

Polyelectrolyte Effects Exerted by Poly(ethyleneimine) on the Ionization Constant of Substituted Phenols

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The ionization constants of sixteen substituted phenols, some of which have a second protogenic group (CO₂H, SO₃H) on the aromatic ring, have been determined spectrophotometrically at 25 °C in water in the presence of poly(ethyleneimine) (PEI). The most remarkable effect exerted by PEI is the enhancement of the acidity of the phenolic group, more relevant (up to 2.9 pK units) when there is a second ionizable group in the molecule. In some cases the acidity constants of the two protogenic groups are sufficiently close for their ionizations to overlap. The results are ascribed to an electrostatic interaction of the positively charged polyelectrolyte with the phenols containing ionized carboxylate or sulphonate groups. A semiempirical equation has been developed to interpret the shape of the spectrophotometric titration curve of the weaker diprotic phenols as being due to the progressive detachment of the phenol from the polyelectrolyte, as the pH increases. Furthermore, two separate linear relationships have been found for monoprotic and for diprotic compounds, respectively, which correlate the acidity of the phenolic group in the presence of PEI with those determined in absence of PEI. The goodness of the correlations denotes the absence of effects due to the structure of the phenols and therefore appears of general validity.

In a previous paper¹ it was reported that the rate of aminolysis of 8-acetoxyquinoline-5-sulphonate by poly(ethyleneimine) (PEI) was higher than that of 8-acetoxyquinoline. In contrast an unremarkable difference in the rates was found when the aminolysis of the two substrates was performed using a monomeric amine of comparable nucleophilicity to that of PEI. The results were tentatively ascribed to an increase in the acid dissociation constant of the conjugate acid of the leaving group of the sulphonated compound in the presence of PEI.

For a better understanding of the behaviour of the above-mentioned and other esters² we have examined the effect of PEI on the acid dissociation equilibria of a set of substituted phenols.

Other examples of the increase in acidity constants of phenols covalently or electrostatically bonded to natural³⁻⁵ or synthetic⁶ polymers have been reported. However, such an apparently simple phenomenon as the ionization of a protogenic compound in the presence of a polyelectrolyte is not well understood in spite of its potential importance as a model for the ionization equilibria in the presence of far more complicated systems such as biological macromolecules.

Experimental

Materials.—Substituted phenols were purchased from Carlo Erba, Merck, Lancaster Synthesis, or Aldrich and in some cases were recrystallized from suitable solvents. 5-Hydroxyisophthalic acid was crystallized from ethanol and then sublimed under vacuum at 260 °C. The sodium salt of 4-hydroxy-3-nitrobenzenesulphonic acid was prepared according to ref. 7 and 3-hydroxy-*N,N,N*-trimethylphenylammonium iodide (m.p. 179 °C from absolute ethanol) was prepared by a procedure given for its acetate ester.⁸ N.m.r. spectra of both compounds were compatible. Titrimetric determination of functional groups (OH and I) was 99.9%.

Buffers were HCl (0.05 mol dm⁻³), CH₃CO₂H–CH₃CO₂Na (0.025 mol dm⁻³), KH₂PO₄–Na₂HPO₄ (0.015 mol dm⁻³), H₃BO₃–NaOH (0.05 mol dm⁻³), NaHCO₃–Na₂CO₃ (0.015 mol dm⁻³). The ionic strength was kept constant at 0.05 mol dm⁻³ with added KCl.

Poly(ethyleneimine) was Polymin P from BDH. The absolute concentration (47.6% by weight and monomer molecular weight (59), were both determined as reported elsewhere.^{9,†} Buffer solutions of PEI were prepared by mixing solutions of suitable concentration with HCl (0.1–8.5 mol dm⁻³) up to the desired pH. Unless otherwise specified, no adjustment for ionic strength was made. Solutions were kept closed under nitrogen atmosphere and used within a day.

Poly(diallyldimethylammonium chloride) (PDDA) (15% in water, monomer molecular weight 143) and poly[trimethyl(vinylbenzyl)ammonium chloride] (PVBA) (33.5% in water, monomer molecular weight 222) were from Polysciences. Other materials were of analytical grade. Water was deionized and freshly distilled from KMnO₄.

Apparatus.—Konron Uvikon 860 and Sigma ZWS-II (Biochem) spectrophotometers equipped with thermostatted cell holders were used. The pH meter was a KNICK 643 equipped with an INGOLD HA-405 combined glass electrode standardized before use with phosphate, phthalate, and borate buffers.¹¹ A pH precision of 0.01 was allowed.

Spectrophotometric Determination of Ionization Constants.—Measurements of optical absorption and of pH were carried out at 25 ± 0.1 °C in buffered solution according to the procedures described by Albert and Serjeant.^{12a}

A stock solution of the substituted phenol (0.3–3.5 × 10⁻³ mol dm⁻³; 5 cm⁻³) was added to the buffer solution (20 cm⁻³). The ratio of moles of PEI monomers per mole of substrate was *ca.* 1 000 for monoprotic and *ca.* 180 for diprotic substrates. PEI concentrations were high enough to assure a buffer capacity and an excess over the substrate; in a preliminary experiment carried out with compound (16) (sodium 4-hydroxy-3-nitro-

† PEI is a branched polyelectrolyte containing primary (25%), secondary (50%), and tertiary (25%) amino groups. Its p*K*_{app} and the value *n* of the modified Henderson–Hasselbalch equation are not constant depending on the concentration, on the degree of ionization of PEI, and on the concentration of an added salt.¹⁰

benzenesulphonate) at a concentration of 1.77 mol dm^{-3} no difference was observed between the u.v.-vis spectra registered in the presence of 1.22×10^{-2} or $2.1 \times 10^{-3} \text{ mol dm}^{-3}$ of PEI monomer. Furthermore, the concentrations of the polyelectrolyte were such that hydrolysis of the acetates of the phenols² occurred under saturation conditions. This will be referred to in a following paper. In some experiments, two different polycations instead of PEI were used: poly[diallyl(dimethyl)ammonium chloride] (PDDA) and poly[trimethyl(vinylbenzyl)ammonium chloride] (PVBA) at the concentration of 0.05 mol dm^{-3} monomer in $0.0085 \text{ mol dm}^{-3}$ oxyanion buffers.

The u.v. absorption at various pH values was initially recorded for each compound. A more precise determination of the absorbance was then performed at a suitable analytical wavelength at several pH values.

For phenols not having an ionizable carboxylic group* the 'mixed' acidity constants K_m of the phenolic group were calculated from the pH dependence of the optical density (OD) in the range of $\text{pH} = \text{p}K \pm 0.5$. A simple computer program was used for equation (1) where OD_i is the absorbance of

$$\text{p}K_m = \text{pH} + \log[(\text{OD}_i - \text{OD})/(\text{OD} - \text{OD}_n)] \quad (1)$$

the phenolate anion and OD_n is the absorbance of the unionized phenol, previously determined at $\text{pH} = \text{p}K_a \pm 2.5$. When too high a pH value was needed for the determination of OD_i in the presence of PEI, OD_i was obtained from the intercept of the plot of OD against $[\text{H}^+]$ ($\text{OD} - \text{OD}_n$).^{12a}

For phenols containing an additional carboxylic group, the two values of pK, which can be sufficiently close to overlap, were determined according to the procedure of Albert and Serjeant^{12a} using the precautions suggested therein.

These authors reported a FORTRAN IV iterative computer program for overlapping pKs of a diprotic acid, which calculates the molar absorption coefficient of the monoprotonated species and the thermodynamic ionization constants of the two acidic groups. The treatment is based on the well known equation (2) which expresses, at a selected wavelength, the dependence of the optical density on the proton activity a_{H^+} for solutions of a diprotic acid:

$$\text{OD} = c_m \frac{\epsilon_D a_{\text{H}^+}^2 + \epsilon_M K_1 a_{\text{H}^+} + \epsilon_N K_1 K_2}{a_{\text{H}^+}^2 + K_1 a_{\text{H}^+} + K_1 K_2} \quad (2)$$

where optical path = 1 cm, c_m is the molar concentration of the phenol, K_1 and K_2 are the 'mixed' ionization constants of the two protogenic groups (in our case CO_2H and the phenolic OH, respectively), ϵ_D , ϵ_M , and ϵ_N are the molar absorption coefficients of the diprotonated, monoprotonated, and unprotonated species, respectively, initially determined at a suitable pH.† The data are divided into two segments which cover the pH range in which both the stronger and the weaker group are ionized. In our experiments the optical density was determined at *ca.* 20

different pH values; in the presence of PEI we considered for calculation only the absorbance values at $\text{pH} < 7$, which is a critical value for the electrostatic interaction of anions with the polyelectrolyte (see below). We 'translated' into BASIC, the original program to adapt it to our APPLE IIe PC and, in order to verify the confidence of the results, we integrated the program to recalculate, using equation (2) and the parameters given by the program, the pH dependence of the absorbance. The procedure allowed the optimization of the results after selection of the best segments of data to use in computation or, when necessary, to modify the computed parameters to find the best fit.‡ The accepted agreement between the computed and experimental values of OD was 2–5%. Finally, we added a routine for graphical display. Visual inspection of the results revealed a difference of 0.05 units in the value of $\text{p}K_2$.

For 5-hydroxyisophthalic acid, which contains three protogenic groups, the pK of the phenolic group was determined using the program for overlapping pK, as for a diprotic acid. This procedure was adopted since, at the chosen analytical wavelength, the ionization of the two carboxylic groups are spectroscopically indistinguishable. Adequate correction for ionic strength was made.

The 'thermodynamic' ionization constants were obtained by the correction for ionic strength of the 'mixed' constants. The ionic strength at various pH values in the presence of PEI was calculated, as reported in ref. 15, from equation (3) where c_p is

$$I = 0.5[(2ic_p) + 2c_a + 2c_s] \quad (3)$$

the concentration of the polyelectrolyte expressed as mol dm^{-3} monomer, c_a is the molar concentration of added HCl, c_s is the molar concentration of the added salt (if any) and i is the degree of ionization of PEI, calculated by potentiometric titration. Because the ionic strength of PEI varies with pH, we assumed it to be constant at the median value at $\text{pH} = \text{p}K(\text{phenol group}) \pm 0.5$.

With buffers other than PEI, the ionic strength was calculated as usual. In both cases, when the ionic strength was higher than 0.1 mol dm^{-3} the correction term (0.055I) was added.¹⁶

Experimental details, pK values, and molar extinction coefficients are reported in Table 1.

Results and Discussion

The phenols were grouped into two sets: those having only one ionizable group (monoprotic) and those having a second ionizable group (diprotic) such as CO_2H or SO_3H . The latter group is fully ionized in the range of pH considered. For the sake of brevity the results obtained with buffer other than PEI are cited as 'in water.'

Monoprotic Phenols [compounds (1)–(7)].—The plot of absorbance versus wavelength at various pH values showed, for compounds (2) and (3) in the presence of PEI, a small drift at alkaline pH (1–4 nm at the maximum of the curve), therefore it was not possible to determine the isosbestic point. It may be that the effect could depend on interactions between the phenolate ions with PEI. In fact, the *N,N,N*-triethylammonium derivative, which because of its positive charge cannot be attracted by the protonated PEI, showed a clean isosbestic point. Molar absorption coefficients at the analytical wavelength in the presence of PEI, were not significantly different from those found in water.

The plots of absorbance versus pH, not reported here, showed the usual sigmoidal shape. The plot of $\log[(\text{OD}_i - \text{OD})/(\text{OD} - \text{OD}_n)]$ vs. pH gave a straight line as required by the Henderson–

* The sulphonate group was considered to be fully ionized at all pH values.

† Owing to the high acidity of the carboxy group, the optical density of the diprotonated species of 3,5-dinitrosalicylic acid in water and in PEI was determined by extrapolating the value of the acidity function, $H_o = -2.12$ (HCl 20%) from the values of OD measured at $H_o = -1.01$ (HCl 10%) and -1.57 (HCl 15%) from ref. 13(a). A $\text{p}K_1$ value of 0.35 was found (*cf.* $\text{p}K_1 = 0.54$ reported in ref. 14) because a different value of the optical density of the diprotonated species was used.

‡ The dissociation constants were introduced into the program as 'thermodynamic' constants and automatically corrected by the ionic strength to the 'mixed constants.'

Table 1. Acidity constants of the carboxylic (pK_1) and phenolic (pK_2) groups and optical absorption coefficients of monoprotic and diprotic phenols^a in the absence (W) and in presence of poly(ethyleneimine) (PEI) at 25 ± 0.1 °C.

Compd.	R ¹ R ² R ³ C ₆ H ₃ OH			λ /nm ^b	PEI (mono- mer)/mol dm ⁻³	pK_1 (W) ^c	pK_2 (W) ^c	pK_1 (PEI)	pK_2 (PEI)	log ^d		
	R ¹	R ²	R ³							$\epsilon_{\text{diprot.}}$	$\epsilon_{\text{monoprot.}}$	$\epsilon_{\text{non-prot.}}$
(1)	H	H	H	288	0.90		9.99		10.05		1.58	3.42 ^e
(2)	<i>o</i> -NO ₂	H	H	420	0.55		7.23		6.50		2.47	3.67
(3)	<i>p</i> -NO ₂	H	H	402	0.98		7.14		6.64		2.94	4.29
(4)	<i>p</i> -CONH ₂	H	H	294	0.78		8.56		8.05		2.33	4.29
(5)	<i>m</i> -Cl	H	H	295	0.98		9.12		8.63		1.72	3.49 ^e
(6)	<i>o</i> -NO ₂	<i>p</i> -NO ₂	H	390	0.56		4.07		3.26		2.46	4.09
(7)	<i>m</i> -N ⁺ (CH ₃) ₃ I ⁻	H	H	294	0.09		8.03		8.13		1.79	3.53
(8)	<i>p</i> -CO ₂ H	H	H	280	0.052	4.40 ^{f,g}	9.44 ^{f,g}	3.50	7.14	3.52	3.15	4.25
(9)	<i>p</i> -CH ₂ CO ₂ H	H	H	295	0.056	4.24 ^f	10.38 ^f	3.71	8.18	1.32	1.88	3.38
					0.096			3.71	8.18	(1.52)	(1.72)	(3.38)
(10)	<i>p</i> -SO ₃ ⁻ Na ⁺	H	H	254	0.05		9.06 ^f		6.58		2.95	4.19
(11)	<i>o</i> -Cl	<i>p</i> -CO ₂ H	H	273	0.064	4.25 ^f	7.89 ^f	3.35	5.16	3.68	3.49	4.15
(12)	<i>o</i> -NO ₂	<i>p</i> -CO ₂ H	H	410	0.050	3.79 ^f	6.67 ^f	3.10	3.75	2.15	0.79	3.64
										(2.15)	(2.58)	(3.64)
(13)	<i>o</i> -NO ₂	<i>p</i> -NO ₂	<i>o'</i> -CO ₂ H	370	0.05	0.35 ^{f,h}	7.45 ^{f,h}	0.36	4.56	2.55	3.85	4.15
										(2.55)	(3.84)	(4.18)
(14)	<i>m</i> -CO ₂ H			313	0.064	4.07	10.09 ^f	3.41	7.68	3.03	2.13	3.40
				(318)						(1.62)	(3.40)	
(15)	<i>m</i> -CO ₂ H	<i>m'</i> -CO ₂ H	H	330	0.052	3.48 ⁱ	10.39 ^f	2.35 ⁱ	7.29	2.72	1.89	3.56
				(328)						(2.91) ^l	(2.40)	(3.56)
(16)	<i>o</i> -NO ₂	<i>p</i> -SO ₃ ⁻ Na ⁺	H	405	0.052		6.08 ^f		3.43		2.38	3.66
											(2.41)	(3.65)
					0.062				3.42			

^aThe accuracy of the pK values is within ± 0.08 . ^bAnalytical wavelength, not necessarily the λ_{max} of the non-protonated phenol. ^cFrom ref. 12(b) unless otherwise indicated. ^dThe units of ϵ are $\text{dm}^3 \text{mol}^{-1} \text{cm}^{-1}$. In parentheses the values found without PEI. ^eValues found by spectral extrapolation (see text). ^fThis paper. ^g pK_1 (W) 4.57 and pK_2 (W) 9.46 in ref. 12(c). ^h pK_1 (W) 0.54 and pK_2 (W) 7.38 in ref. 14. ⁱThe pK values of the two carboxylic groups are indistinguishable at the wavelength employed. ^l ϵ of protonated species.

Table 2. Effect of KCl on the acidity constants of 4-hydroxy-3-nitrobenzenesulphonate and 4-hydroxybenzoic acid in the presence of PEI at 25 ± 0.1 °C.^a Parameters used in equations (4) and (5).

Acid		KCl/mol dm ⁻³				
		0	0.008	0.021	0.087	0.256
4-Hydroxy-3-nitrobenzenesulphonate ^b	pK_2 (PEI)	3.43	3.75	4.03		5.46
	pK_1 (PEI)	3.50	3.90		4.10	4.30
4-Hydroxybenzoic ^c	pK_2 (PEI)	7.14	7.30		8.60	9.00
	pK_3 (PEI)	9.60	9.60		9.45	9.45
	log ϵ ^d	3.15	3.04		3.20	3.08
	pK_0	7.10	7.15		8	8
	n	1.06	1.07		1	1

^a Experimental conditions are given in Table 1. ^b Plots of OD vs. pH are reported in Figure 1. pK_2 (PEI) Values were calculated using equation (1) and the data given in Table 1. Molar absorption coefficients do not differ from those reported in Table 1. ^c Plots of OD vs. pH are shown in Figure 3. pK values were calculated using equations (4) and (5) and other parameters in Table 1. ^d Molar absorption coefficient of monoprotated species.

Hasselbalch equation in the range of $\text{pH} = \text{pK} \pm 0.5$ (at least). The resulting slopes were 1 ± 0.05 except for 3-chlorophenol for which the slope was 1.3. The acidity constants of the phenolic groups (Table 1) were slightly higher in the presence of PEI; differences of 0.49–0.81 pK units were observed for phenols having more polar substituents, except for the positively charged *N,N,N*-trimethylammonium derivative [compound (7)] for which no significant difference was observed.

Diprotic Phenols.—A red shift of 2–6 nm of the maximum of absorbance was found for the unprotonated species of compounds (12), (13), and (16) in the presence of PEI. Molar absorption coefficients at the analytical wavelength of diprotonated and of unprotonated species of all the diprotic phenols were not significantly affected by PEI. Some differences

were found between the calculated absorptions of the monoprotated species in PEI and in water.

Among the diprotic phenols two types of behaviour were observed for the pH dependence of the absorbance. In compounds (11), (12), and (13) the presence of PEI increases the acidity constants of the phenolic group more than that of the carboxy group. An extreme case is 4-hydroxy-3-nitrobenzoic acid [compound (12)] for which the difference of 2.9 pK units between pK_1 and pK_2 in water, was reduced to 0.65 pK units in the presence of PEI with a large overlap of the ionization steps of the two groups. The effect of increasing the ionic strength is surprisingly relevant in the presence of PEI. An illustrative example (Table 2 and Figure 1) is 4-hydroxy-3-nitrobenzenesulphonic acid [compound (16)]. As the concentration of KCl was increased, the pK_{app} of the phenolic group was shifted

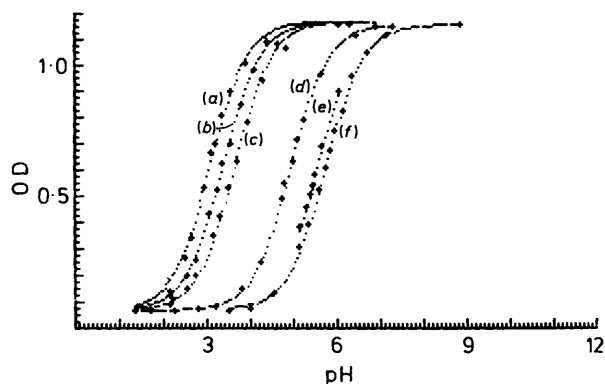


Figure 1. Plots of optical density vs. pH for 4-hydroxy-3-nitrobenzenesulphonate in the presence of monomer ($0.052 \text{ mol dm}^{-3}$) of PEI buffers (a), and with added KCl, 0.008 (b), 0.021 (c), 0.256 (d) mol dm^{-3} . In oxyanions with $0.256 \text{ mol dm}^{-3}$ (e), and without KCl (f). Experimental points (+). Dotted lines are calculated from equation (1) and data in Table 2.

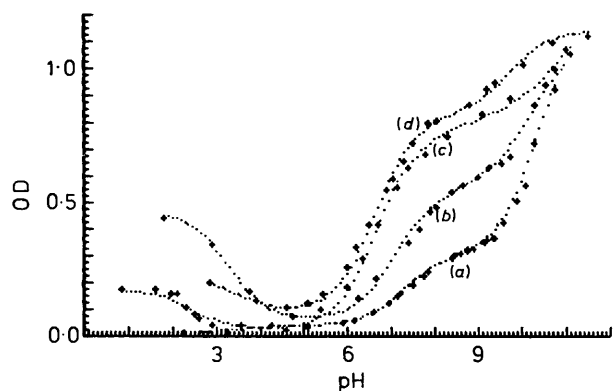


Figure 2. Plots of optical density vs. pH. Experimental points (+). Dotted lines are calculated from equations (4) and (5). For each acid, pK_1 (PEI), pK_2 (PEI), and other parameters are given in Table 1, pK_3 (PEI), pK_0 and n are as follows: (a) 4-hydroxyphenylacetic, 10.6, 7.30, and 1.05; (b) 3-hydroxybenzoic, 10.3, 7.25, and 1.08; (c) 4-hydroxybenzoic, 9.6, 7.1, and 1.05; (d) 5-hydroxyisophthalic, 10.6, 7.0, and 1.08.

towards that observed in water (without PEI). On the other hand the addition of KCl ($0.256 \text{ mol dm}^{-3}$ final concentration) in water induced a normal decrease of the phenolic pK_{app} (Figure 1). The experiment supports an electrostatic interaction between the polyion and the anionic sulphonate group of the substrate. In view of the fact that even small quantities of salt are highly effective, in the experiments in the presence of PEI, we did not adjust the ionic strength to a constant value as is usually done.

In compounds (8), (9), (14), and (15) the shape of the absorbance–pH plots was largely modified by the PEI in comparison with those found in water and suggested the presence of three different values of pK despite there being no more than two protogenic groups in the molecule (Figure 2). For this reason the absorbance values obtained from equation (2) with the computed parameters were only partly in agreement with the experimental data. A good fit over the entire pH range was achieved by substituting K_2 in equation (2) with the term

$$K = K_2\alpha + K_3(1 - \alpha) \quad (4)$$

K [equation (4)]. K_3 is, in principle, an arbitrary value and α is a pH-dependent parameter given by a modified form of the Henderson–Hasselbalch equation (5).

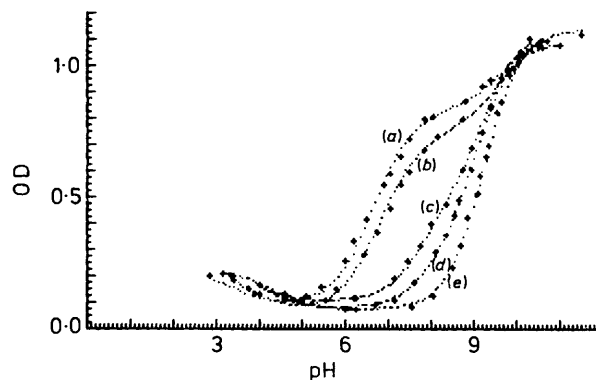


Figure 3. Plots of optical density vs. pH for 4-hydroxybenzoic acid in the presence of monomer ($0.052 \text{ mol dm}^{-3}$) of PEI buffers (a), and with KCl added: 0.008 (b), 0.087 (c), 0.256 (d) mol dm^{-3} ; in the absence of PEI (e). Experimental points (+). Dotted lines are calculated from equations (4) and (5) and the data given in Table 2.

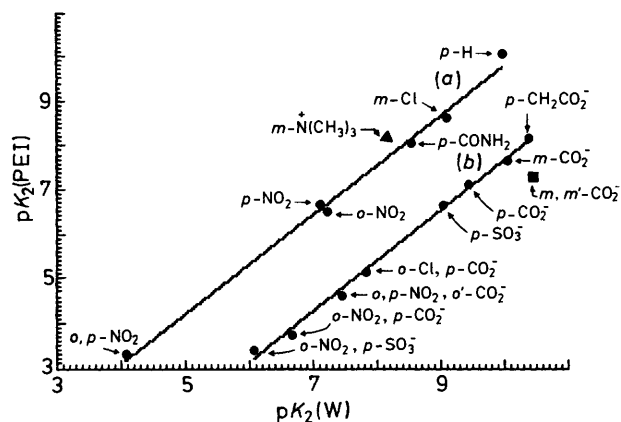


Figure 4. Plots of pK_2 (PEI) vs. $pK_2(W)$: (a) monoprotic phenols; (b) diprotic phenols. (■) 5-Hydroxyisophthalic acid and (▲) 3-hydroxy- N,N,N -trimethylphenylammonium iodide are not computed.

$$\alpha = 1/[1 + 10 \exp(\text{pH} - pK_0)/n] \quad (5)$$

In this way it is possible to ‘weight,’ depending on pH, the contribution to the optical density of the terms containing K_2 or K_3 . The best fit was achieved, as shown in Figure 2, using the computed values of K_1 and K_2 in PEI, and giving to K_3 values equal or very close to the acidity constants of the phenols in water [$K_2(W)$ of Table 1]. pK_0 values in the range 7.1–8.0 and n values in the range 1–1.07 were satisfactory. As an insight into the significance of the parameters α , K_0 , and n , note that α can formally correspond to the degree of ionization of a monomeric ($n = 1$) or polymeric ($n > 1$) (ref. 10) amine in which $pK = pK_0$.

The effect of varying the ionic strength on phenols of this type is shown in Figure 3 for 4-hydroxybenzoic acid. The presence of KCl modified the curve in the part due to K_2 , which was shifted towards that obtained in the absence of PEI. The computed value of pK_1 , pK_2 , ϵ_M and the parameters pK_3 , pK_0 , and n used to obtain the best fit of the spectrophotometric titration curves are reported in Table 2.

The effect of polycations, other than PEI, on the pK of the phenolic group was tested with PDDA on 4-hydroxybenzoic acid [$pK_2(W)$ 9.44] and with PVBA on 4-hydroxy-3-nitrobenzenesulphonate [$pK_2(W)$ 6.08]. pK_2 values 8.77 and 5.02 were found, respectively, in the presence of the polycations and no inflection indicative of a ‘third’ protogenic group was observed in the curve OD vs. pH. Both polycations were less efficient than PEI although both contain quaternary ammonium groups

which can participate in electrostatic interactions with carboxylate or sulphonate groups.

In order to ascertain the generality of the effect of PEI we have correlated the values of pK found in PEI with those found in water without the polyelectrolyte (Figure 4). The pK values of compounds (7) and (15) were not computed because of the singularity of their structure (cationic and triprotic, respectively). For monoprotic phenols [compounds (1)–(6)] we found the relationship (6).

$$pK_2(\text{PEI}) = (1.12 \pm 0.04) pK_2(\text{W}) - (1.39 \pm 0.35) \quad (6)$$

The slightly higher acidity of the phenolic groups in PEI, as expressed by the slope and the intercept, appears in the same direction as the electronic effect of the substituents (the greater the withdrawing effect the greater the difference in pK^*).

For diprotic phenols [compounds (8)–(16)] the correlation with the acidity of the carboxy group is unreliable because the pK_a values are closely grouped [3.79–4.40 in water, except for that of 3,5-dinitrosalicylic acid (0.35)] so that the slope is practically defined only by the pK of the latter compound. In any case the acidity constant is affected by the presence of the polyelectrolyte, by a lowering of the pK by, at most, 0.9 units. The correlation of the pK values of the phenolic groups is expressed by equation (7).

$$pK_2(\text{PEI}) = (1.14 \pm 0.04) pK_2(\text{W}) - (3.76 \pm 0.31) \quad (7)$$

The closeness of the slopes of equations (6) and (7) to unity reveals that the sensitivity of pK to the nature of the substituents in the presence or absence of a second ionizable group, is not modified by PEI. However, the difference of 2.37 pK units in the intercept reveals that the presence of an anionic group in the substrate introduces a further interaction, seemingly electrostatic in nature, with a gain of 13.5 kJ mol^{-1} in the free energy of ionization.

Conclusions

The acidity constants of various phenols in aqueous solution are increased by the presence of PEI, especially when there is a second ionizable group on the molecule. We can tentatively rationalise the facts on the premise that the phenolic group would be in a microenvironment in which proton transfer could be facilitated compared with a simple aqueous solution. The effect is more relevant if the phenol possesses an anionic carboxylate or sulphonate group which can be attracted by the polycation as the counter-ion.

The addition of KCl in the presence of PEI, causes a shift in the pK of the phenolic group towards the higher values found in the absence of the polymer. The Cl^- ions would shield the

electrostatic interaction, so that the ionization of the phenolic group would occur further and further away from the polyion surface. Moreover, when the acidity of the phenolic group in the presence of PEI is rather low, [$pK_2(\text{PEI}) > 7$] its complete ionization occurs at values of pH so high that the polyamine is hardly protonated. Owing to the lack of positive charges the polymer can no longer attract the anionic carrier and consequently exerts no effect on the dissociation of the phenol. This results in the appearance of the third unexpected protegenic group, that belonging to the free phenol no longer bonded to the polymer. A common feature of the compounds that show such behaviour [(8), (9), (14), and (15)] is that the acidity of the phenolic group allows complete neutralization at $\text{pH} \geq 7$. This value of pH is of particular importance: according to Manning¹⁷ the distribution of mobile ions on a polyelectrolyte of degree of ionization i , depends on a charge parameter ξ which for PEI at 25 °C assumes the value $\xi = 1.88$. For $\xi < 1$ the counter-ions are assumed to be no longer condensed on the polymer chain although still 'territorially bound' to it.¹⁸ At a PEI concentration of monomer of *ca.* 0.05 mol dm^{-3} at pH 7, $i = 0.52$ and then $\xi = 0.99$ which is very close to the critical value for the association.

On this basis, the complete ionization of a phenol of pK_a *ca.* 7 will occur at a pH well above the mentioned critical value, when it is no longer electrostatically associated with the polymer by its carboxylate group.

The lesser effect exerted by the quaternary ammonium polycations PDDA and PVBA which have a pH -independent charge parameter 1.55† and 2.8 (ref. 19), respectively, suggests that hydrogen-bonding stabilization of the phenolate anion could play an important role with PEI.

It has been ascertained that the microenvironment polarity in synthetic polymers containing nitrogen bases such as poly(vinylpyridine),^{20,21} poly[4(5)vinylimidazole],²² and linear poly(ethyleneimine),²³ is usually lower than the polarity of the bulk solution. This condition would destabilize the ions and would therefore result in an increase in the pK as found for the dissociation constants of phenols in solvents of lower dielectric constant than water.^{13b} In contrast, hydrogen bonding to the amino group could be favoured by electrostatic forces as in enzyme–substrate interactions.²⁴

A semiempirical way of recalculating the pH dependence of the optical density for the weaker phenols is offered by equation (2) in the form modified by equations (4) and (5). It allows the introduction of, depending on pH , the contribution of the bonded and unbonded phenol. We have further verified its validity with a phenol of substantially different structure, namely, bromothymol blue. Also in this case, a sigmoidal curve with two inflections is observed in the presence of PEI, in which the pK of the phenolic group is lowered by 2.0 with respect to that of water.‡

Finally the goodness over a large pK range (*ca.* 5 pK units) of the correlations of pK in PEI to those without it, for both types of phenols that we have examined, rules out any specific interaction of substrates with PEI, despite the non-homogeneity of its structure and of the variety of the substituents on the phenols. Moreover, the results could be reasonably extended to similar phenols in which the pK values are too high to be determined experimentally in the presence of PEI, *e.g.* salicylic acid [$pK_2(\text{W}) = 13.82$ (ref. 12(a))].

An alternative interpretation of the results is possible, in which the activity of water or the pH in the proximity of the polymer, where the phenol is associated, could be different from that of the bulk solution. The ratio dissociated:undissociated phenol [assuming that the pK is not influenced by PEI in the use of equation (1) or (2)] would operate as an indicator of a local acidity, which would be higher than that expected from the pK_{app} of PEI.

* We considered that the pK values in water are known with a higher precision than those in PEI. The estimated standard errors of the two correlations (6) and (7) are slightly higher than in the inverse correlation.

† The charge parameter for PDDA was calculated according to ref. 19 taking $b = 0.46$ nm as the interchange distance.

‡ The pH dependence of the absorbance of an aqueous solution of bromothymol blue (BTB) (1.42×10^{-5} mol dm^{-3}) and PEI monomer (4.1×10^{-3} mol dm^{-3}) gave a sigmoidal curve with two inflections. Values of pK_2 5.3, pK_3 7.3, pK_0 6.0 and $n = 1$ in equations (4) and (5) showed close agreement between the experimental and recalculated values of the optical density *vs.* pH . In ref. 6, under very similar conditions, a unique value of pK_{app} 6.1 is reported. In water, the $pK = 7.3$ (thermodynamic).²⁵ We have also observed that the u.v.–visible spectrum of BTB was significantly affected by the ratio PEI/BTB. Furthermore, at a fixed molar ratio of PEI to BTB (280), not only was the spectrum obviously modified by pH , but the isosbestic point was lost. These observations suggest the existence of complex equilibria in the dye–polyelectrolyte system.

Whatever the correct interpretation, the determination of the pK of the phenolic group is a way of quantifying the interaction of the polyion with the associated substrate. In fact, the pK_a of the conjugate acid of the leaving group and the basicity of nucleophiles is also essential in some reactions, e.g. aminolysis of phenylacetates, in determining the reaction rate and for information about the mechanism on the basis of linear free-energy relationships.²⁶

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