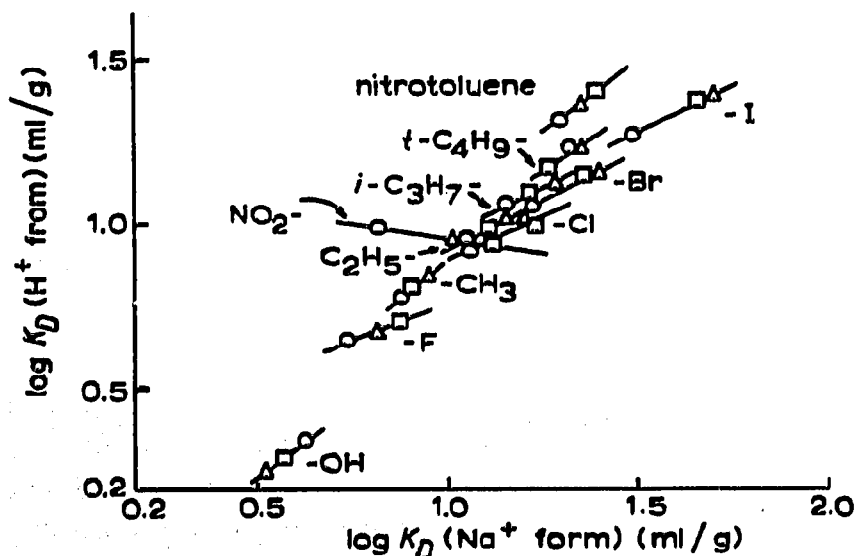


Fig. 2. Relationship between $\log K_D$ values of monosubstituted phenols on the Na^+ and H^+ forms of Bio-Rad AG 50W X8. Column temp.: 60° . Flow rate: 0.36 ml/min. Eluent: water. \circ , ortho; \square , meta; \triangle , para.

plots is represented by the dotted line in Fig. 1. The order of the K_D values in non-polar compounds was hydroxymethyl < aldehyde < acetyl < methoxy < methyl, and this order agreed with the order of the R_F values of *m*-substituted phenols containing these groups found by GUMPRECHT⁴ and GUMPRECHT AND SCHWARTZENBURG⁵ in partition paper chromatography using toluene saturated with water as a solvent. This fact would clearly indicate the contribution of adsorption on the resin skeleton.

The K_{DH} and K_{DNa} values of halogenobenzenes increased in the order: fluoro, chloro, bromo and iodo; and this order follows the order of the size of Van der Waals' ionic radius and the decrement of solubility in water.

The relationship between the carbon number of the alkyl group of alkyl phenyl ethers and $\log K_{DH}$ and $\log K_{DNa}$ indicated additivity, and the increment of a methylene unit was found to be 0.18 to 0.20 $\log K_D$ units. The increments in $\log K_{DH}$ and $\log K_{DNa}$ obtained for these compounds were nearly as equal as would be expected from the line shown in Fig. 1. The K_{DH} and K_{DNa} values of isopropyl phenyl ether were smaller than of the *n*-propyl compound.

Monosubstituted phenols and nitrotoluenes

The plots of $\log K_{DH}$ versus $\log K_{DNa}$ of the *ortho*, *meta* and *para* isomers of the phenols gave straight lines, the slopes of which differ from each other according to substituent group (Fig. 2). The order of K_D values was *ortho* < *meta* < *para* in alkylphenols and halogenophenols except for fluorophenols; *ortho* < *para* < *meta* in fluorophenols; *para* < *meta* < *ortho* in hydroxyphenols; *meta* < *para* < *ortho* in nitrophenols; and *ortho* < *para* < *meta* in nitrotoluenes. *o*-Hydroxyphenol and *o*-nitrophenol tend to form intramolecular hydrogen bonds, and thus the former compound on the hydrogen and sodium forms of the resin, and the latter on hydrogen form, are adsorbed more strongly than the other isomers.

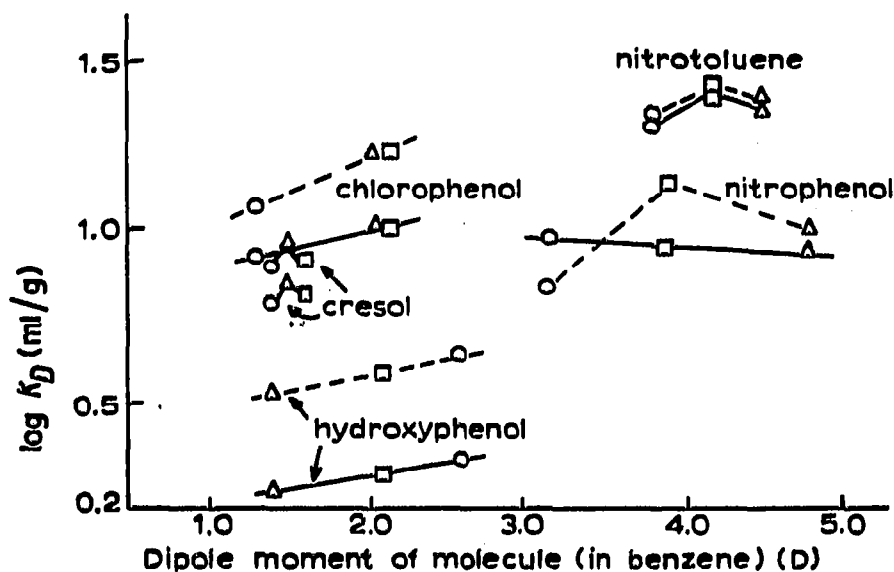


Fig. 3. Relationship between dipole moments of molecules¹⁹ and $\log K_D$ values on the H^+ and Na^+ forms of Bio-Rad AG 50W X8. —, H^+ form; ---, Na^+ form. Column temp.: 60°. Flow rate: 0.36 ml/min. Eluent: water. O, *ortho*; □, *meta*; △, *para*.

The reason why the hydroxyphenols were less adsorbed than phenol might depend on the increased solubility owing to two hydroxyl groups.

With regard to the adsorption mechanisms of phenols, the following aspects have been discussed: (1) formation of a hydrogen bond by the phenolic hydroxyl group on silica²⁷, alumina²⁸, Sephadex²⁹, and polyamide¹², and (2) elution of the phenols (not always in the order according to the pK_a values) and also adsorption by non-ionic affinity to the resin^{17,18}.

In our studies, the correlations of $\log K_D$ with pK_a values³⁰ and new σ values found by McDANIEL AND BROWN³¹ were not confirmed. Consequently, adsorption on the ion-exchange resin as a result of hydrogen bonding with the hydroxyl group is not considered.

On the other hand, while the dipole moment in aqueous solution is not very important, a correlation between the dipole moments³² of the phenols in benzene and their $\log K_{DH}$ and $\log K_{DNa}$ values was obtained for each of the isomers: *ortho*, *meta* and *para* (Fig. 3). The K_{DH} and K_{DNa} values of chlorophenols and hydroxyphenols increased with increasing molecular dipole moment, but the K_{DH} values of the nitrophenols decreased, and the abnormality of their K_{DNa} values was attributed to exchange with the sodium ion.

Considering only the molecular dipole moment instead of the kind of substituent, there was no correlation with the K_D value of the phenols. It can however be presumed that the slope of the line joining plots of *ortho*, *meta* and *para* is related to the kind of substituent.

The relationships between the number of carbons in the alkyl group in alkylphenols and $\log K_{DH}$ and $\log K_{DNa}$ are depicted in Fig. 4. The straight-line relationship probably exists for carbon numbers 1 to 3 in the case of straight-chain groups, and additivity could be expected as in the case of the alkyl phenyl ethers. In the case

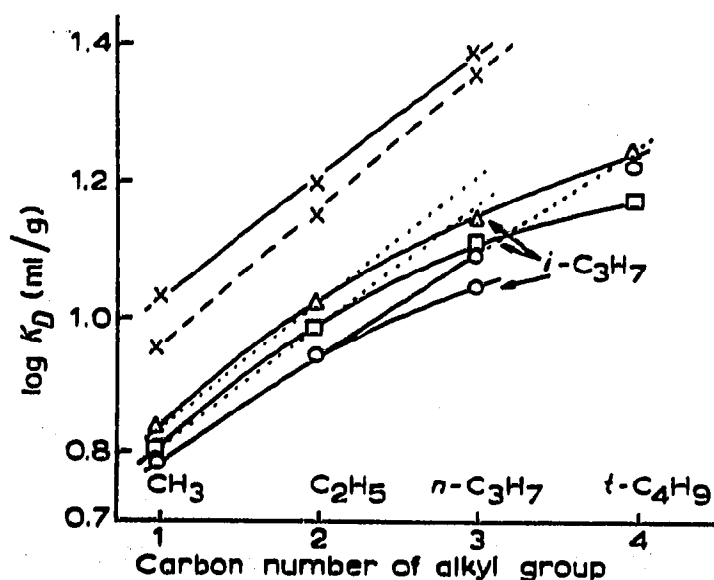


Fig. 4. Relationship between $\log K_D$ values on the H^+ and Na^+ forms of Bio-Rad AG 50W X8 and carbon number of the alkyl groups in alkyl phenyl ethers and alkyl phenols. —, H^+ form; ---, Na^+ form. Column temp.: 60° . Flow rate: 0.36 ml/min. Eluent: water. ○, *ortho*; □, *meta*; △, *para*; ×, alkyl phenyl ether.

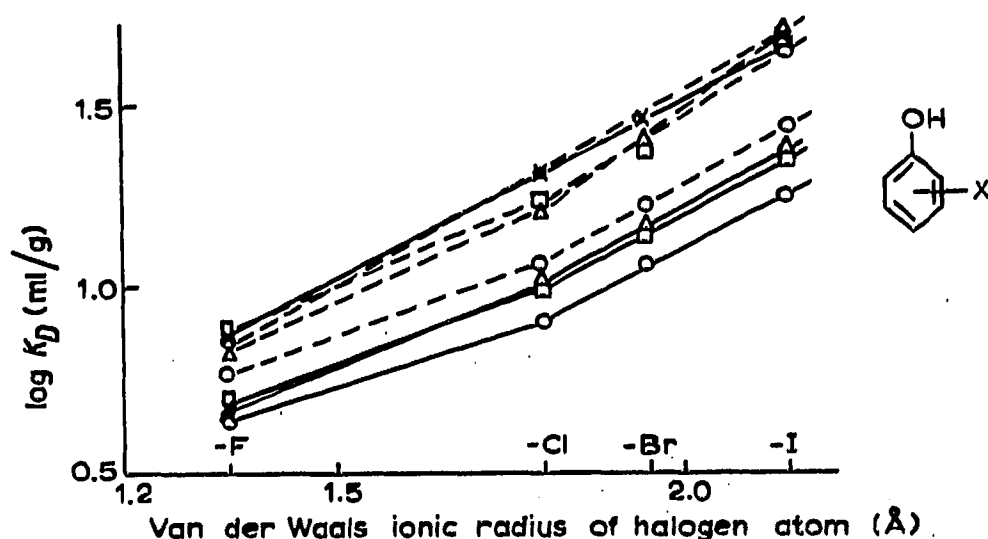


Fig. 5. Relationship between $\log K_D$ values on the H^+ and Na^+ forms of Bio-Rad AG 50W X8 and Van der Waals' ionic radius of halogen atoms³⁴. —, H^+ form; ---, Na^+ form. Column temp.: 60°. Flow rate: 0.36 ml/min. Eluent: water. O, *ortho*; □, *meta*; △, *para*; ×, halogenobenzene.

of branched-chain groups, the plots were out of line, and the K_D values were smaller than those which would be expected for straight-chain alkyl groups.

Steric hindrance, the *ortho* effect of the alkyl group on the phenolic hydroxyl group in adsorption chromatography has been already pointed out^{27,33}. In our study, *ortho*-alkyl substituted compounds, except for *tert.*-butyl, are the ones which are adsorbed most weakly among the isomers, and such an effect is possible, but the stronger adsorption of the larger alkyl-substituted compounds opposes that view. The larger K_D value of *ortho tert.*-butylphenol clearly represents a different *ortho* effect, probably a deforming effect.

The K_D values of halogenophenols increase in the order: fluoro, chloro, bromo and iodo and follow the order of the size of the Van der Waals' ionic radii³⁴ of the

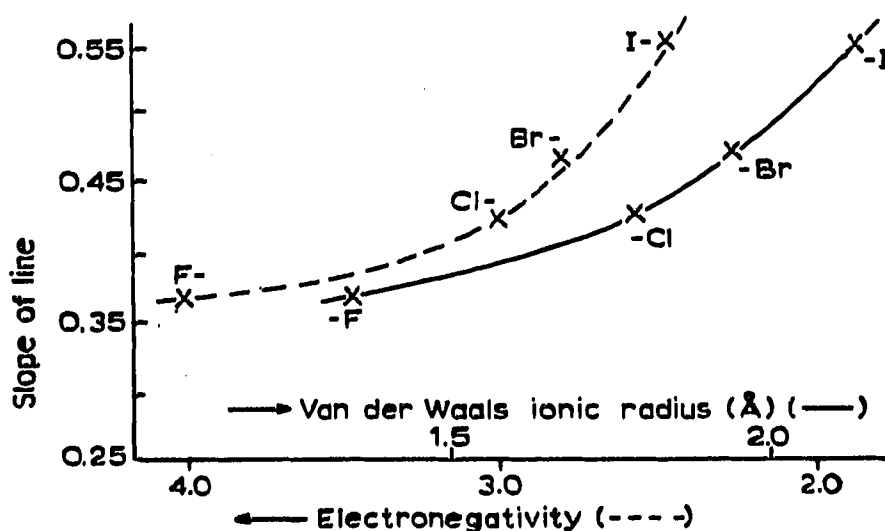


Fig. 6. Relationships between the slopes of straight lines joining plots of $\log K_D$ values of *ortho*, *meta* and *para* halogenophenols on the H^+ form of Bio-Rad AG 50W X8 vs. $\log K_D$ values on the Na^+ form (Fig. 2) and Van der Waals' ionic radius and electronegativity of halogen atoms³⁴.

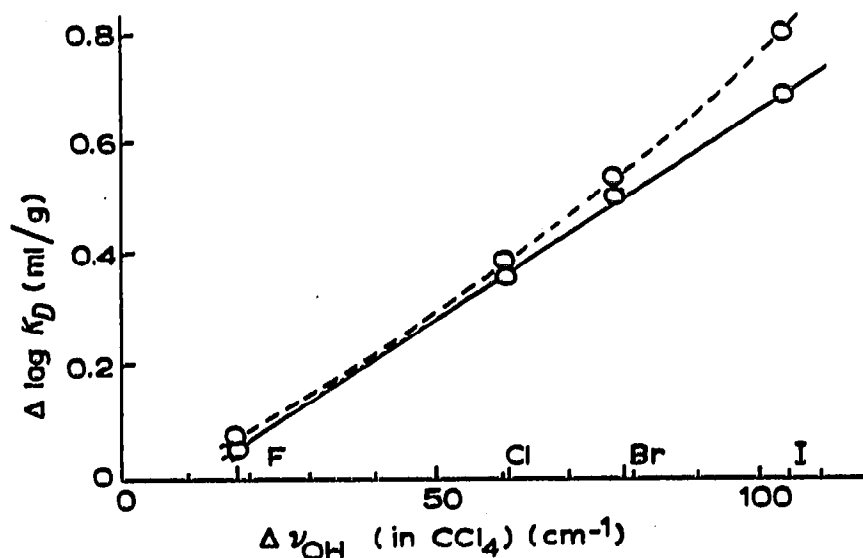


Fig. 7. Relationship between $\Delta \log K_D$ values on the H^+ and Na^+ forms of Bio-Rad AG 50W X8 and $\Delta \nu_{OH}$ values of IR spectra in carbon tetrachloride by BAKER AND SHULGIN³⁶ for *ortho* halogenophenols. —, H^+ form; ---, Na^+ form. $\Delta \nu_{OH} = \nu_{OH} - \nu_{OH}(\text{phenol})$; $\Delta \log K_D = \log K_D / K_D(\text{phenol})$.

halogen atoms, as in the case of the halogenobenzenes (Fig. 5). This fact agrees with MARCINKIEWICZ AND GREEN'S⁸ and BARK AND GRAHAM'S¹¹ results that the chromatographic behaviour of halogenophenols is influenced by the size of the halogen atom. Furthermore, the slopes of the straight lines joining the plots of $\log K_{DH}$ of *ortho*, *meta* and *para* isomers versus $\log K_{DNa}$ are related to the Van der Waals' ionic radii and the electronegativity³⁴ of the halogen atoms (Fig. 6). The intramolecular hydrogen bonding of *ortho* halogenophenols in non-polar solvents, an *ortho* effect, has been discussed in connection with the dipole moment³⁵, and IR³⁶ and NMR spectrometry³⁷. The K_D values of *ortho*-substituted compounds were in general smaller than those of the *meta* and *para* isomers and therefore an *ortho* effect is to be expected. Plots of $\Delta \log K_{DH}$ and $\Delta \log K_{DNa}$ of their compounds versus $\Delta \nu_{OH}$ in carbon tetrachloride in IR spectroscopy by BAKER AND SHULGIN³⁶ give a straight line and a slight curve,

TABLE II

THE INCREMENTS OF $\log K_D$ VALUES OF INDIVIDUAL SUBSTITUENTS IN MONOSUBSTITUTED BENZENE DERIVATIVES ON THE H^+ AND Na^+ FORMS OF BIO-RAD AG 50W X8

Column temp.: 60°. Flow rate: 0.36 ml/min. Eluent: water.

Substituent	$\Delta \log K_D^a$	
	H^+ form	Na^+ form
OH	-0.266	-0.058
CH ₃	0.298	0.358
NO ₂	0.230	0.358
F	0.026	0.094
Cl	0.472	0.576
Br	0.605	0.712
I	0.821	0.945

^a $\Delta \log K_D = \log K_D(\text{substituted benzene}) - \log K_D(\text{benzene})$.

TABLE III

COMPARISON OF THE EXPERIMENTAL $\log K_D$ VALUES WITH THE CALCULATED $\log K_D$ VALUES FOR PHENOLS AND NITROTOLUENESColumn: BIO-RAD AG 50W X8, H⁺ and Na⁺ forms. Column temp.: 60°. Flow rate: 0.36 ml/min. Eluent: water.

Substituent of phenols	Experimental $\log K_D$			Calculated $\log K_D^a$
	Ortho	Meta	Para	
<i>A (H⁺ form)</i>				
OH	0.340	0.290	0.253	0.310
CH ₃	0.786	0.802	0.835	0.874
NO ₂	0.982	0.938	0.940	0.806
F	0.641	0.687	0.671	0.602
Cl	0.915	1.004	1.013	1.048
Br	1.072	1.140	1.158	1.181
I	1.263	1.371	1.380	1.397
Nitrotoluene	1.316	1.396	1.364	1.370
<i>B (Na⁺ form)</i>				
OH	0.645	0.578	0.532	0.630
CH ₃	0.905	0.912	0.965	1.046
NO ₂	0.829	1.143	1.045	1.046
F	0.765	0.885	0.833	0.782
Cl	1.068	1.236	1.225	1.264
Br	1.233	1.380	1.407	1.400
I	1.495	1.685	1.713	1.633
Nitrotoluene	1.318	1.415	1.371	1.462

^a Calculated value: $\log K_D$ (substituted phenol) = $\log K_D$ (phenol) + $\Delta \log K_D$ (substituent).

respectively (Fig. 7). In this case, the hydrogen bonding weakens their adsorption on the resin, in contrast to the case of the *ortho* hydroxy- and nitrophenols.

The additivity of K_D values is very important and given the requisite indices can be used to explain the adsorption mechanism to estimate the strength of the adsorption applied to separations.

Now, the additivity of K_D values was examined in the case of methyl-, hydroxy-, nitro-, fluoro-, chloro-, bromo- and iodophenols and nitrotoluenes. An increment for each substituent is calculated as follows and the results are given in Tables II and III.

$$\Delta \log K_{D(\text{substituent})} = \log K_{D(\text{substituted benzene})} - \log K_{D(\text{benzene})}$$

$$\log K_{D(\text{substituted phenol})} = \log K_{D(\text{phenol})} + \Delta \log K_{D(\text{substituent})}$$

Considerable agreement is found between the experimental and calculated values for both *meta*- and *para*-substituted compounds, with a few exceptions¹ (hydroxy- and fluorophenols). In *ortho*-substituted compounds, the experimental values failed to agree with the calculated because of *ortho* effects.

CONCLUSION

The following facts were obtained by adsorption chromatography of benzene derivatives on the hydrogen and sodium forms of a styrene-based cation-exchange resin using water as eluent: (1) Non-polar monosubstituted benzene derivatives were scarcely affected by the ionic form of the resins and were adsorbed on the resin

skeleton. (2) The differences in the adsorption on the resin of the *ortho*, *meta* and *para* isomers of monosubstituted phenols are related to their molecular dipole moments in benzene. (3) In alkyl phenyl ethers, additivity of $\log K_D$ according to the carbon number of the alkyl group was found; this also appeared to hold for the alkylphenols. (4) The adsorption of halogenophenols was related to the Van der Waals' ionic radius of the halogen atom.

ACKNOWLEDGEMENTS

The authors are deeply grateful to Dr. TOYOHICO NAONO (Jeol Co., Ltd.) for useful discussions, and to Mr. SHIGEYOSHI-HIRAKI for his experimental assistance.

REFERENCES

- 1 T.-C. L. CHANG AND C. KARR, JR., *Anal. Chim. Acta*, 21 (1959) 474.
- 2 W. SANDERMANN AND G. WEISSMANN, *Z. Anal. Chem.*, 189 (1962) 137.
- 3 A. ONO, *Nippon Kagaku Zasshi*, 91 (1970) 72, 92 (1971) 242, 429, 433.
- 4 D. L. GUMPRECHT, *J. Chromatogr.*, 18 (1965) 336.
- 5 D. L. GUMPRECHT AND F. SCHWARTZENBURG, JR., *J. Chromatogr.*, 23 (1966) 134.
- 6 S. MARCINKIEWICZ, J. GREEN AND D. McHALE, *J. Chromatogr.*, 10 (1963) 42, 158.
- 7 S. MARCINKIEWICZ AND J. GREEN, *J. Chromatogr.*, 10 (1963) 184, 354, 366.
- 8 S. MARCINKIEWICZ AND J. GREEN, *J. Chromatogr.*, 10 (1963) 372.
- 9 L. R. SNYDER, in J. C. GIDDINGS AND R. A. KELLER (Editors), *Advances in Chromatography*, Vol. 4, M. Dekker, New York, 1967, p. 35.
- 10 L. S. BARK AND R. J. T. GRAHAM, *J. Chromatogr.*, 23 (1966) 120, 417.
- 11 L. S. BARK AND R. J. T. GRAHAM, *J. Chromatogr.*, 25 (1966) 347, 357.
- 12 L. S. BARK AND R. J. T. GRAHAM, *J. Chromatogr.*, 27 (1967) 109, 116, 131.
- 13 C. A. STREULI, *J. Chromatogr.*, 47 (1970) 355.
- 14 N. KAMEYAMA, Y. MIYAZAKI AND T. SAKUMA, *Ann. Meet. Chem. Soc. Jap.*, 23rd, Tokyo, Japan, April 1970.
- 15 T. UNO AND H. OKUDA, *Yakugaku Zasshi*, 90 (1970) 335.
- 16 L. R. SNYDER, in E. HEFTMANN (Editor), *Chromatography*, 2nd Ed., Reinhold, New York, 1967, p. 65.
- 17 T. SEKI, *Nippon Kagaku Zasshi*, 75 (1954) 1297.
- 18 T. SEKI, *J. Chromatogr.*, 4 (1960) 6.
- 19 J. SHERMA AND L. V. S. HOOD, *J. Chromatogr.*, 17 (1965) 307.
- 20 R. E. ANDERSON AND R. D. HANSEN, *Ind. Eng. Chem.*, 47 (1955) 71.
- 21 J. SHERMA AND W. RIEMAN, *Anal. Chem.*, 18 (1958) 214.
- 22 A. EVANS AND W. A. MUNDAY, *J. Appl. Chem.*, 9 (1959) 145.
- 23 J. S. FRITZ AND A. TATEDA, *Anal. Chem.*, 40 (1968) 2115.
- 24 W. FUNASAKA, T. ANDO, K. FUJIMURA AND T. HANAI, *Ann. Meet. Chem. Soc. Jap.*, 23rd, Tokyo, Japan, April, 1970.
- 25 N. NOMURA, S. HIRAKI, M. YAMADA AND D. SHIHO, *J. Chromatogr.*, 59 (1971) 373.
- 26 N. NOMURA, D. SHIHO, K. OHSUGA AND M. YAMADA, *J. Chromatogr.*, 42 (1969) 226.
- 27 J. K. CARLTON AND W. C. BRADBURG, *J. Amer. Chem. Soc.*, 78 (1956) 1069.
- 28 L. S. SNYDER, *J. Chromatogr.*, 16 (1964) 55, 20 (1965) 463.
- 29 A. J. W. BROOK AND K. C. MUNDAY, *J. Chromatogr.*, 47 (1970) 1.
- 30 H. C. BROWN, D. H. McDANIEL AND O. HAFLIGER, in E. A. BRAUDE AND F. C. NACHOD (Editors), *Determination of Organic Structures by Physical Method*, Vol. 1, Academic Press, New York, 1955, p. 589.
- 31 D. H. McDANIEL AND H. C. BROWN, *J. Org. Chem.*, 23 (1958) 420.
- 32 Y. MORINO, in M. KOTAKE (Editor), *Series of Comprehensive Organic Chemistry, Constants of Organic Compounds*, Asakura, Tokyo, 1963, p. 500.
- 33 B. SMITH, *Acta Chem. Scand.*, 16 (1962) 843.
- 34 L. PAULING, *The Nature of Chemical Bond*, 3rd Ed., Cornell University Press, Ithaca, 1960, Chap. VII.
- 35 E. V. GOODE AND D. A. IBBITSON, *J. Chem. Soc.*, (1960) 4265.
- 36 A. W. BAKER AND A. T. SHULGIN, *J. Amer. Chem. Soc.*, 80 (1958) 5358.
- 37 L. M. JACKMAN, *Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, Pergamon, New York, 1959, p. 69.