First pKa Values of Some Acid-Base Indicators

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Abstract ☐ An attempt was made to estimate the first pKa values of bromocresol green, bromocresol purple, bromophenol blue, cresol red, and phenol red using a method similar to that of Reilley and Sawyer. Values of −0.75 (−2.13 on the Hammett acidity scale) for bromocresol purple, +1.05 for cresol red, and +1.03 for phenol red were estimated. pKa values of cresol red and phenol red were not estimated on the Hammett acidity scale, since this scale is good only for acidic solutions stronger than 0.1 M. Trials to estimate the first pKa values of bromocresol green and bromophenol blue were not successful due to the upper limitation on the strength of commercially available hydrochloric acid. Values of −0.85 (approximately −2.7 on the Hammett acidity scale) or less for bromocresol green and −0.95 (−3.2 on the Hammett acidity scale) or less for bromophenol blue have been predicted.

Keyphrases ☐ Indicators, acid-base—first pKa determination ☐ pKa determination, first—acid-base indicators ☐ Dyes, organic—first pKa determination

Many organic dyes are used as acid-base indicators by scientists in a variety of analytical and industrial applications. Some of these dyes have also found use as diagnostic agents in medicine (1–4). Some of them are used in the quantitative determination of many pharmaceutical amines, since they form stable salts with this group of chemicals (5–8). These amine dye salts can be extracted with organic solvents and the dye component measured spectrophotometrically (9).

Preliminary investigations on bromothymol blue, reported by Gupta and Cadwallader (10), indicated that these dyes may have more than one pKa value. For example, the literature value of about 6.3 for bromocresol purple (11) may be the pKa₂ rather than the pKa₁ value.

The purpose of this research was to determine the first pKa values for: (a) bromocresol green (BCG); (b) bromocresol purple (BCP); (c) bromophenol blue (BPB); (d) cresol red (CR); and (e) phenol red (PR). The usefulness of this information is well documented. For example, without knowing the first pKa value, it is not possible to determine the true partition coefficients of these dyes.

EXPERIMENTAL

Reagents—All chemicals and reagents used were either USP, NF, or A.C.S. grade. All of the dyes were used without further purification.[1]

Preparation of Solutions—Each dye (50.0 mg.) was dissolved in 10 ml. of ethyl alcohol in a 100-ml. glass-stoppered volumetric flask, and sufficient distilled water was added to make a total volume of 100 ml. Solutions of lower dye concentration were prepared by diluting this stock solution with hydrochloric acid of various concentrations. The concentrations of the various dyes are reported in Table I. Hydrochloric acid USP was diluted with distilled water to obtain the dilutions needed.

Determination of pKa Values—The pKa values were determined according to the procedure of Reilley and Sawyer (12). Solutions

Table I—Concentrations of Various Dyes Used

Dye	Concentration, % w/v
BCG	0.001
BCP	0.001
BPB	0.001
CR	0.001[a]
	0.0005[a]
PR	0.001[a]
	0.0005[a]
	0.00025[a]

[a] More than one concentration was used to obtain readings within the scale of the spectrophotometer.

of each dye in hydrochloric acid solutions of various concentrations were scanned between 360 and 600 mμ, using a Beckman DK2 spectrophotometer. Distilled water was used as the blank. Two wavelengths were chosen where the (H₂I) and (HI⁻) forms of each dye showed a maximum difference in their absorbance. Plots of absorbance *versus* the theoretical pH value (−log H⁺) were prepared for each of the two wavelengths selected. Two horizontal lines across each of the plots were drawn, one corresponding to the absorbance of the dye solution having a theoretical pH value of −1.0 and the other corresponding to the absorbance of the dye solution having a theoretical pH value of −0.398 or higher.

Line A represents the absorbance of the dye, *i.e.*, the indicator dye represented as "I," when present entirely in the (H₂I) form. Line B represents the absorbance of the dye when present entirely in the (HI⁻) form. The midpoint of each curve, between Lines A and B,
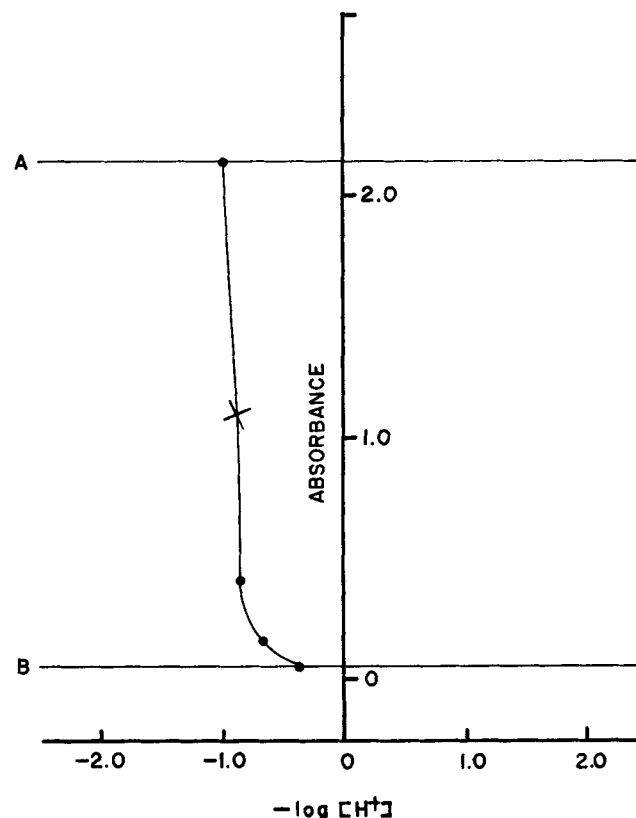

Figure 1—*Determination of the first pKa value of BCG using absorbance values at 564 mμ.*

Table II—First pKa Values of Various Dyes

Dye	First pKa Value	Average	First pKa Value Using Hammett Acidity Function	Average
BCP	−0.78		−2.15	
BCP	−0.73		−2.11	
BCP	−0.75		−2.12	
BCP	−0.75		−2.13	
		−0.75[a]		−2.13[a]
CR	1.08			
CR	0.97			
CR	1.10			
CR	1.05			
		1.05[a]		
PR	1.03			
PR	0.95			
PR	1.05			
PR	1.07			
		1.03[a]		

[a] Average of the four values.

represents the equal concentration of the (H_2I) and (HI^-) forms of each dye. This was marked as the midpoint on each curve. The results are presented in Table II. Figures 1–3 are presented as samples. In the case of BCP, the pKa values were also estimated using H_0 (Hammett acidity function) instead of theoretical pH. Results are presented in Table II. From these figures, the ratio of (HI^-) to (H_2I) at various pH values was obtained by measuring the relative distances of the point from the (HI^-) and (H_2I) lines. Plots of log (HI^-/H_2I) (vertically) versus theoretical pH were prepared for each of the two wavelengths selected. The point where the line crossed
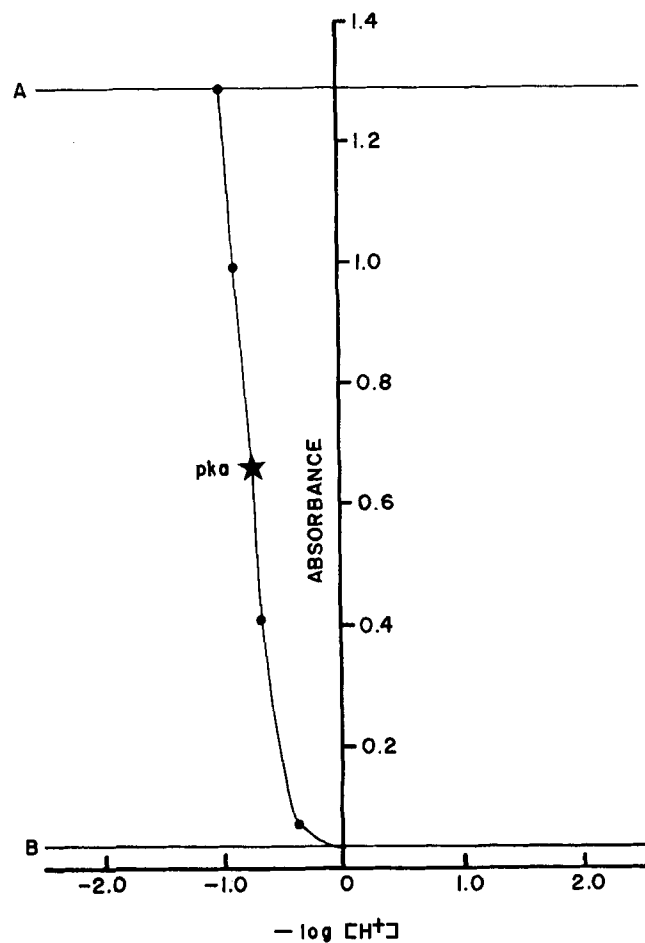
the pH axis corresponded to the pKa_1 value, since (H_2I) ⇌ (HI^-) + (H^+). The dissociation of (HI^-) to (I^{--}) and (H^+) can be neglected in the pH range of −1.0 to approximately 2.0, since K_2 values of these dyes range from 1×10^{-4} to 5×10^{-9}. The results are presented in Table II. Figure 4 is presented as a sample. In the case of BCP, the pKa values were also estimated using H_0 instead of pH. Results are presented in Table II.

DISCUSSION AND CONCLUSIONS

Bromocresol Green—Trials to estimate the first pKa value of this dye were not successful, since the difference between the absorbance readings at the theoretical pH values of −0.875 and −1.0 was so high (Fig. 1) that it was not possible to assume that the whole dye existed in the (H_2I) form at the lowest theoretical pH value of −1.0. It was not possible to prepare dye solutions of much lower theoretical pH values due to the upper limit on the strength of commercially available hydrochloric acid. From Fig. 1, it appears that the first pKa value of this dye is −0.85 (approximately −2.7 on the Hammett acidity scale) or less.

Bromocresol Purple—The first pKa value of this dye was estimated to be −0.75 or −2.13 on the Hammett acidity scale (Figs. 2 and 4 and Table II). The true pKa value may be somewhat lower, since the dye might not be totally in the (H_2I) form at the theoretical pH value of −1.0. This is due to the fact that the difference between the absorbance values at the theoretical pH values of −0.875 and −1.0 (Fig. 2) is not negligible.

Bromophenol Blue—Trials to estimate the first pKa value of this dye were not successful due to the reasons reported for BCG. From Fig. 3, it appears that the first pKa value of this dye is −0.95 (approximately −3.2 on the Hammett acidity scale) or less.

Cresol Red—The first pKa value of this dye was estimated to be +1.05 (Table II). This value appears to be correct, since a transition interval of +0.2 to +1.8 (red to yellow) for this dye has been reported (13). The pKa value of this dye was not estimated on the Hammett acidity scale, since this scale is good only for acidic solutions stronger than 0.1 M.
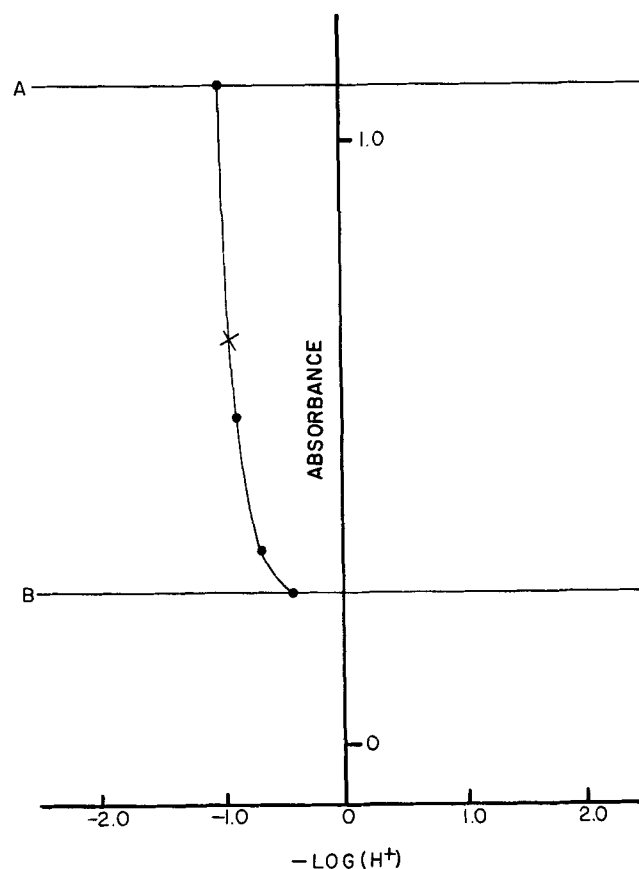

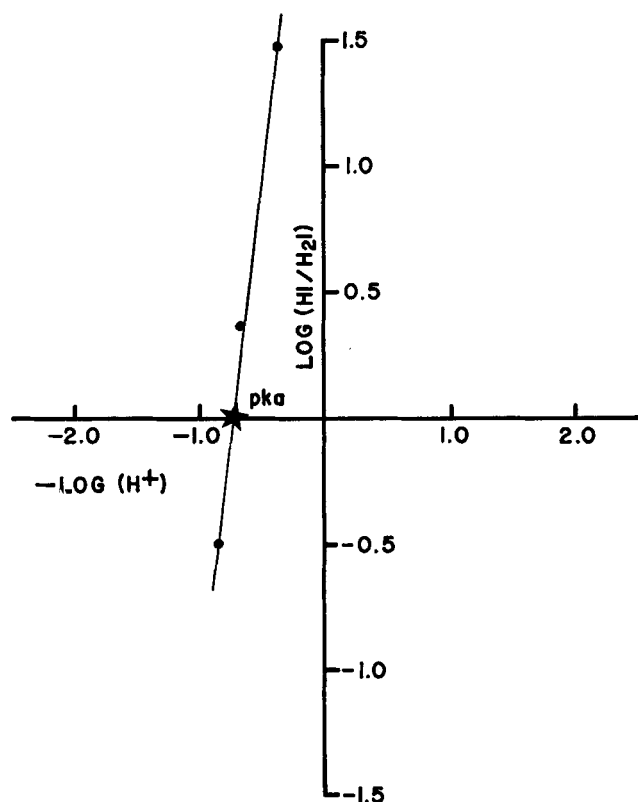**Figure 2**—*Determination of the first pKa value of BCP using absorbance values at 530 mμ.*

Figure 3—*Determination of the first pKa value of BPB using absorbance values at 530 mμ.*

Figure 4—*Determination of the first pKa value of BCP using log* (HI^-/H_2I) *(from Fig. 2) versus* $- log(H^+)$ *plot.*

Phenol Red—The first pKa value of this dye was estimated to be +1.03 (Table II). The Hammett acidity scale was not used due to reasons previously explained.

It was not possible to take into account the activity coefficients at these higher concentrations of hydrochloric acid. This will, no doubt, cause some error in the determination of the first pKa values

of these dyes. Wherever possible, the Hammett acidity scale was also used as explained previously.

Analytical Applications—The information provided is very useful for the determination of the true partition coefficients as reported by Gupta and Cadwallader (10). This information could also be useful to correlate the structural formulas of the dyes.

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Dipole Moment and Structure of Thiophene Derivatives and Benzene Analogs

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Abstract ☐ The dipole moments of 2-halothiophene, 2,2'-bithiophene, 2-thiophenecarboxylic acid derivatives, and the corresponding benzene analogs have been measured in benzene and in dioxane. Evidence is presented that the conformation in 2-thiophenecarboxylic acid derivatives has the thiophene dipole (which has the sulfur negative) opposed to the resultant dipole of the carboxyl or ester group. The conformation in 2,2'-bisthiophene is shown to be *cis*. In dioxane, there is more resonance interaction between the thiophene ring and the functional groups than between the benzene ring and these groups. The chemical shift and the coupling constant of the NMR spectra of the 2-halothiophenes and 5,5'-dihalo-2,2'-bithiophenes have been assigned.

Keyphrases ☐ Thiophene derivatives, benzene analogs—dipole moment, structure determination ☐ NMR spectroscopy—structure

The dipole moment has been shown to be a useful electronic parameter in some structure–activity correlation studies (1), *e.g.*, the insecticidal activity of chlorphenothane (DDT) isomers (2), the cholinesterase inhibitory activity of *N*-alkylsubstituted amides (3), the

respiratory stimulation activity of cyclic ureas and thioureas (4), and the inhibition of viral neuraminidase by dihydroisoquinoline derivatives (5).

The usefulness of dipole moments in structure–activity correlation is more restricted than other physico-