Contribution of Substituent Groups to the Extractability of Phenols and Benzoic Acids

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The contribution of substituent groups to the extractability of phenols and benzoic acids was examined by using a substituent constant, π, derived from the distribution coefficients of nonionic substances. This constant is defined as $\pi_X = \log K_{D(X)} - \log K_{D(H)}$, where $K_{D(X)}$ is the distribution coefficient of a derivative and $\log K_{D(H)}$ is that of the parent compound. The substituent constants of the groups at the *ortho*-position of phenol were found to vary with a variation of the extraction solvent, possibly due to competition between the hydration and solvation of an organic solvent. From the K_D values of the phenols and benzoic acids determined between chloroform and water, the substituent constants of halogeno, cyano, trifluoromethyl and nitro groups were calculated. In phenols, the π values of the *ortho*-substituting group (π^o) were greater than those of the *meta*- and *para*-substituting group, π^m and π^p, respectively, whereas in benzoic acids π^o are smaller than π^m and π^p. Such results can be explained by a masking effect and the overlapping effect: the masking effect increases the π^o values, whereas the overlapping effect decreases the π^o values. A method for predicting the total π values of di- and tri-substituted phenols and benzoic acids is proposed.

Keywords Solvent extraction, phenol, benzoic acid, extractability, substituent group contribution

Among the various separation techniques, liquid-liquid extraction is one of the most useful and versatile. In the liquid-liquid extraction of nonionic species methods for predicting the distribution coefficient of the species have been studied and successfully applied to studies of biologically active molecules in the field of pharmacochemistry by using the substituent constant, π, or the fragmental constant, f.[1-4] Among the π values of groups substituting in an aromatic ring, those obtained by using mono-substituted benzenes have often used.[3-4] However, experimentally obtained π values for phenol and benzoic acid are often considerably different from those of mono-substituted benzenes; furthermore, the π values of groups substituting at the *ortho*-position of phenol and benzoic acid are very different from the π values of *meta*- and *para*-substituents. Such matters have scarcely been considered, though they are very interesting and fundamental. The derivatives of phenol and benzoic acid are usually encountered in analytical chemistry, both as an analyte and as an organic reagent: for example, most chelating agents contain a hydroxyphenyl or a carboxyphenyl group in them.

In this paper, the authors consider the various factors which contribute to the π values of *ortho*-substituted phenols and benzoic acids.

Experimental

Reagents

All chemicals used were of analytical-reagent grade, except for such organic acids as the derivatives of phenol and benzoic acid.

Organic acids: phenols and benzoic acids. These were purchased from suppliers (Tokyo Kasei Kogyo Co., Wako Pure Chemical Ind. and Aldrich Chemical Co.), and were used without further purification. The purity of most of the reagents attained from suppliers were more than 98%. They were dissolved in an aqueous solution containing an equivalent amount of sodium hydroxide.

Extraction solvent. Chloroform was used after washing with distilled water.

Apparatus

The absorbances were measured with a Shimadzu 140-02 spectrophotometer and a Shimadzu UV-300 recording spectrophotometer with 10-mm quartz cells. The pH was measured with a Corning 130 pH meter equipped with a Ross combination pH electrode (Orion Research). A Taiyo SR-1 horizontal shaker was used.

Procedures

Determination of the distribution coefficients of the organic acids between an aqueous and an organic phase. Transfer suitable volumes of an organic acid solution and a pH-adjusting solution (sulfuric acid or buffer solution) into a 25-ml test tube fitted with a stopper, and dilute the mixture to 5 ml with distilled water. Shake the solution with 5 ml of chloroform for 30 min in a temperature-controlled room (25°C). After phase separation, transfer a 4 ml portion of the aqueous phase into a glass vessel. To it, add 1 ml of a NaOH solution (1 - 10 M) to make the organic acid be completely in its basic form. Then measure the absorbance at the maximum wavelength (λ_{max}) of the basic form of the organic acid. Determine the concentration of the organic acid in each phase by using a calibration curve; then calculate the distribution coefficient. For phenol and some derivatives (2-F, 2-NO_2, 2-Br, 4-I, 4-CN, 2,4-NO_2, 2,6-NO_2, 2,6-Cl), naphthol and benzoic acid and some derivatives (4-NO_2, 4-CN, 4-F, 4-Cl), pH dependency of the extraction equilibrium was examined using acetate (CH_3COOH-CH_3COONa), phosphate (KH_2PO_4-Na_2HPO_4) and ammonium (NH_3-$(NH_4)_2SO_4$) buffer solutions, sodium hydroxide solution and sulfuric acid solution (concentration of buffer: 0.01 M; ionic strength: 0.1 M with Na_2SO_4). For other derivatives of phenol and benzoic acid, the distribution coefficients were obtained at the pH region below (pK_a-2), where K_a is the acid dissociation constant of an organic acid.

Results and Discussion

Distribution coefficients for phenol and benzoic acid, and their derivatives

The liquid-liquid equilibrium constants of phenol, 2-naphthol and benzoic acid were obtained using the aqueous phases of various pH values. The distribution coefficient and distribution ratio, K_D and D, respectively, are defined as

$$K_D=[HA]_o/[HA],$$
$$D=[HA]_o/([HA]+[A^-])$$
$$=K_D\{1+(K_a/[H^+])\}^{-1}, \qquad (1)$$

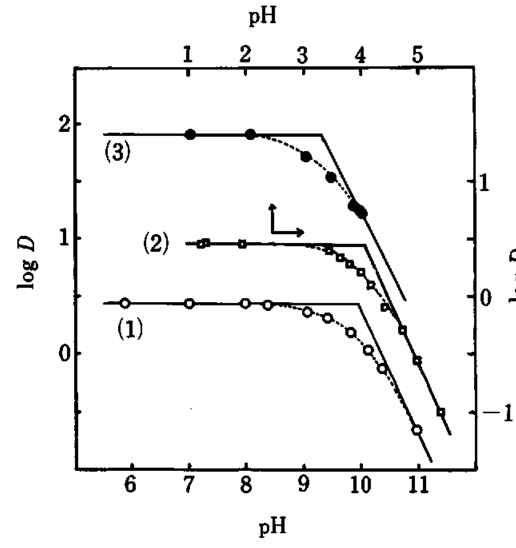
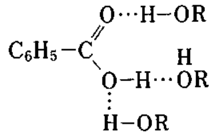


Fig. 1 Plots of log D of organic acids against pH. Organic acid: 1×10^{-4} M. (1) phenol; (2) benzoic acid; (3) 2-naphthol.

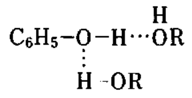
where HA and A^- are a protonated and a dissociated form of an acid HA, respectively, K_a is an acid dissociation constant, subscript "o" refers to the organic phase, and symbols without subscript refer to the aqueous phase. The values of log D were plotted against pH. As examples, the graphs of phenol, naphthol and benzoic acid are shown in Fig. 1: the graphs show a normal shape. Such a result shows that these organic acids are present as monomers in the organic phase at concentrations near 10^{-4} M, and that the distribution equilibriums follow Eq. (1). The values of pK_a calculated by using Eq. (1) were 9.95±0.02, 9.50±0.04 and 4.10±0.03 for phenol, 2-naphthol and benzoic acid, respectively. These are in good agreement with those obtained in aqueous solutions.[5] The values of log K_D of phenol, 2-naphthol and benzoic acid were obtained from both the horizontal lines and calculations using Eq. (1): they were 0.44, 1.91 and 0.46, respectively. The difference in log K_D between phenol and 2-naphthol is 1.47, which is in good agreement with the value obtained from ion association extraction (1.53).[6]

The substituent constants of the hydroxyl and carboxyl groups were obtained with 1-octanol by Hansch *et al.*: $\pi_{OH}=-0.67$ and $\pi_{COOH}=-0.32$.[3] The difference in log K_D between phenol and benzoic acid obtained in this work is smaller than that between π_{OH} and π_{COOH}. In 1-octanol, a carboxyl group is more solvated by 1-octanol (H–O–R) than is a hydroxyl group, and can be illustrated as I and II:



log K_D=1.87
(ref. 8)

(I)



log K_D=1.46
(ref. 8)

(II)

Sucn a solvation contributes to increasing the lipophilicity of the solute. In chloroform, however, solvation of solvent molecules is weak, compared with 1-octanol. This weak solvation results in a low lipophilicity of the solute, and the values of log K_D are smaller than those obtained with 1-octanol.

The values of log K_D of the derivatives of phenol and benzoic acid were determined in a pH region below (pK_a-2), except for *ortho*-substituted and poly-substituted benzoic acids. In the *ortho*- and poly-substituted benzoic acids, the pK_a values of which are sometimes below 3, the values of log K_D were determined in 0.25 - 1 M H_2SO_4. The values of log K_D obtained in this work are summarized in Table 1.

Substituent constant of groups substituting at the 3- and 4-positions, π^m and π^p

Table 2 shows the values of π obtained in both this and other studies (Hansch *et al.*[8]). Regarding the π

Table 1 Distribution coefficients ($\log K_D$) of monosubstituted phenols and benzoic acids between water and chloroform

Substituents (-X)	Phenols		Benzoic acids	
	pK_a[a]	$\log K_D$[b]	pK_a[a]	$\log K_D$[b]
-H	9.95(10.0)	0.44±0.01	4.20(4.1)	0.46±0.01
2-I	8.52		2.85	0.93±0.01
3-I	9.06	1.46±0.01	3.80	1.50±0.02
4-I	9.31(9.3)	1.45±0.01	3.99	1.56±0.04
2-Br	8.44(8.5)	1.83±0.01	2.84	0.61±0.01
3-Br	9.03	1.17±0.00	3.86	1.23±0.02
4-Br	9.36	1.12±0.01	3.98	1.18±0.07
2-Cl	8.48	1.64±0.01	2.92	0.57±0.04
3-Cl	9.02	0.95±0.01	3.82	1.01±0.07
4-Cl	9.38	0.94±0.01	3.98(4.0)	1.08±0.06
2-F	8.81(8.8)	0.81±0.01	3.27	0.24±0.04
3-F	9.28	0.43±0.00	3.86	0.60±0.01
4-F	9.95	0.38±0.01	4.14(4.1)	0.58±0.04
2-CN	6.7[c]	0.18±0.00		
3-CN	8.61	0.21±0.01	3.58	0.06±0.00
4-CN	7.95(7.8)	0.09±0.00	3.50(3.4)	0.20±0.01
2-CF_3		1.07±0.03		0.63±0.02
3-CF_3	8.89	1.06±0.01	3.74	1.17±0.05
4-CF_3	8.74[c]	1.00±0.00	3.67	1.18±0.01
2-NO_2	7.23(7.3)	2.52±0.10	2.16	−0.16±0.01
3-NO_2	8.40	0.40±0.00	3.47	0.47±0.01
4-NO_2	7.15	0.21±0.01	3.41(3.4)	0.49±0.01

a. Ref. 5. The values in parentheses are the ones obtained in this work, according to the plots in Fig. 1.

b. Mean values of three determinations.

c. These are predicted according to the calculation with Hammet σ values (ref. 7).

obtained with 1-octanol, the values for phenols are the largest, and the values for mono-substituted benzenes the smallest. This is also attributed to solvation. Among these three series of compounds, phenol derivatives are the most polarized by electron-withdrawing groups, and mono-substituted benzenes the least, as is illustrated below.

(III)

(IV)

Since octanol is considered to be more nucleophilic than water[8], it can solvate phenol derivatives (III) more effectively than mono-substituted benzenes (IV). Thus, the electron-withdrawing groups effectively increase the distribution coefficients or π values of phenols.

In this work using chloroform as an extraction solvent, the values of π for phenols are almost the same as those for benzoic acids, and the values for the groups at the 3-position, π^m, are almost the same as those for the groups at the 4-position, π^p. Furthermore, the values of π^m and π^p are smaller than those for the mono-substituted benzenes obtained with octanol. These results indicate that the effect of the solvation of chloroform on the distribution coefficients of solutes is very small, compared with 1-octanol.

Table 2 Substituent constants, π

Substituents (-X)	This work		Other works		
	Phenols	Benzoic acids	(1)[a]	(2)[b]	(3)[c]
-H	0	0	0		
2-I	(1.7)[d]	0.47	1.19		1.12
3-I	1.02	1.04	1.47	1.28	
4-I	1.01	1.10	1.45	1.14	
2-Br	1.39	0.15	0.89		0.86
3-Br	0.73	0.77	1.17	0.99	
4-Br	0.68	0.72	1.13	0.98	
2-Cl	1.20	0.11	0.69		0.71
3-Cl	0.51	0.55	1.04	0.83	
4-Cl	0.50	0.62	0.93	0.87	
2-F	0.37	−0.22	0.25		0.14
3-F	−0.01	0.14	0.47	0.28	
4-F	−0.06	0.12	0.31	0.19	
2-CN	−0.26				−0.57
3-CN	−0.23	−0.40	−0.24	−0.37	
4-CN	−0.35	−0.26	0.14	−0.31	
2-CF_3	0.63	0.17			
3-CF_3	0.62	0.71			
4-CF_3	0.56	0.72	1.49	1.07	
2-NO_2	2.08	−0.62	0.33		−0.28
3-NO_2	−0.04	0.01	0.54	−0.05	
4-NO_2	−0.23	0.02	0.50	0.02	

a. These were obtained for monosubstituted phenols with octanol as extraction solvent, and the $\log K_D$ value of phenol was 1.46 (ref. 8).

b. These were obtained for monosubstituted benzoic acids with octanol as extraction solvent, and the $\log K_D$ values of benzoic acid was 1.87 (ref. 8).

c. These were obtained for monosubstituted benzenes with octanol as extraction solvent, and the $\log K_D$ values of benzene was 2.13 (ref. 8).

d. A predicted value obtained from the graph in Fig. 2.

A characteristic point is that in chloroform extraction we can use the same values for π^m and π^p, as well as for phenols and benzoic acids. The substituent constants obtained in this work are therefore considered to show a more realistic contribution of the substituent groups to the distribution coefficient of the solute than those obtained with 1-octanol.

As many workers have reported, the surface areas or volumes of substituent groups contribute to the distribution coefficients or π values: the larger the surface area or volume, the larger are the distribution coefficients or the π values. Thus, the order of the π values for halogeno groups is -I>-Br>-Cl>-F. Hereafter, this effect of the surface area or volume is called the "volume effect" of a substituent group, P_V. Figure 2 shows the relations between π and the van der Waals volume. From Fig. 2 we can see that the π values of the cyano

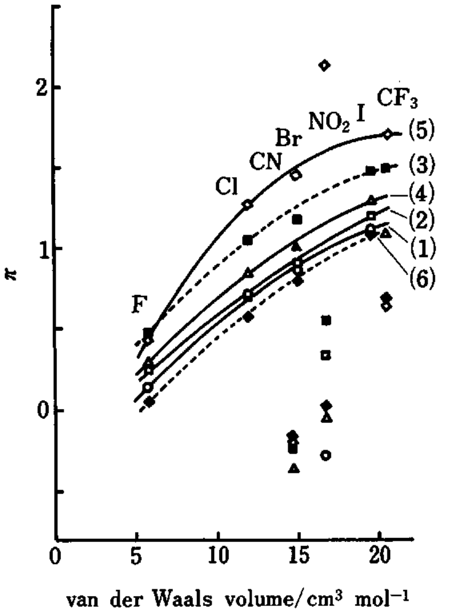
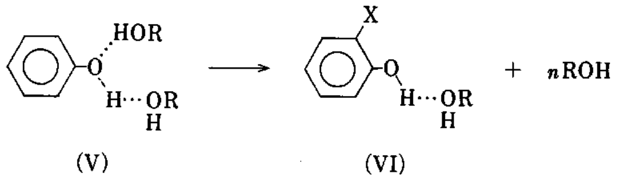


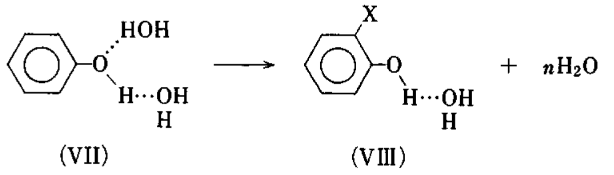
Fig. 2 Relationships between the substituent constant, π, and the van der Waals volume. (1) benzene derivatives (ref. 8); (2) *ortho*-substituted phenols (ref. 8); (3) *meta*-substituted phenols (ref. 8); (4) *meta*-substituted benzoic acids (ref. 8); (5) *ortho*-substituted phenols (this work); and (6) *meta*-substituted phenols (this work). van der Waals volume (ref. 9): F 5.80; Cl 12.0; Br 15.12; I 19.64; CN 14.70; NO$_2$ 16.8; CF$_3$ 20.49 cm^3 mol^{-1}.

and nitro groups deviate considerably from curves for the halogeno groups. This negative deviation is mainly due to much solvation of water to these groups, whereas the abnormally positive deviation of the nitro group adjacent to the hydroxyl group is due to the formation of an intramolecular hydrogen bonding.

Substituent constant for 2-substituting groups, π^o

Table 2 shows that in octanol extraction, the π^o for the phenols is smaller than π^m and π^p, whereas in chloroform extraction the π^o for the phenols is larger than π^m and π^p. It is also very interesting that π^o for the phenols obtained in this work are larger than those obtained with octanol. These facts can be explained by the difference in the solvation strength between the extraction solvents. Phenols are strongly solvated at the hydroxyl group by octanol or water. As already mentioned, octanol is more nucleophilic than water, resulting in an increase in the lipophilicity of the phenols. However, the substituent groups at the 2-position of phenol inhibit octanol and water from solvating the HO-group; such inhibition is probably more effective for octanol solvation than for water solvation, since octanol has a long alkyl chain. This results in a large decrease in the lipophilicity of -OH of phenols, which can be illustrated as follows:



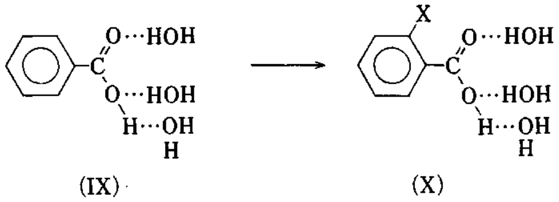


Lipophilicity of -OH, LP (V)>(VI)
(VIII)>(VII)
Difference in LP, ΔLP $\Delta LP_{(V)-(VI)} > \Delta LP_{(VIII)-(VII)}$

As a result, π^o becomes smaller than π^m and π^p in phenol derivatives.

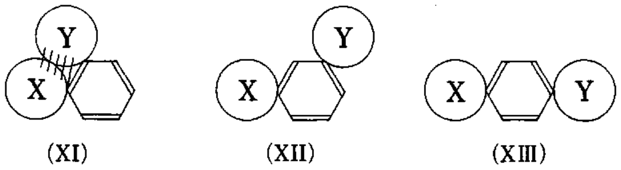
In chloroform extraction the substituent groups at the 2-position of phenol also inhibit solvent molecules (water in our case) from solvating the HO-group. This results in a large increase in the lipophilicity of phenols, as illustrated by formulae (VII) and (VIII). The distribution coefficients of 2-substituted phenols are therefore larger than those of the 3- and 4-substituted phenols. Such a contribution of the 2-substituting group plays an important role in inhibiting water from solvating the HO-group and is called "masking effect of the 2-substituting group, P_M".

The contribution of P_M seems to be negligibly small in benzoic acids, since the substituent group at the 2-position of benzoic acid is far from the oxygens of the carboxyl group, as can be seen in (IX) and (X):



Thus, the distribution coefficients of 2-substituted benzoic acids are not so large as those of 2-substituted phenols.

The other interesting thing is why π^o is smaller than π^m and π^p in the extraction of benzoic acids with chloroform. This cannot be explained from the solvation of solutes. It is considered that the two substituent groups, which substitute at the *ortho*-position in benzene ring, share some parts of their surfaces and volumes, as can be seen below:



$$\Sigma\pi \quad (\mathrm{XI}) < (\mathrm{XII}) \simeq (\mathrm{XIII}),$$

where $\Sigma\pi$ is the total contribution of the substituent groups, -X and -Y, to the distribution coefficient. Such an effect is called the "overlapping effect, P_O". The contribution of this effect to the distribution coefficients is always negative. Therefore, π^o of benzoic acids is smaller than π^m or π^p.

Estimation of the factors contributing to the distribution coefficient

The volume effect and hydrogen bonding effect: Figure 2 shows that π_X increases with an increase in the van der Waals volume, where X is a halogeno group. However, cyano, nitro and trifluoromethyl groups, which form strong bonds to water through a hydrogen bond, deviate negatively from the curves of the halogeno group. Such a deviation from the curves seems to be brought about by competition between the solvation of water and the extraction solvent. In chloroform extraction, the deviations for -CN, -NO_2 and -CF_3 are −0.94, −0.90 and −0.46, respectively; we can use these deviations as a hydrogen bonding effect, P_H. Therefore, the strength of hydrogen bonding seems to be in the order -CN>-NO_2>-CF_3.

For convenience, we use the averaged values of π^m and π^p as a measure of the sum of the volume effect (P_V) and the hydrogen bonding effect (P_H), $P_{V,H}$. Therefore, $P_{V,H}$ can be expressed as

$$P_{V,H} = P_V + P_H \simeq \pi^m \simeq \pi^p.$$

The P_H of halogeno groups seems to be negligibly small, whereas the P_H of -CN, -NO_2 and -CF_3 is negative.

Overlapping effect, P_O: It may be considered that in *ortho*-substituted phenols and benzoic acids π^o is composed of P_O, $P_{V,H}$ and P_M, and can be expressed as

$$\pi^o = P_{V,H} + P_O = \pi^m \text{ (or } \pi^p) + P_O \quad \text{(in benzoic acids)} \qquad (2)$$

and

$$\pi^o = P_{V,H} + P_O + P_M$$
$$= \pi^m \text{ (or } \pi^p) + P_O + P_M \quad \text{(in phenols).} \qquad (3)$$

The values of P_O for benzoic acids were calculated from Eq. (2); they are summarized in Table 3. We cannot obtain P_O and P_M for phenols separately from Eq. (3), since we only know the values of π^o and $P_{V,H}$ in phenols. Therefore, we assume that P_O for phenols is approximately equal to that for benzoic acids. The values of P_M were thus calculated from Eq. (3). The estimated values of P_V, P_H, $P_{V,H}$, P_O and P_M are summarized in Table 3.

As is shown in Fig. 3, the absolute value of P_O increases with an increase in the volume of the substituent group, and reaches a maximum, as do the values of P_M. From Fig. 3, we can estimate the values for the substituent groups, the P_H of which are negligibly small: for example, we can estimate the values for the methyl group. The estimated values are listed in Table 3. The estimated value for P_V is in good agreement with the reported value, 0.56.[4]

The abnormally large value of P_M for the nitro group is attributed to an intramolecular hydrogen bond, as follows:

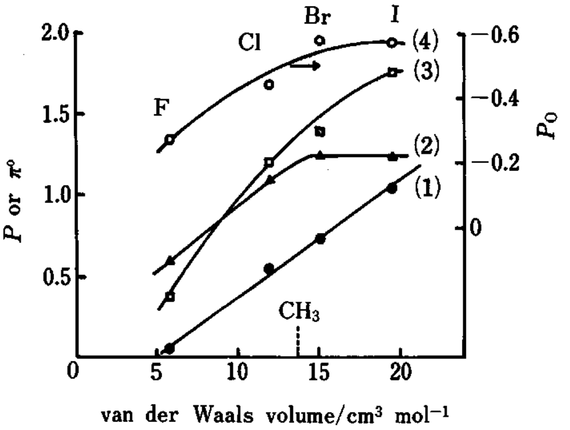
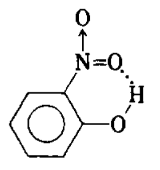


Fig. 3 Relations between the van der Waals volume and factors contributing to substituent constants. (1) P_V; (2) P_M; (3) π^o for phenols; (4) P_O. van der Waals volume (ref. 9): CH_3 13.67 cm^3 mol^{-1}.

Table 3 Factors contributing to the distribution coefficients or substituent constants

	P_V	P_H	$P_{V,H}$	P_O	P_M	π^m, π^p	π^o	
							Benzoic acids	Phenols
-I	1.04	0	1.04	−0.57	1.29	1.04	0.47	1.76
-Br	0.73	0	0.73	−0.58	1.24	0.73	0.15	1.39
-Cl	0.55	0	0.55	−0.44	1.09	0.55	0.11	1.20
-F	0.05	0	0.05	−0.27	0.59	0.05	−0.22	0.37
-NO_2	0.84	−0.90	−0.06	−0.56	2.70	−0.06	−0.62	2.08
-CN	0.63	−0.94	−0.31			−0.31		
-CF_3	1.11	−0.46	0.65	−0.48	0.46	0.65	0.17	0.63
-CH_3[a]	0.65	0	0.65	−0.51	1.17	0.65	0.14	1.30

a. These values were estimated from Fig. 4.



Prediction of the distribution coefficients for poly-substituted phenols and benzoic acids

The distribution coefficients can be predicted by calculating the total π value of the substituent groups. The total π value, $\Sigma\pi$, is obtained summing the contribution of the substituent groups to the distribution coefficient. The method for predicting $\Sigma\pi$ for benzoic acids is rather simple.

The values of $\Sigma\pi$ for poly-substituted benzoic acids are estimated as follows:

$$\Sigma\pi = 2\pi_X^o \qquad \text{(2,6-disubstituted benzoic acids)},$$

$$\Sigma\pi = \pi_X^o + \pi_X \ (\pi_X\text{: } \pi_X^p \text{ or } \pi_X^m) \qquad \text{(2,3- or 2,4-disubstituted benzoic acids)},$$

and

$$\Sigma\pi = 2\pi_X^o + \pi_X^p \qquad \text{(2,4,6-trisubstituted benzoic acids)}.$$

In Table 4 both the predicted and the experimental values are listed. They are in fairly good agreement.

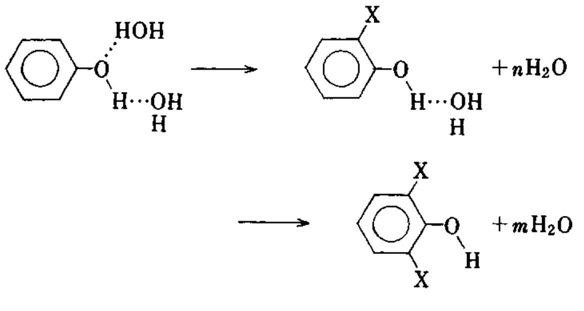
Table 4 Prediction of the total π values ($\Sigma\pi$) for phenols and benzoic acids

Substituent	log K_D	$\Sigma\pi$		Diff.[b]
		Experimental[a]	Calcd.	
Benzoic acids				
2,6-NO_2	−0.62±0.10	−1.08	−1.24	0.16
2,4-NO_2	−0.22±0.05	−0.68	−0.68	0.00
2-Cl,4-NO_2	0.69±0.04	0.23	0.05	0.18
2-Cl,5-NO_2	0.72±0.04	0.26	0.05	0.21
2,3,5-I	2.87±0.02	2.41	2.55	−0.14
2,4,6-Br	1.74±0.03	1.28	1.03	0.25
Phenols				
2,6-Br	2.54±0.00	2.10	2.16	−0.06
2,6-Cl	2.17±0.01	1.73	1.85	−0.12
2,6-NO_2	2.63±0.01	2.19	2.81	−0.62
2,4-Br	2.42±0.02	1.98	2.12	−0.14
2,4-NO_2	2.36±0.01	1.92	2.02	−0.10
2-NO_2,5-F	2.19±0.03	1.75	2.13	−0.38
2-NO_2,4-Cl	3.26±0.02	2.82	2.63	0.19
2-Cl,4-NO_2	1.35±0.01	0.91	1.14	−0.23
2,4,6-1	4.20±0.07	3.76	3.94	−0.18
2,4,6-Br	3.66±0.06	3.22	2.89	0.33
2,4,6-Cl	2.57±0.01	2.13	2.40	−0.27
2,6-CH_3,4-NO_2	2.22±0.01	1.78	1.95	−0.17

a. The log K_D of phenol and benzoic acid were 0.44 and 0.46, respectively.

b. Differences between the experimental and calculated values.

Regarding phenol derivatives, one question is how great is the contribution of two *ortho*-substituted groups. An *ortho*-substituted group inhibits water from solvating the oxygen and hydrogen of the -OH group through a hydrogen bond, as follows:



However, the second or 6-substituting group in phenol probably contribute less to the inhibition of water from solvating than does the first group or 2-substituting group; that is, the number of dissociated water molecules seems to be $n > m$. We therefore consider that the inhibition effect of the second *ortho*-substituting group is half that of P_M, though this is only an empirical estimation. Thus, the $\Sigma\pi$ of poly-substituted phenols are calculated as follows:

$$\Sigma\pi = \pi_X^o + (\pi_X^o - P_M/2) \qquad \text{(2,6-disubstituted phenols)},$$

$$\Sigma\pi = \pi_X^o + \pi_X \ (\pi_X\text{: } \pi_X^m \text{ or } \pi_X^p) \qquad \text{(2,3- or 2,4-disubstituted phenols)},$$

and

$$\Sigma\pi = \pi_X^o + (\pi_X^o - P_M/2) + \pi_X^p \qquad \text{(2,4,6-trisubstituted phenols)}.$$

In Table 4 the predicted values for the phenols are shown: they are in good agreement with the experimental values, except for that of 2,6-dinitrophenol. The reason why the predicted value for 2,6-dinitrophenol is larger than the experimental one is that only one of the two nitro groups adjacent to the -OH group forms a hydrogen bond with the hydrogen of the -OH group, and the other can not.

We estimated the factors for the methyl group. By using these values we can predict $\Sigma\pi$ for 2,6-dimethyl-4-nitrophenol: $\Sigma\pi = 1.30 + (1.30 - 0.59) - 0.06 = 1.95$. The experimentally obtained value was 1.78, which is in good agreement with the predicted value.

In conclusion, the factors contributing to the distribution coefficient or the substituent constant were considered, and a method for predicting the total π values, $\Sigma\pi$, was proposed. By the proposed method, though it is still empirical, the $\Sigma\pi$ for poly-substituted phenols and benzoic acids were calculated and compared with the experimental values. Such a method for predicting distribution coefficients is useful for designing new extractants, while predicting the extractability of analytes and reagents.

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(Received September 5, 1990)
(Accepted November 28, 1990)