

DETERMINATION OF THE FIRST pK_a VALUES
OF SOME SULFONPHTHALEIN DYES

A Thesis

Presented to

The Faculty of the College of Pharmacy

University of Houston

In Partial Fulfillment

of the Requirements for the Degree

Master of Science

by

John B. Reed, Jr.

May 1969

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ABSTRACT

An attempt was made to estimate the first pK_a values of Bromocresol Green, Bromocresol Purple, Bromophenol Blue, Cresol Red and Phenol Red using a method similar to that of Reilley and Sawyer. A value of -0.75 for Bromocresol Purple; +1.05 for Cresol Red and +1.03 for Phenol Red was estimated. Trials to estimate the first pK_a values of Bromocresol Purple and Bromophenol Blue were not successful due to the upper limitation on the strength of commercially available hydrochloric acid. A value of -0.85 or less for Bromocresol Green, and -0.95 or less for Bromophenol Blue has been predicted.

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CHAPTER I

INTRODUCTION

Many organic dyes are used as acid-base indicators by scientists all over the world 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 have also been 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, et al., (10) indicated that these dyes may have more than one pK_a value. For example, the literature value of 6.05 to 6.3 for Bromocresol Purple (11) may be the pK_{a_2} rather than the pK_{a_1} value.

The purpose of this research was to determine the first pK_a values for (1) Bromocresol Green (BCG), (2) Bromocresol Purple (BCP), (3) Bromophenol Blue (BPB), (4) Cresol Red (CR), and (5) Phenol Red (PR). The usefulness of this information is well documented. For example, without knowing the first pK_a value, it is not possible to determine the true partition coefficients of these dyes.

CHAPTER II

HISTORY

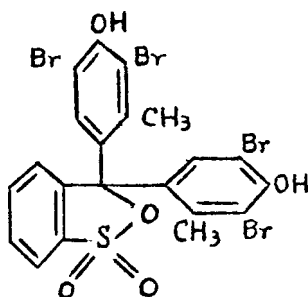
Acid-base indicators (dyes) are able to assume a color, which varies with the pH of the solution in which they are contained. Several investigators have attempted to define indicators in relation to mechanism of color change. Ostwald (12) defined indicators as weak acids or bases, which were able to exhibit a different color in the undissociated form from that of their ionic forms. Hantzsch (13) demonstrated that color change was a result of a change in the structural formula of the dye. Subsequently, Kolthoff (14) proposed that indicators were weak acids or bases, of which the ionogenic form possessed a color and constitution different from the color and structure of the pseudo- or normal dye compound. All of the indicators which were investigated belong to the sulfonphthalein group of dyes. The preparation of various sulfonphthalein dyes (15-18) from o-sulfobenzoic acid, molten zinc chloride, and a phenol (which may be halogenated) has been described (19-21).

Brode (22) found that the positions of the absorption bands in the visible range of various indicators do not change as the hydrogen ion concentration is varied, but that the intensity of the transmitted light diminishes or increases. When the ratio of the maximum to the minimum quantity of transmitted light is plotted as a function of the pH, a curve results which yields the dissociation constant of the indicator. Kolthoff (23) has summarized the data in the literature regarding the effect of ionic strength and temperature on the pK_a values of various indicators. All pertinent available information

the dyes studied is presented in Tables I-VII. Table I presents the structures and chemical names of the indicators studied. Table II presents a description of the dyes and some of their physical constants. Tables III-VII present a review of the pK_{a_1} values as reported in the literature.

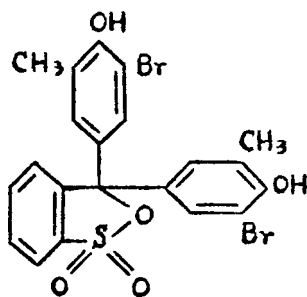
TABLE I. CHEMICAL STRUCTURES AND NAMES OF VARIOUS DYES

BROMOCRESOL GREEN



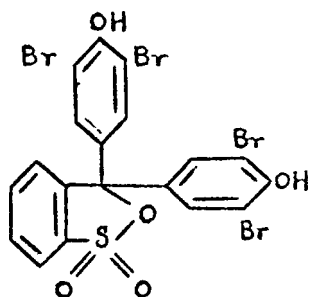
3, 3', 5, 5' Tetrabromo-M-cresol sulfonphthalein

BROMOCRESOL PURPLE



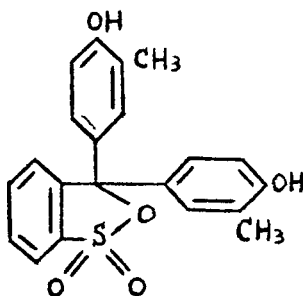
5, 5', Dibromo-O-cresol sulfonphthalein

BROMOPHENOL BLUE



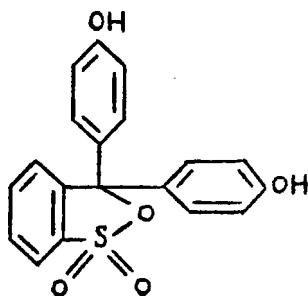
3, 3', 5, 5' Tetrabromo phenolsulfonphthalein

CRESOL RED



O-cresol sulfonphthalein

PHENOL RED



Phenolsulfonphthalein

TABLE II. PHYSICAL CONSTANTS OF VARIOUS DYES

Name	Empirical Formula	Molecular Weight	pK _a	Transformation Range	Appearance
Bromocresol Green (BCG) ^a	C ₂₁ H ₁₄ Br ₄ O ₅ S	698.05	4.7	3.8 - 5.4 Yellow-Blue Green	Minute slightly yellow crystals
Bromocresol Purple (BCP) ^b	C ₂₁ H ₁₄ Br ₂ O ₅ S	540.24	6.3	5.2 - 6.8 Yellow-Purple	Minute slightly yellow crystals
Bromophenol Blue (BPB) ^c	C ₁₉ H ₁₀ Br ₄ O ₅ S	670.02	4.0	3.0 - 4.6 Yellow-Purple	
Cresol Red (CR) ^d	C ₂₁ H ₁₈ O ₅ S	382.42	8.3	7.2 - 8.8 Yellow - Red	Reddish brown crystalline powder
Phenol Red (PR) ^e	C ₁₉ H ₁₄ O ₅ S	354.37	7.9	6.8 - 8.4 Yellow - Red	Bright to dark red crystals

^a From Ref. 11, p. 164. ^b From Ref. 11, p. 164. ^c From Ref. 11, p. 171. ^d From Ref. 11, p. 293. ^e From Ref. 11, p. 811.

TABLE III. LITERATURE REVIEW OF THE pK_a VALUES OF BROMOCRESOL GREEN^a

TEMPERATURE	METHOD	BUFFER SOLUTION	pK_1
27°	spectrophotometric	Clark and Lubs	4.68
30°	spectrophotometric	Clark and Lubs	4.67
Room temp.	spectrophotometric	citrate	4.7
20°	colorimetric	acetate	4.64
38°	colorimetric	acetate	4.68

^aReproduced from Ref. 12, p. 286.

TABLE IV. LITERATURE REVIEW OF THE pK_a VALUES OF BROMOCRESOL
PURPLE^a

TEMPERATURE	METHOD	BUFFER SOLUTION	pK_1
18°	spectrophotometric	citrate (Sørensen)	6.15
Room temp. (18°?)	spectrophotometric	citrate (Sørensen)	6.3
Room temp. (25°?)	spectrophotometric	Clark and Lubs	6.3
20°	colorimetric	Clark and Lubs	6.3
30°	colorimetric	Clark and Lubs	6.26
20°	colorimetric	Clark and Lubs	6.28
Room temp. (25°?)	colorimetric	Clark and Lubs	6.3
15°	colorimetric	Clark and Lubs	6.07
20°	colorimetric	acetate, citrate	6.15
38°	colorimetric	acetate, citrate	6.05

^a Reproduced from Ref. 12, p. 286.

TABLE V. LITERATURE REVIEW OF THE pK_a VALUES OF BROMOPHENOL BLUE^a

TEMPERATURE	METHOD	BUFFER SOLUTION	pK_1
(Approx. 25°?)	spectrophotometric	Clark and Lubs	4.05
(Approx. 18°?)	spectrophotometric	Sørensen	4.0
(Approx. 18°?)	spectrophotometric	acetate	4.10
20°	colorimetric	Clark and Lubs	4.1
15°	colorimetric	Clark and Lubs	4.00±0.05
30°	colorimetric	Clark and Lubs	4.10±0.1
30°	colorimetric	Clark and Lubs	4.1
18°	colorimetric	<u>very</u> dil. HCl	4.09
18°	colorimetric	same+0.05 N KCl	4.10
18°	colorimetric	same+0.1 N KCl	3.84
18°	colorimetric	same+0.5 N KCl	3.77
18°	colorimetric	same+1 N KCl	3.71

^a Reproduced from Ref. 12, p. 285.

TABLE VI. LITERATURE REVIEW OF THE pK_a VALUES OF CRESOL RED^a

TEMPERATURE	METHOD	BUFFER SOLUTION	pK_1
Room temp. (25°?)	spectrophotometric	Clark and Lubs	8.20
Room temp. (18°?)	spectrophotometric	borate (Sørensen)	8.2
Room temp. (18°?)	spectrophotometric	borate (Palitzsch)	8.30
20°	colorimetric	Clark and Lubs	8.3
24°	colorimetric	Clark and Lubs	8.08
15°	colorimetric	Clark and Lubs	8.17
Room temp. (25°?)	colorimetric	Clark and Lubs	8.3

^aReproduced from Ref. 12, p. 287.

TABLE VII. LITERATURE REVIEW OF THE pK_a VALUES OF PHENOL RED^a

TEMPERATURE	METHOD	BUFFER SOLUTION	pK_1
18°	spectrophotometric	phosphate (Sørensen)	7.86
Room temp. (18°?)	spectrophotometric	phosphate, borate	7.9
Room temp. (25°?)	spectrophotometric	Clark and Lubs	7.90
20°	colorimetric	Clark and Lubs	7.87
20°	colorimetric	Clark and Lubs	7.78
20°	colorimetric	Clark and Lubs	7.9
Room temp. (25°?)	colorimetric	Clark and Lubs	7.9
29°	colorimetric	Clark and Lubs	7.72
25°	colorimetric	Clark and Lubs	7.76
15°	colorimetric	Clark and Lubs	7.85
20°	colorimetric	phosphate (Sørensen)	7.74
38°	colorimetric	phosphate (Sørensen)	7.61

^aReproduced from Ref. 12, p.287.

CHAPTER III

EXPERIMENTAL

Reagents: All chemicals and reagents used were either U.S.P., N.F., or A.C.S. grade. The dyes were purchased from Curtin Scientific Company, Houston, Texas, and used without further purification.

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 VIII. Hydrochloric acid, U.S.P., was diluted with distilled water to obtain the dilutions needed.

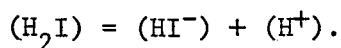
Determination of pK_a' Values: The pK_a' value was determined according to the procedure of Reilley and Sawyer (24). Solutions of each dye in hydrochloric acid solutions of various concentrations were scanned between 360 and 600 μ using a Beckman DK2 Spectrophotometer. Distilled water was used as the blank. Two wavelengths were chosen where the (H_2I) 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 -.398 or higher. Line A represents the absorbance of the dye, i.e., the indicator dye represented

TABLE VIII. 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 in order to obtain readings within the scale of the spectrophotometer.

as "I", when present entirely in the (H_2I) 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, 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 Figures 1 through 10. From Figures 3,4, and 7 through 10, 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 pH concentration were prepared for each of the two wavelengths selected. The point where the line crossed the pH axis corresponded to the pK_{a_1} value, since



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} .

Therefore,

$$K_1 = \frac{(HI^-) (H^+)}{(H_2I)}$$

or

$$\log K_1 = \log (HI^-) + \log (H^+) - \log (H_2I);$$

hence,

$$\text{first } pK_a' = \text{pH} - \log (\text{HI}^-) + \log (\text{H}_2\text{I})$$

or

$$\log (\text{HI}^-/\text{H}_2\text{I}) = \text{pH} - pK_a'$$

when

$$(\text{HI}^-) = (\text{H}_2\text{I}),$$

$$\log (\text{HI}^-/\text{H}_2\text{I}) = \log 1$$

which is zero, and therefore $\text{pH} = pK_a'$. The results are presented in Figures 11 through 16, and Table IX.

CHAPTER IV

RESULTS

FIGURE 1. DETERMINATION OF THE FIRST pK_a VALUE OF BROMOCRESOL GREEN USING ABSORBANCE VALUES AT 446 MILLIMICRONS

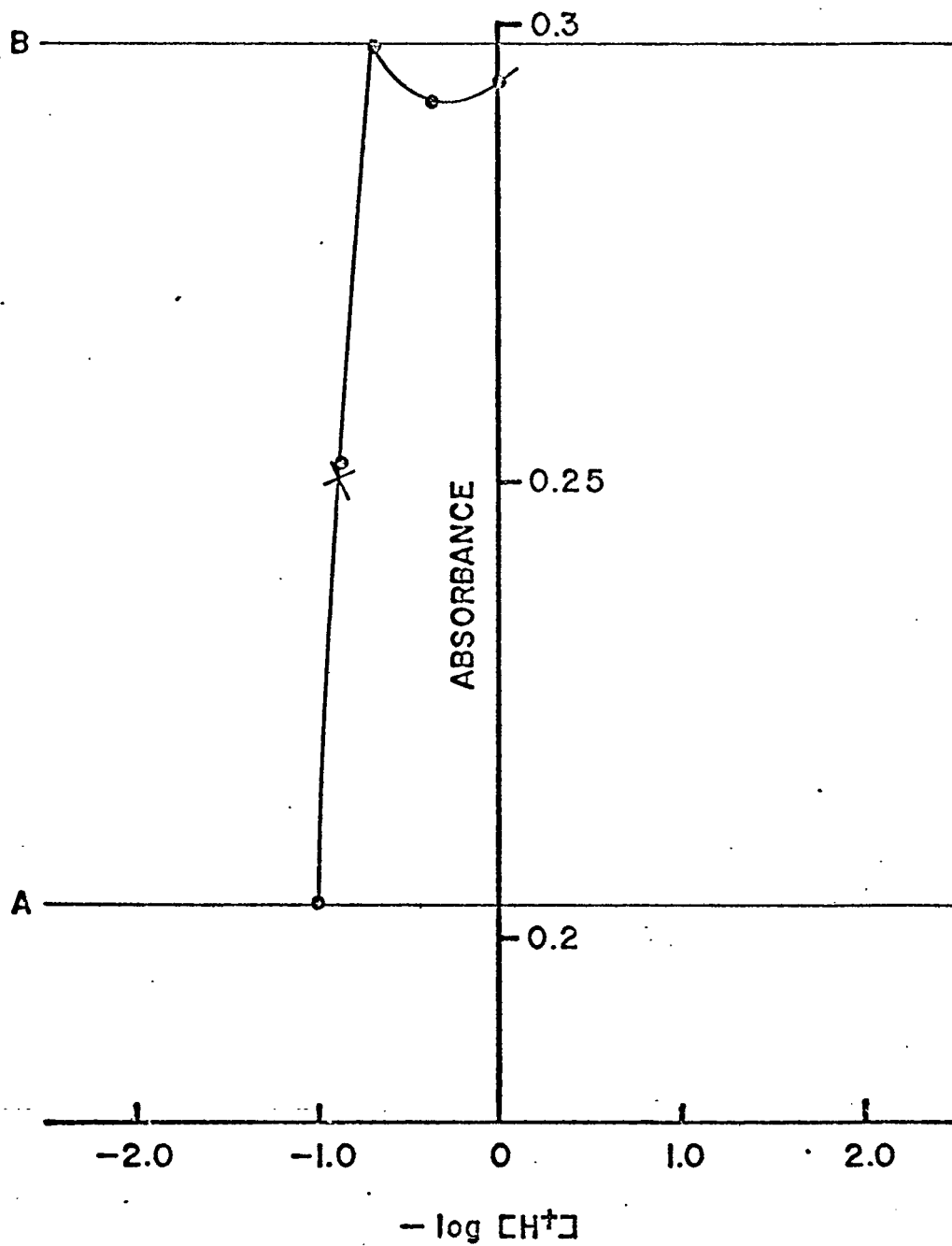


FIGURE 2. DETERMINATION OF THE FIRST pK_a VALUE OF BROMOCRESOL GREEN USING ABSORBANCE VALUES AT 564 MILLIMICRONS

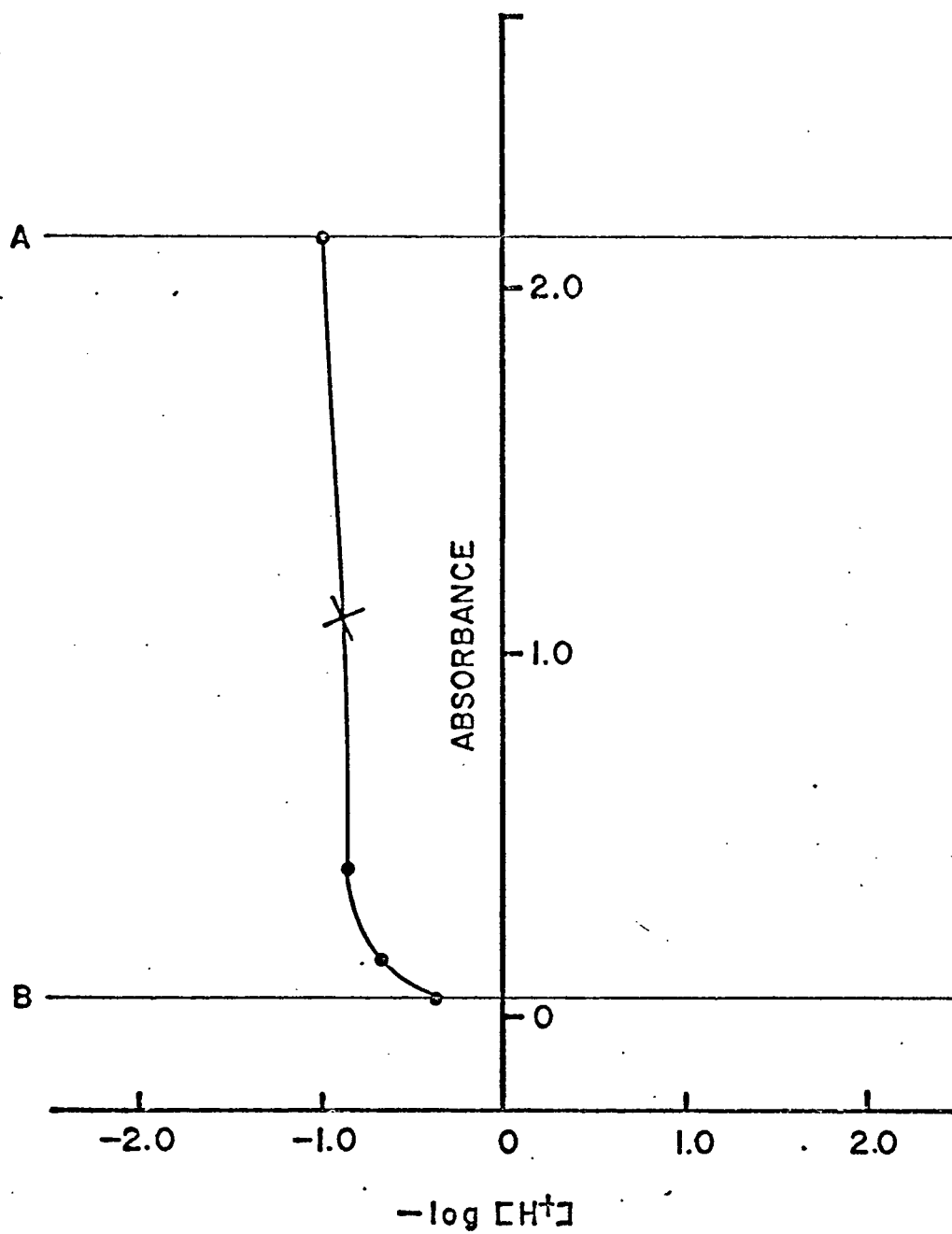


FIGURE 3. DETERMINATION OF THE FIRST pK_a VALUE OF BROMOCRESOL PURPLE USING ABSORBANCE VALUES AT 433 MILLIMICRONS

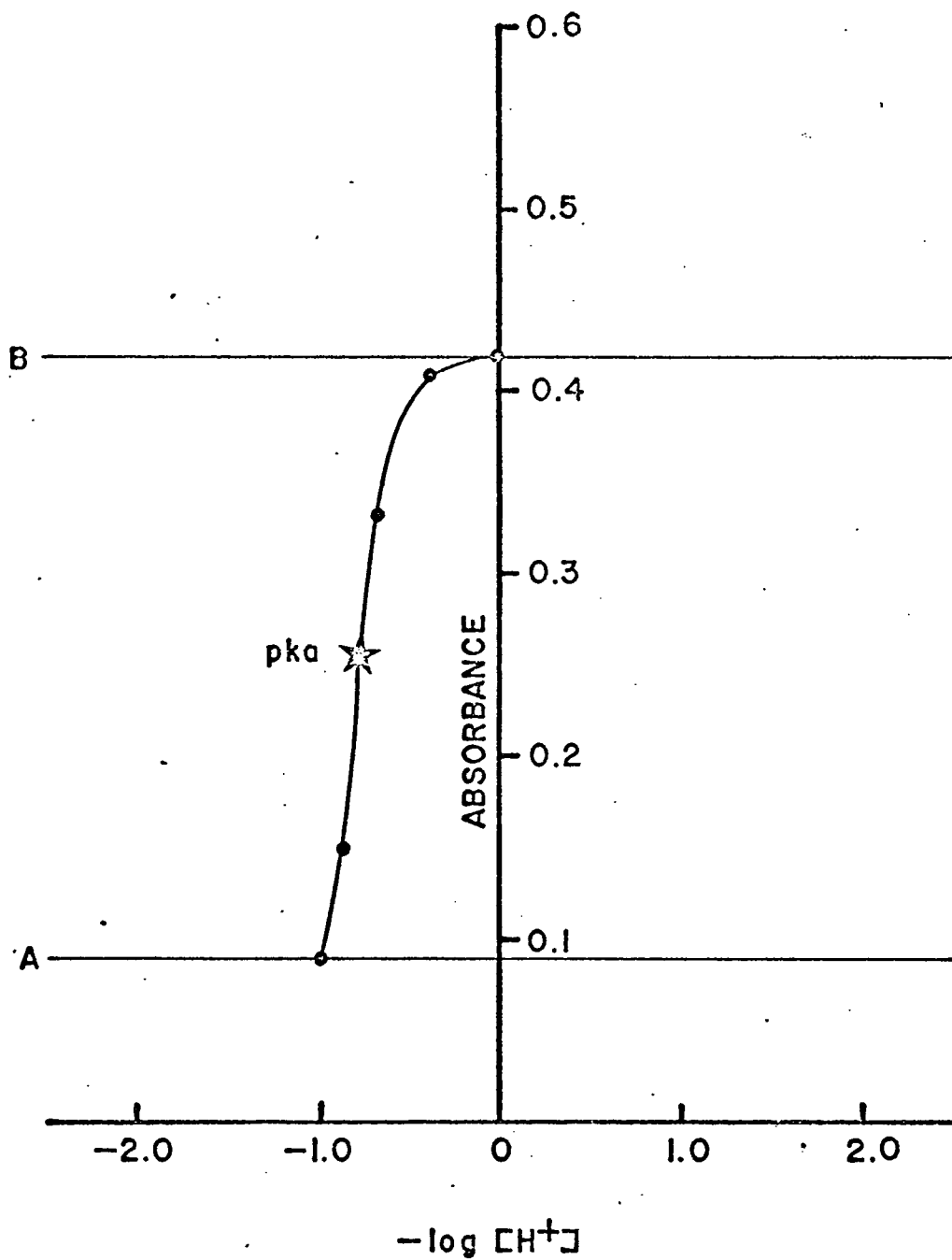


FIGURE 4. DETERMINATION OF THE FIRST pK_a VALUE OF BROMOCRESOL PURPLE USING ABSORBANCE VALUES AT 530 MILLIMICRONS

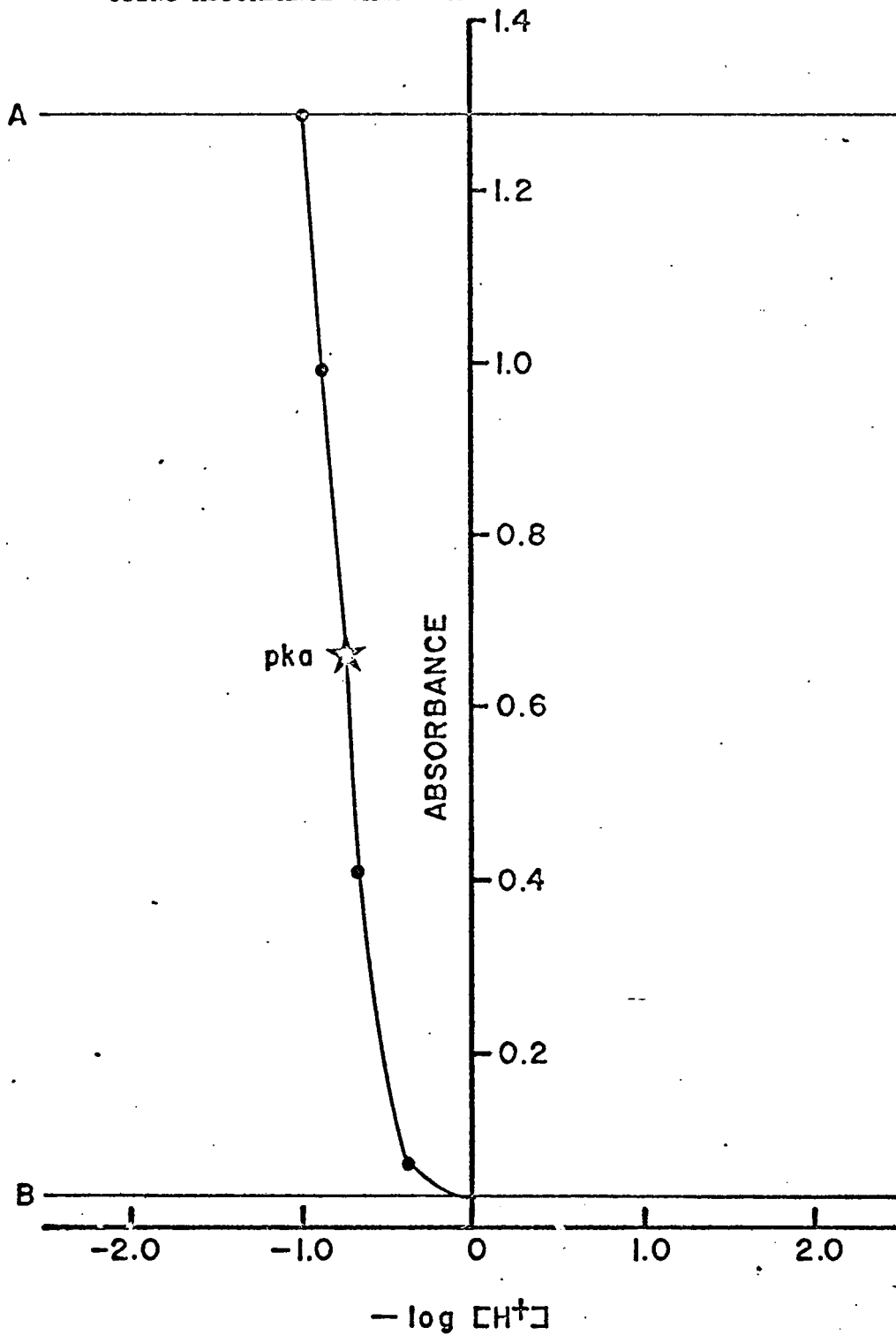


FIGURE 5. DETERMINATION OF THE FIRST pK_a VALUE OF BROMOPHENOL BLUE USING ABSORBANCE VALUES AT 440 MILLIMICRONS

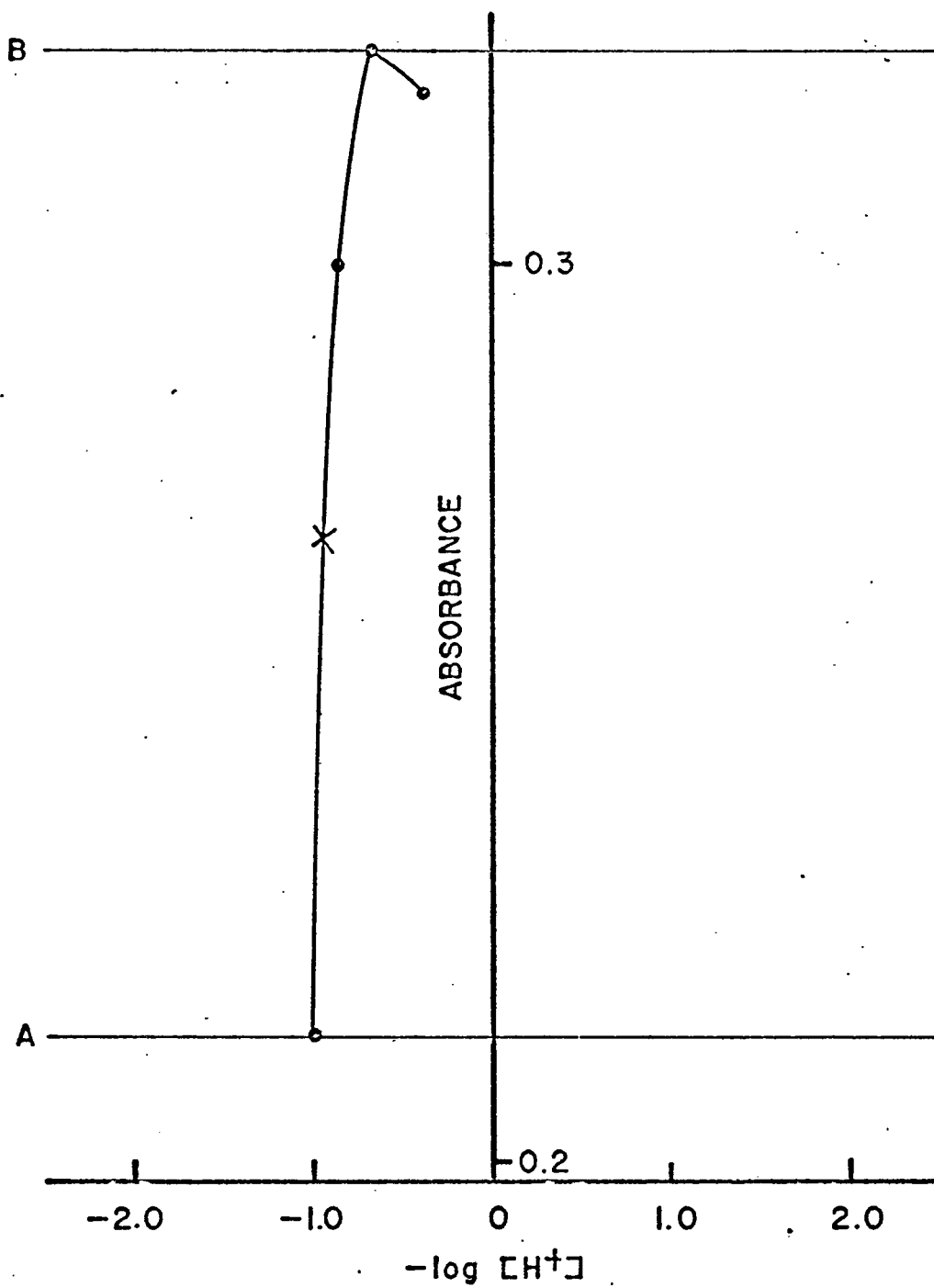


FIGURE 6. DETERMINATION OF THE FIRST pK_a VALUE OF BROMOPHENOL BLUE USING ABSORBANCE VALUES AT 530 MILLIMICRONS

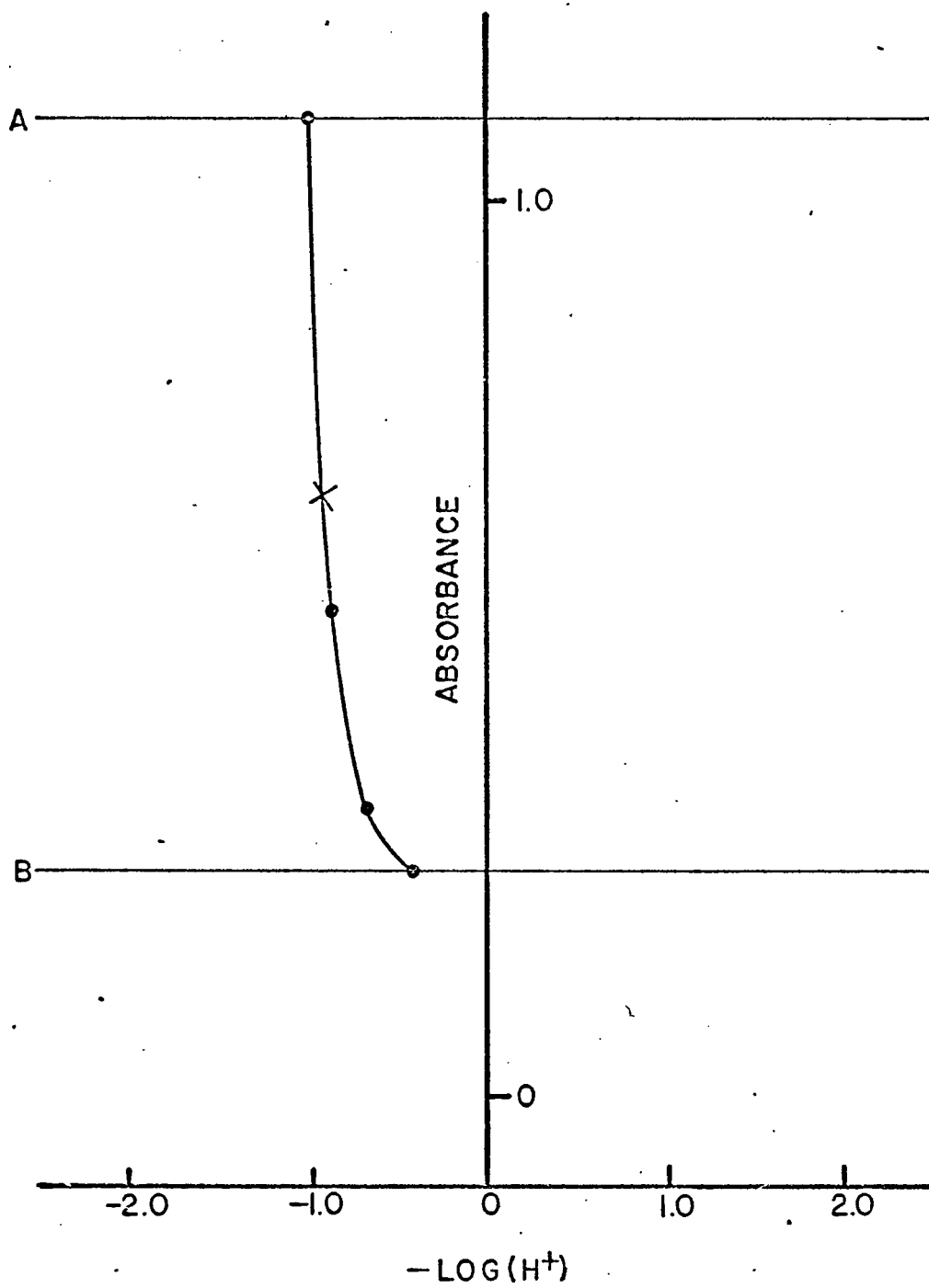


FIGURE 7. DETERMINATION OF THE FIRST pK_a VALUE OF CRESOL RED USING ABSORBANCE VALUES AT 436 MILLIMICRONS

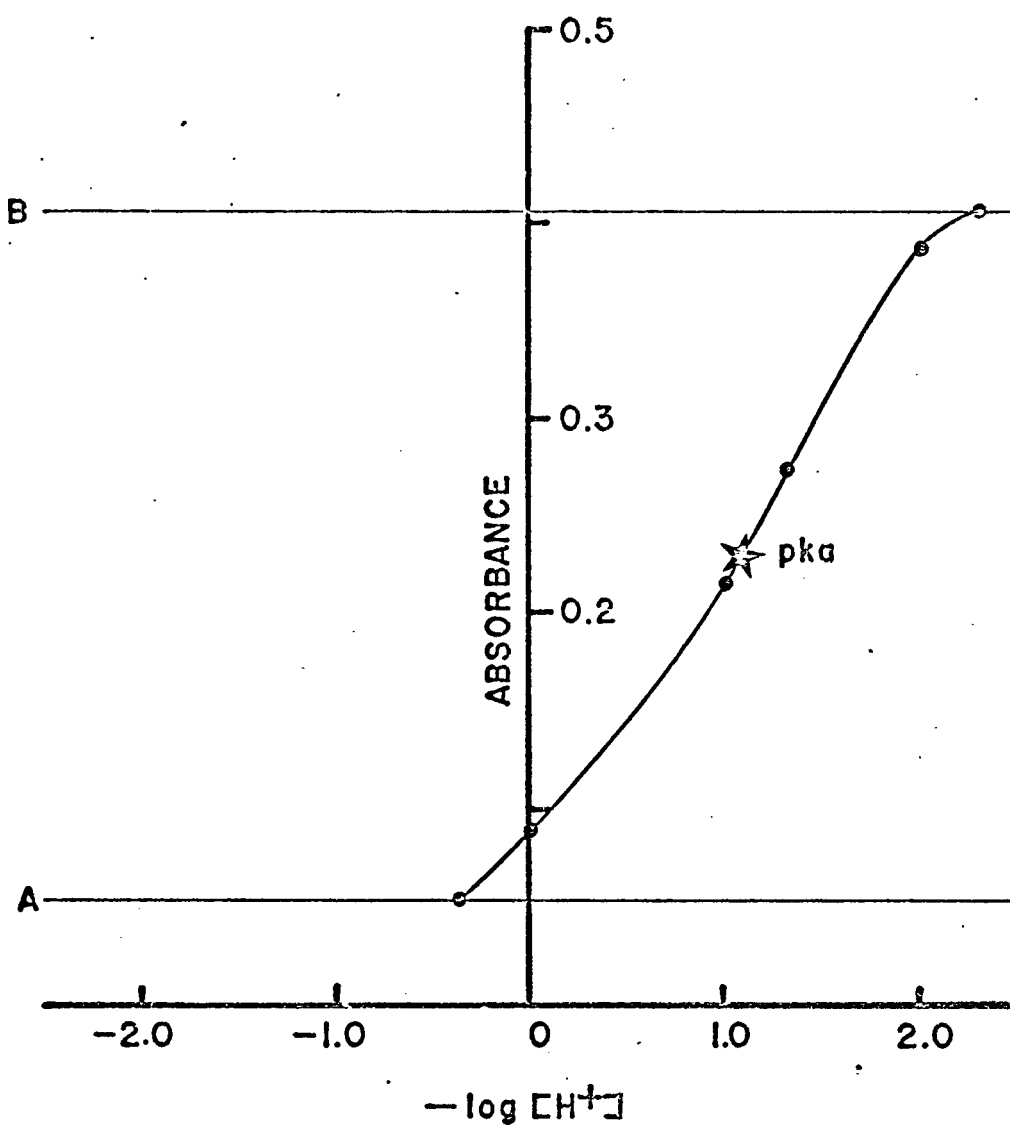


FIGURE 8. DETERMINATION OF THE FIRST pK_a VALUE OF CRESOL RED USING ABSORBANCE VALUES AT 518 MILLIMICRONS

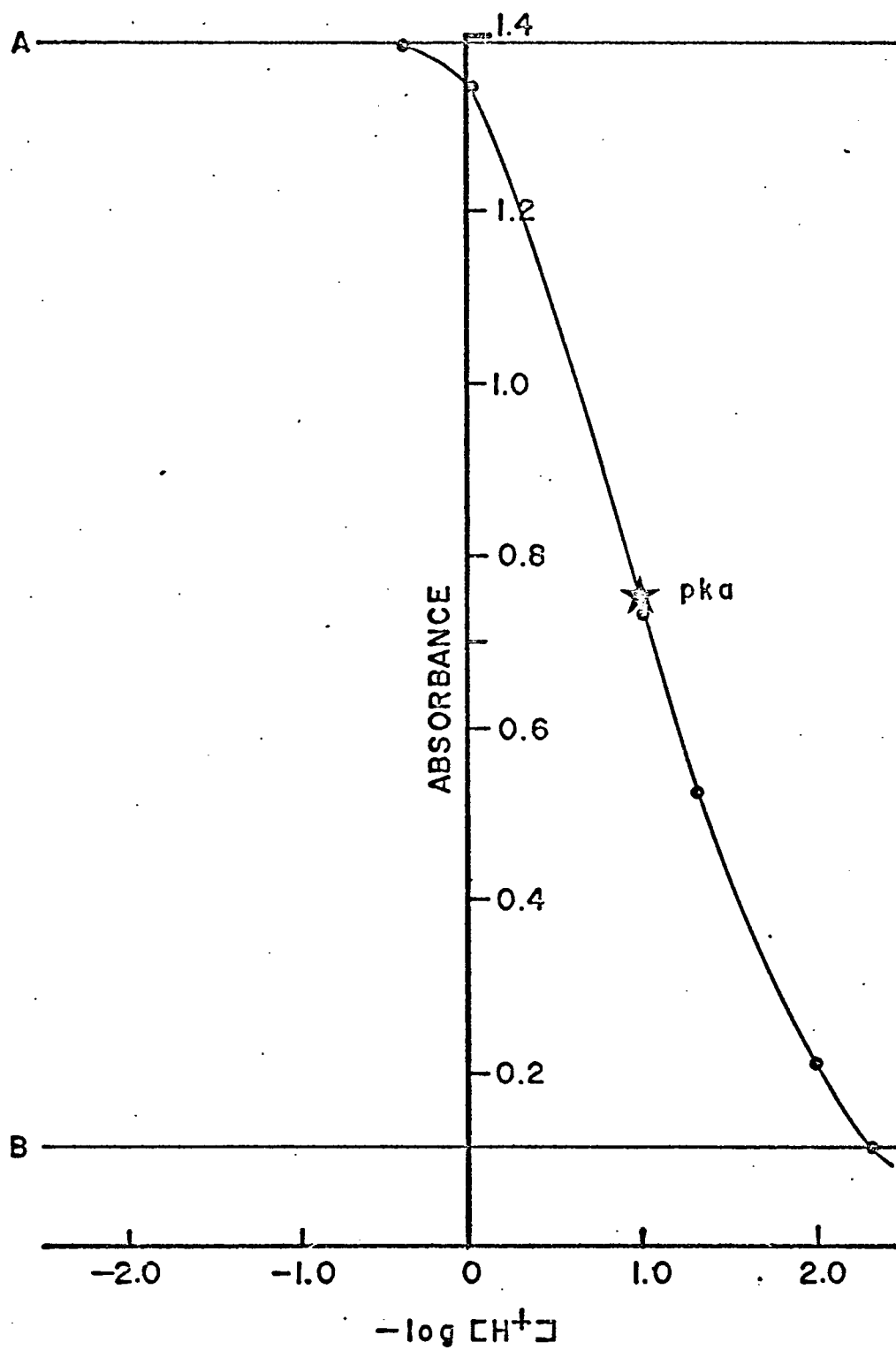


FIGURE 9. DETERMINATION OF THE FIRST pK_a VALUE OF PHENOL RED USING ABSORBANCE VALUES AT 433 MILLIMICRONS

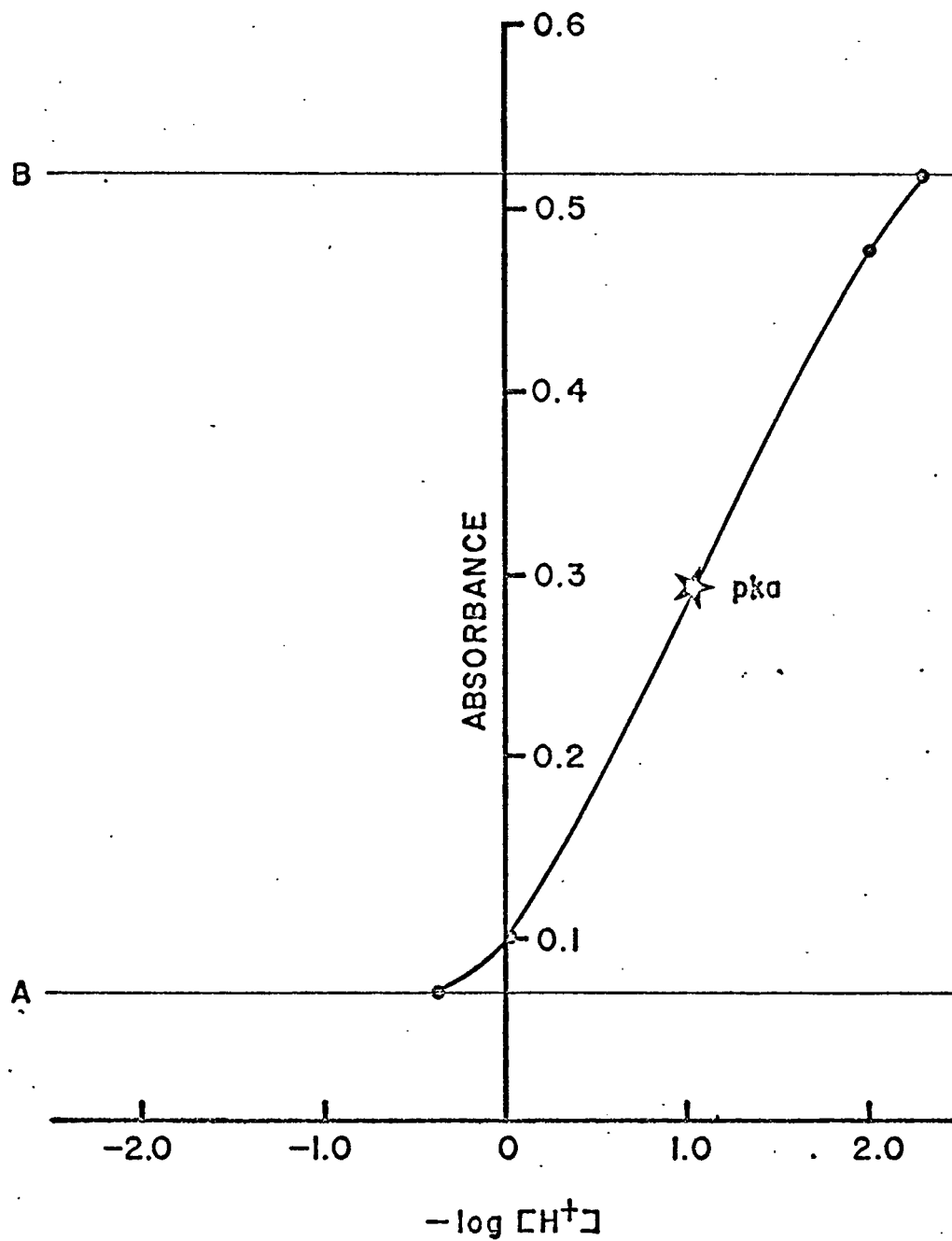
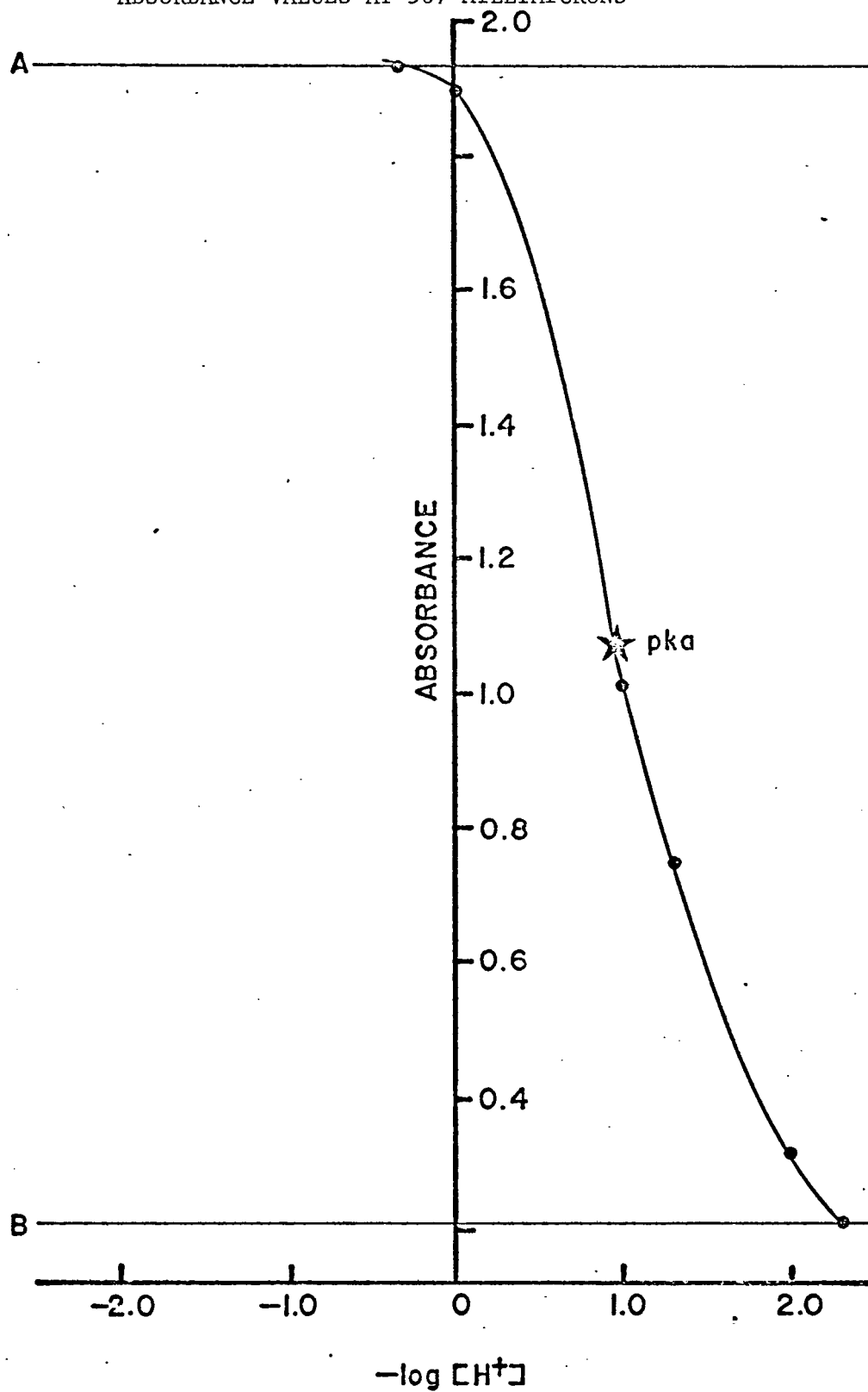


FIGURE 10. DETERMINATION OF THE FIRST pK_a VALUE OF PHENOL RED USING ABSORBANCE VALUES AT 507 MILLIMICRONS



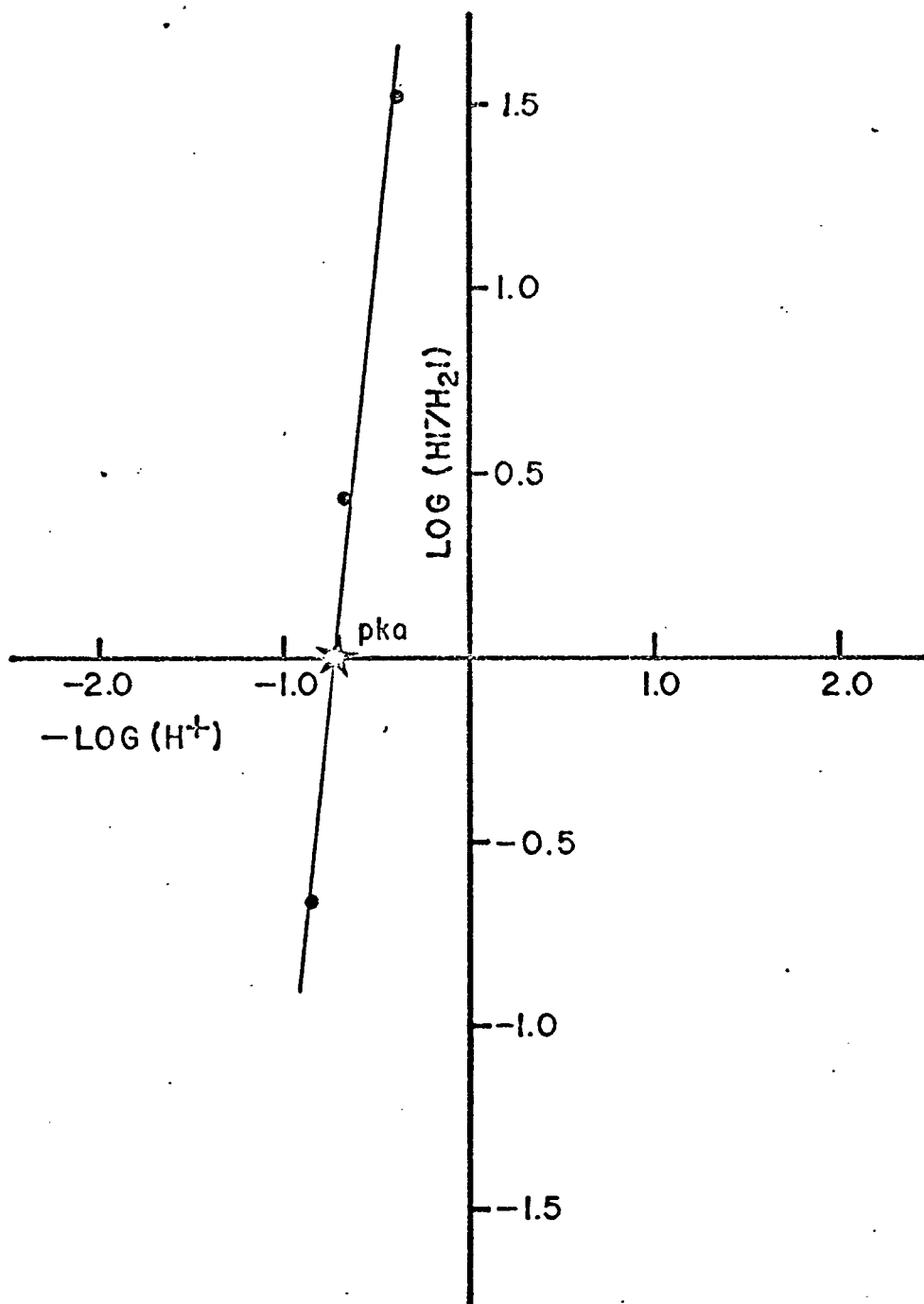


FIGURE 11. DETERMINATION OF THE FIRST pK_a VALUE OF BROMOCRESOL PURPLE USING $\text{LOG (HI}^-/\text{H}_2\text{I)}$ (From Figure 3) VERSUS $-\text{LOG (H}^+)$ PLOT

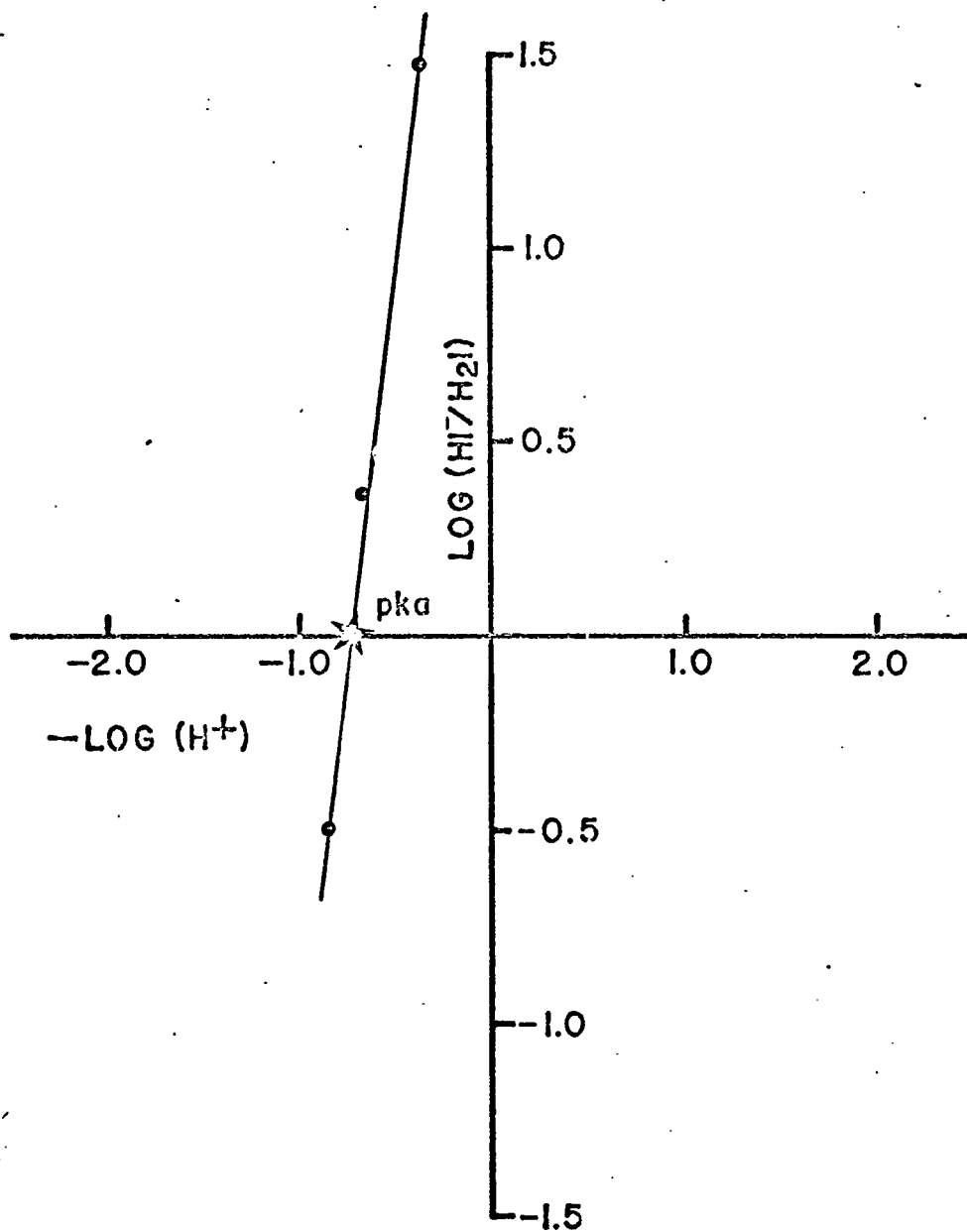


FIGURE 12. DETERMINATION OF THE FIRST pK_a VALUE OF BROMOCRESOL PURPLE USING $\text{LOG}(\text{HI}^-/\text{H}_2\text{I})$ (From Figure 4) VERSUS $-\text{LOG}(\text{H}^+)$ PLOT

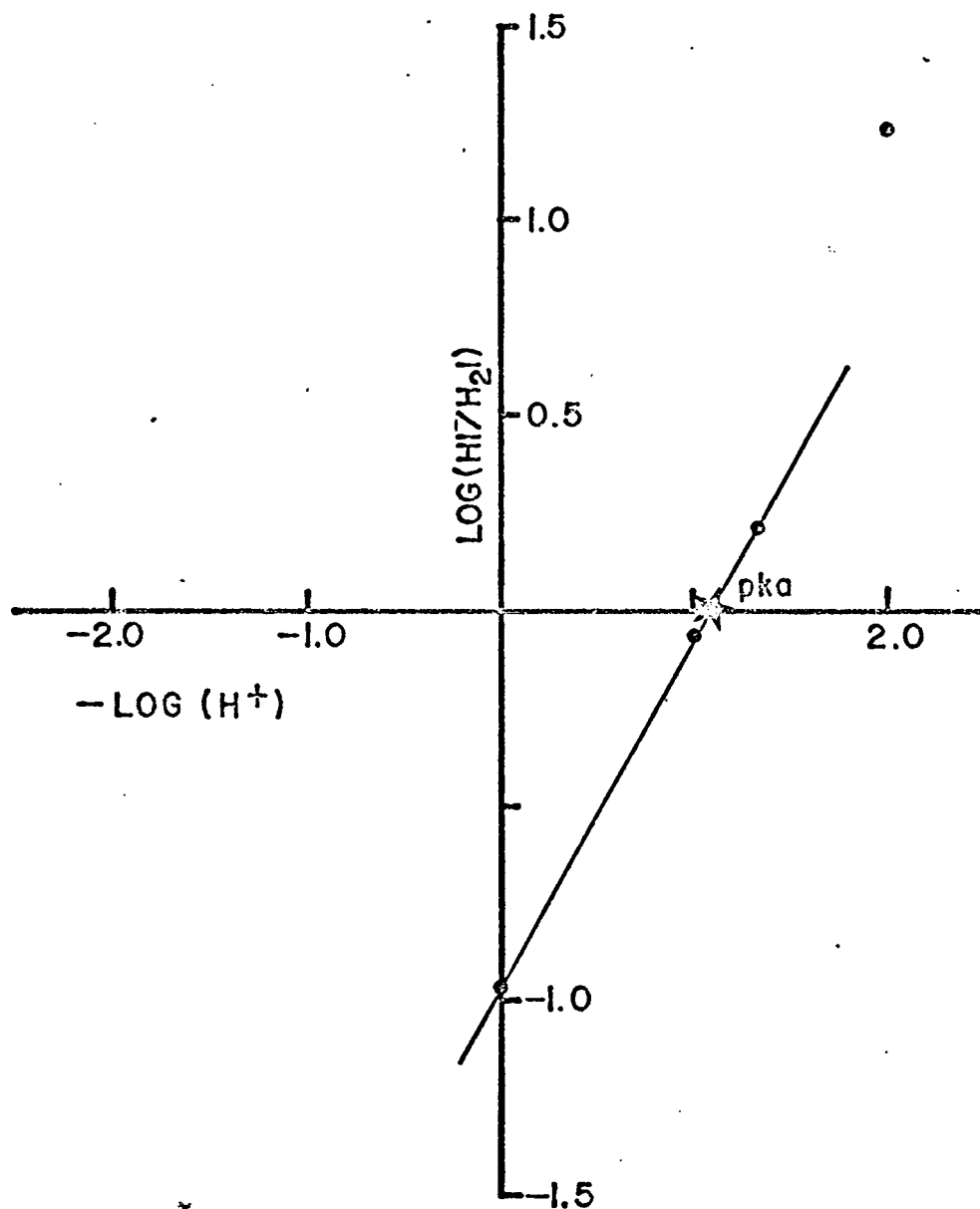


FIGURE 13. DETERMINATION OF THE FIRST pK_a VALUE OF CRESOL RED USING $\text{LOG}(\text{HI}^-/\text{H}_2\text{L})$ (From Figure 7) VERSUS $-\text{LOG}(\text{H}^+)$ PLOT

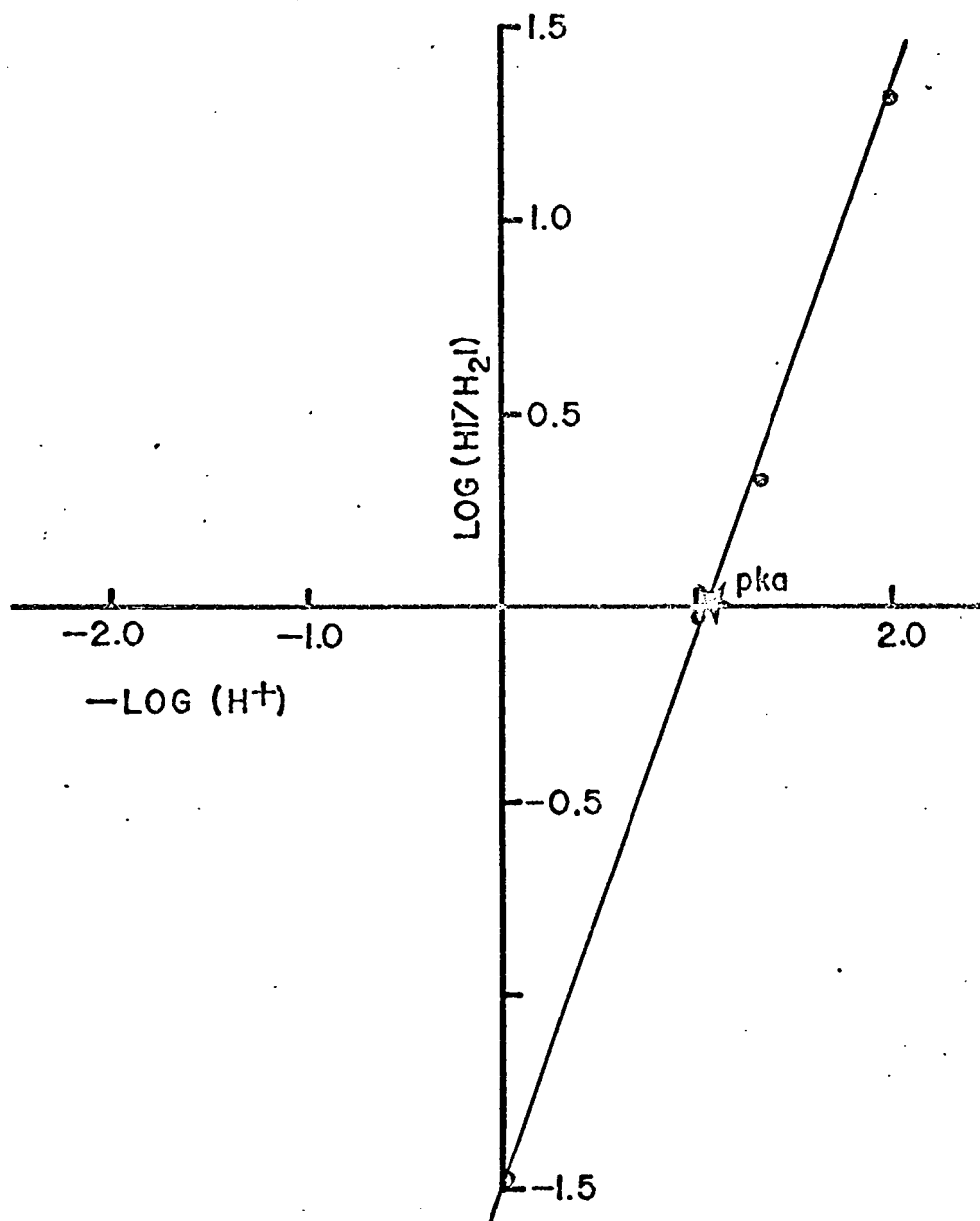


FIGURE 14. DETERMINATION OF THE FIRST pK_a VALUE OF CRESOL RED USING $\text{LOG (HI}^-/\text{H}_2\text{I)}$ (From Figure 8) VERSUS $-\text{LOG (H}^+)$ PLOT

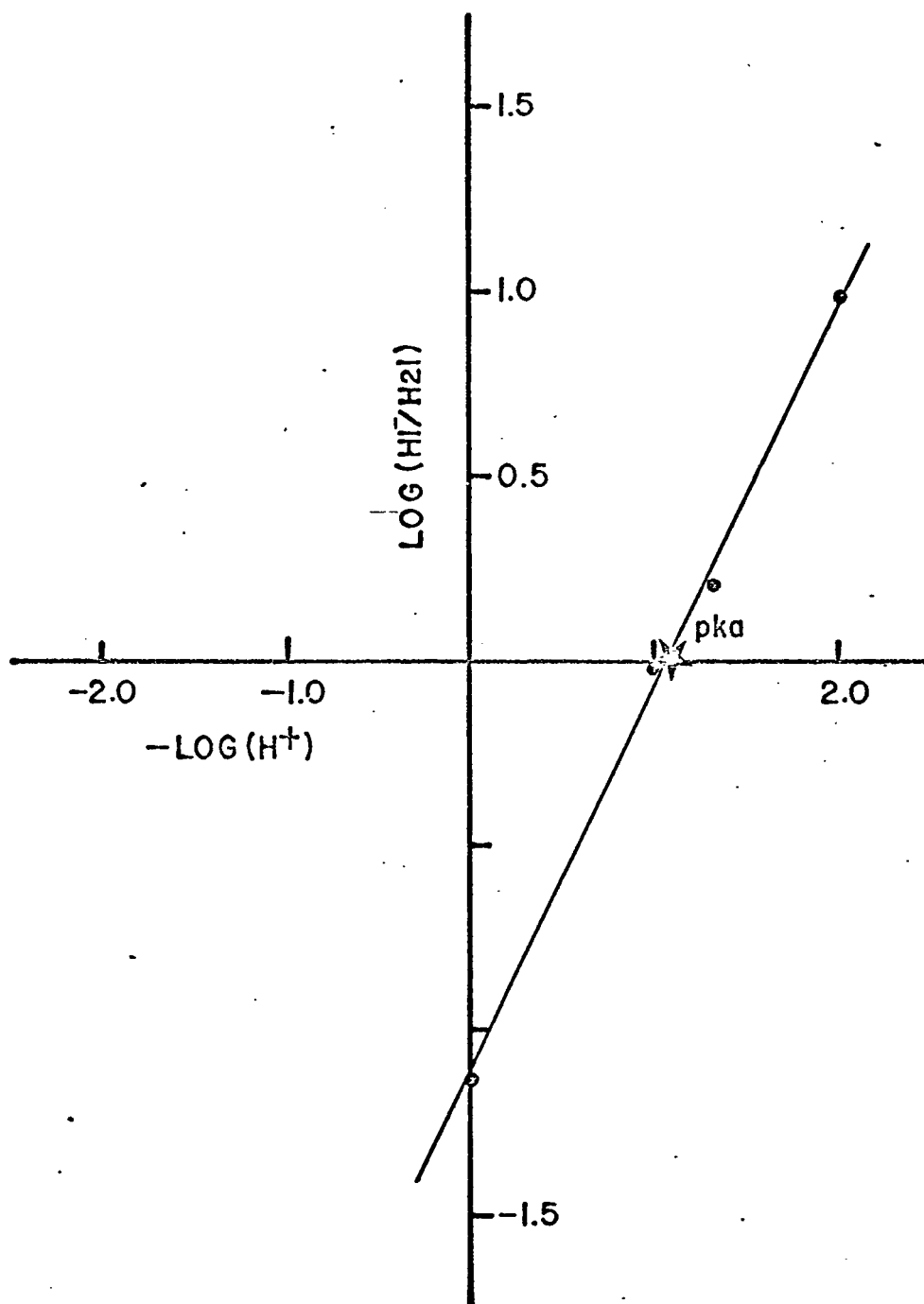


FIGURE 15. DETERMINATION OF THE FIRST pK_a VALUE OF PHENOL RED USING $\text{LOG}(\text{HI}^-/\text{H}_2\text{I})$ (From Figure 9) VERSUS $-\text{LOG}(\text{H}^+)$ PLOT

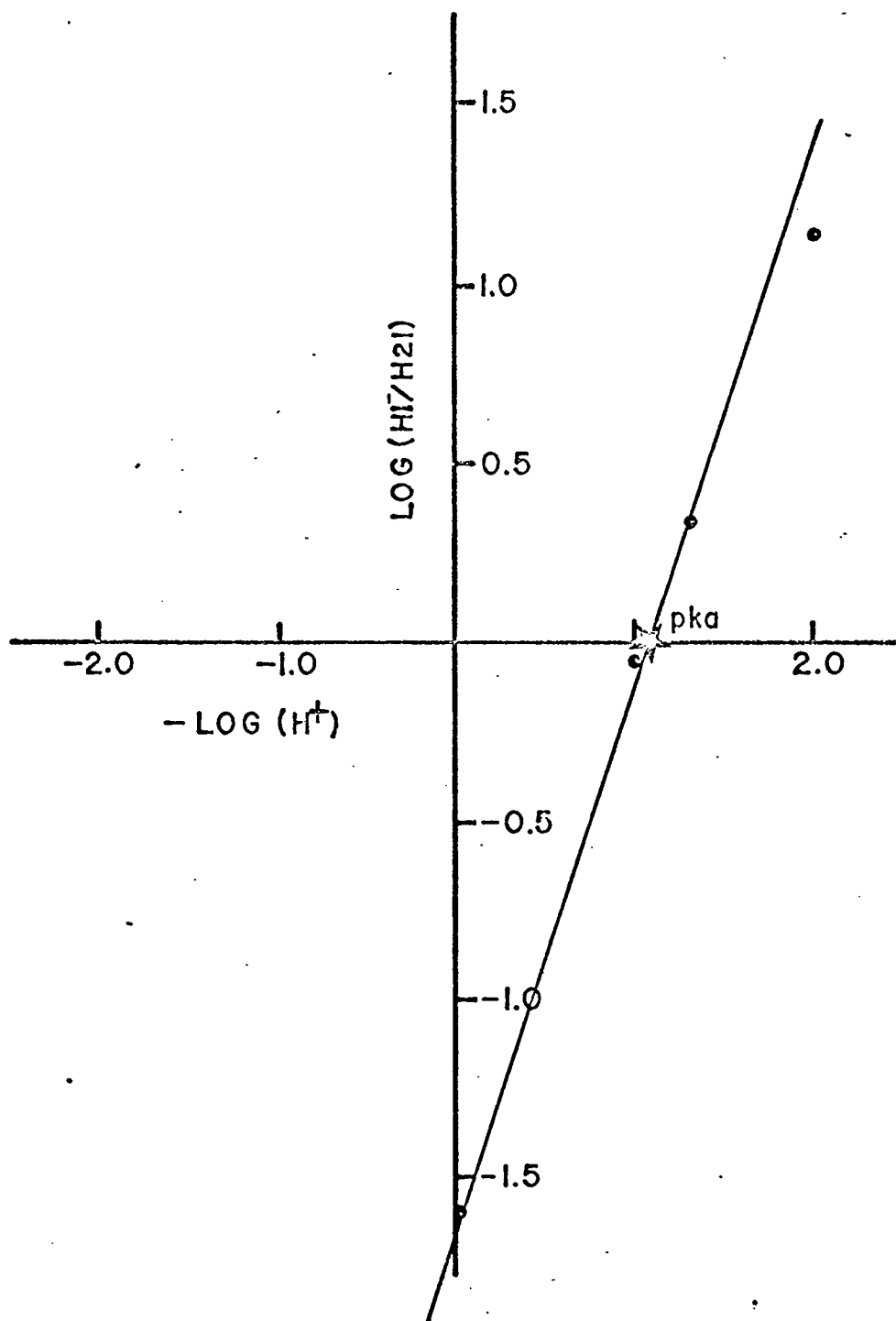


FIGURE-16. DETERMINATION OF THE FIRST pK_a VALUE OF PHENOL RED USING $\text{LOG}(\text{HI}^-/\text{H}_2\text{I})$ (From Figure 10) VERSUS $-\text{LOG}(\text{H}^+)$ PLOT

TABLE IX. FIRST pK_a VALUES OF VARIOUS DYES

DYE	REFERENCE FIGURE NUMBER	FIRST pK_a VALUE	AVERAGE
BCP	3	-0.78	
BCP	4	-0.73	
BCP	11	-0.75	
BCP	12	-0.75	
			-0.75 ^a
CR	7	1.08	
CR	8	0.97	
CR	13	1.10	
CR	14	1.05	
			1.05 ^a
PR	9	1.03	
PR	10	0.95	
PR	15	1.05	
PR	16	1.07	
			1.03 ^a

^a Average of the four values.

CHAPTER V

DISCUSSION AND CONCLUSION

Bromocresol Green: Trials to estimate the first pK_a 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 (Figures 1 and 2) 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 Figures 1 and 2, it appears that the first pK_a value of this dye is -0.85 or less.

Bromocresol Purple: The first pK_a value of this dye was estimated to be -0.75 (Figures 3,4,11 and 12 and Table IX). The true pK_a 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 (Figures 3 and 4) is not negligible.

Bromophenol Blue: Trials to estimate the first pK_a value of this dye were not successful due to the reasons reported under Bromocresol Green. From Figures 5 and 6, it appears that the first pK_a value of this dye is -0.95 or less.

Cresol Red: The first pK_a value of this dye was estimated to be +1.05 (Figures 7, 8, 13 and 14 and Table IX). 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 (25).

Phenol Red: The first pK_a value of this dye was estimated to be +1.03 (Figures 9, 10, 15 and 16 and Table IX).

Some of the points in Figures 11-16 did not fall on the straight line, probably due to the lack of sensitivity in the method used to calculate either (H_2I) or (HI^-) . 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 pK_a values of these dyes.

Analytical Applications: The information provided is very useful for the determination of the true partition coefficients as reported by Gupta and Cadwallader (16). This information may also be useful to correlate the structural formulas of the dyes. A project of this nature is already under investigation.

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