traction of the virus, show that a significant portion of the S^{35} supplied to the plants was taken up and utilized. One can, therefore, conclude that if CV4 had contained S, even in the smallest amount shown by the analytical data, this would have been manifested by appreciable radioactivity in the isolated and highly purified CV4. Confirmation of this conclusion appears to be provided by the outcome of the TMV experiment where, as shown in Table I, 55% of the expected S^{35} activity was found in the highly purified TMV. The author was assisted in these experiments by Miss Jessie Mason McNeil.

Discussion and Summary

The fact that a highly purified preparation of cucumber virus 4 obtained from cucumber plants which had received a nutrient solution containing S^{35}, possessed much less than 1% of the potential, calculated radioactivity of a compound containing 0.6% sulfur, indicates that no sulfur is present in CV4. This conclusion is supported by the finding that 55% of the calculated radioactivity was present in a similar preparation of tobacco mosaic virus, which is known to contain 0.2% of sulfur.[24]

The sulfur values obtained by two different laboratories on portions of the CV4 of the S^{35} experiment illustrate the confusing results which made the isotope experiment imperative, for the analyst who had previously obtained high values for most preparations, reported essentially no sulfur present (0.07%), whereas a second analyst found an amount comparable to that present in TMV, *i. e.*, about 0.2%. The nature of this pseudo-sulfur, found in 90% of the analyses of CV4 thus far, remains to be solved. It seems clear, however, that it is an artifact.

As an incidental point, the S^{35} experiment demonstrated in a graphic manner how a virus can be separated from normal plant materials in a stepwise fashion by the technique of differential centrifugation. The clarified plant sap, from which the virus was separated by an initial high-speed centrifugation, possessed over 2 million units of S^{35} activity. After 3 cycles of centrifugation, the total S^{35} activity of the viral preparation was about 1500 units, and after 5 cycles, 31 units. It seems reasonable in view of these facts, to assign the relatively minute amount of radioactivity in the highly purified CV4 to a residual trace of impurity.

The demonstration that CV4 contains no sulfur constitutes a striking difference between this virus and the other strains of TMV which have been studied chemically thus far, for the latter all contain sulfur, mainly in the form of cysteine.

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[24] A. F. Ross, *J. Biol. Chem.*, **136**, 119 (1940).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, UNIVERSITY OF PENNSYLVANIA]

The Effects of Substituents on the Dissociation Constants of Substituted Phenols. I. Experimental Measurements in Aqueous Solutions[1]

BY CHARLES M. JUDSON[2,3] AND MARTIN KILPATRICK[4]

The Sarmousakis modification[5] of the Kirkwood–Westheimer[6] electrostatic theory of the effects of substituents on the dissociation constants of benzenoid acids was originally tested by a comparison with the experimentally observed constants for the benzoic acids in several different pure solvents. To assist in providing a further test of the Sarmousakis treatment, the dissociation constants of a number of substituted phenols have been measured using a stepwise colorimetric method similar to that used previously in this Laboratory.[7] Complete data for the substituted phenols measured by a consistent method have been reported in the literature only for certain alcohol–water mixtures.[8] Values in a pure solvent are preferred for comparison with the electrostatic theory. The data obtained in the present investigation along with the previously available data have provided a satisfactory set of values for the substituted phenols in aqueous solution. These values have been compared with values calculated by the electrostatic theory and have been used to provide additional support for the theory.[9]

The ratio of the dissociation constant of an indicator A_i to that of an uncolored acid A may be defined by the equation

$$K_{A_IB} = c_{B_I}c_A/c_{A_I}c_B \qquad (1)$$

where B_i and B refer to the corresponding conjugate bases. By placing a small measured amount of the indicator in a buffer solution of known concentration of the uncolored acid with its sodium salt, the ratio of the dissociation constants can be determined from a colorimetric measurement of the concentration of one form of

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[1] Taken from the dissertation presented by Charles M. Judson to the Faculty of the Graduate School of the University of Pennsylvania in partial fulfillment of the requirements for the degree of Doctor of Philosphy, August, 1947. Presented before the 112th meeting of the American Chemical Society held in New York, N. Y., September, 1947.

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[5] Sarmousakis, *J. Chem. Phys.*, **12**, 277 (1944).

[6] Kirkwood and Westheimer, *ibid.*, **6**, 506 (1938); Westheimer and Kirkwood, *ibid.*, **6**, 513 (1938); Westheimer and Shookhoff, THIS JOURNAL, **61**, 555 (1939); Westheimer, *ibid.*, **61**, 1977 (1939).

[7] Mason and Kilpatrick, *ibid.*, **59**, 572 (1937); Minnick and Kilpatrick, *J. Phys. Chem.*, **43**, 259 (1939); Kilpatrick and Mears, THIS JOURNAL, **62**, 3047, 3051 (1940).

[8] Schwarzenbach and Egli, *Helv. Chim. Acta*, **17**, 1176 (1934); Schwarzenbach and Rudin, *ibid.*, **22**, 360 (1939).

[9] Judson and Kilpatrick, THIS JOURNAL, **71**, 3115 (1949)

the indicator. By making a series of such measurements of relative dissociation constants and including in this series one compound, acetic acid, for which the dissociation constant in water had been previously established, the dissociation constants were measured for a series of nitrophenol indicators and uncolored substituted phenols. This procedure was particularly suitable for measurement of phenols with nitrophenol indicators because the extrapolation to zero concentration is simplified when the buffer acid and the indicator have the same charge type, the ratio of the dissociation constants being to a first approximation independent of concentration.

Experimental

Apparatus.—Preliminary measurements were made with a Rubicon photoelectric colorimeter (number 4600) using a galvanometer and a 4400 Å. filter supplied by the manufacturer.

With the object of increasing the precision of the measurements, another colorimeter was constructed by modifying the instrument used by Minnick and Mears.[7] The modified instrument consisted of a projection bulb source, a regulated power supply for the source, a Hilger spectroscope used as a monochromator, a light-tight box within which four absorption cells could be brought successively into the light path, and a 931 multiplier phototube circuit to measure the intensity of the transmitted light.[10]

The optical system was essentially that used by Minnick and Mears. The absorption cells were plane-window, cylindrical glass cells with a path of 25 mm., obtained from the Phoenix Precision Instrument Co. The cells were found to have identical effective solution depths as determined by extinction measurements. The monochromator was calibrated by reference to a mercury arc. All measurements were made at 4450 Å. with a half-width of 24 Å.

The electrical circuits were modified because of the difficulties reported by previous workers. The voltage regulators used for the light source supply was similar to one described by Terman.[11] A three-phase full-wave rectifier circuit with 1120 volt center-tapped transformers supplied the power to the regulator. Using twenty-one 6L6 tubes in parallel in the regulator, an output of one ampere was obtained. The 200 volt output was dropped through a resistance to obtain a 100 volt potential for the source. The resulting potential was constant to 0.002 v. which was shown to be sufficient to ensure regulation of light intensity to 0.01%. The 110 v. projection bulb was operated at 100 v. increasing its life at some expense of intensity.

Two separate filtered half-wave power supply circuits were provided for the dynode and anode potentials of the multiplier phototube. A Sola constant-voltage transformer was used to regulate the input to both supply circuits. The output of the dynode supply was further controlled by an electronic voltage regulator similar to one designed for a Geiger counter supply.[12] This regulator was found more convenient than regulation based on the control characteristics[13] of the tube in which the voltage step at one dynode is made unequal to that at the other dynodes. The potential supplied to the anode was 280 v. The potential supplied to the dynodes was 560 v., constant to 0.1 v. This potential was divided into nine equal portions by a 180,000 ohm divider. The limit of accuracy of the transmittance measurements was apparently set by the regulation of the dynode potentials. Because this regulator was drawing more current than it was designed for, the precision of the transmittance measurements was limited to 0.2%.

The output of the phototube was measured by passing the photocurrent through a high resistance decade (R1 in Fig. 1) and measuring the potential developed across the decade with a type K potentiometer (R2). A second potentiometer (R3) was used to compensate for the dark current of the phototube which generally amounted to about 0.3% of the photocurrent. The balance of the potentiometer was measured with a Rubicon galvanometer (0.0012 μa/mm.) used in conjunction with an Ayrton shunt (not shown in Fig. 1).

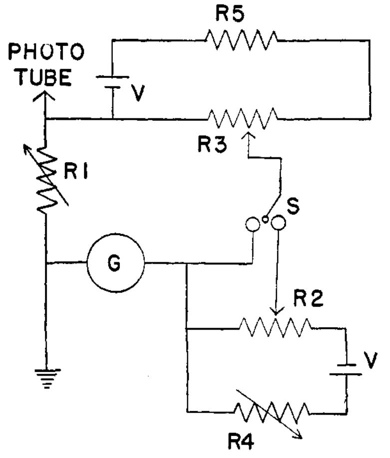

Fig. 1.—Circuit for measuring photocurrent: R1, 100,000ω decade; R2, type K potentiometer; R3, 30ω slide wire; R4, 1000ω decade, R5, 7000ω; V, 1.5 volt batteries; G, galvanometer.

Instead of using a standard cell, the photocurrent for the measured transmittances was always compared with the photocurrent obtained with a cell containing pure water. As the type K potentiometer used was not designed for direct reading of potentials compared to a standard of unity, it was necessary to use the standard cell position, 1.018 v., for the measurement of the reference solution, the ratio of the two photocurrents then being 1.018 times the reading of the potentiometer.

The optical system was placed in a transite air-bath lagged with rock wool. Water cooled to 5° by a mechanical refrigerating unit was circulated through a radiator inside the air-bath. A thyratron relay controlled by a bimetallic regulator operated a nichrome wire heater and simultaneously a mercury switch relay which in turn controlled an impeller pump in the cooling system. Three fans were used to circulate the air. The temperature inside the absorption cell box was 25.0 ± 0.1°. The temperature was measured with a Beckmann thermometer calibrated by comparison with a Bureau of Standards platinum resistance thermometer.

Solutions measured with the Rubicon colorimeter were brought to 25° in a water-bath and were then quickly transferred to the test-tube absorption cells and the transmittance measured immediately. The temperature could be controlled in this way to ±0.5°.

Procedure.—At the beginning of each series of measurements with the photomultiplier instrument, the four absorption cells were cleaned and filled with water and the windows were polished. Using one cell as a reference, the relative transmittances of the other three cells were measured to obtain a calibration of the cells. Three of the cells were then removed, rinsed with the solutions to be measured, filled and replaced without touching the cell

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(10) We are indebted to J. P. Hervey of the Johnson Foundation for Research in Medical Physics of the University of Pennsylvania and to J. Presper Eckert of the Moore School of Electrical Engineering of the University of Pennsylvania for suggestions in the design of the electrical circuits used.

(11) Terman, "Radio Engineers' Handbook," McGraw-Hill Book Co., Inc., New York, N. Y., 1943, p. 615, Fig. 19.

(12) Strong, "Procedures in Experimental Physics," Prentice-Hall, New York, N. Y., 1939, p. 296, Fig. 28.

(13) Rajchman and Snyder, *Electronics*, **13**, 20 (1940)

window. The transmittances of the three solutions were then measured by comparison with the reference cell containing pure water. The cells were then filled with another set of solutions in the same way. At the end of the group of measurements the cells were again filled with water and the cell calibration checked. In filling the cells an air bubble was left just below the stopper to prevent the formation of small bubbles on the window. The light source and the thermostat were allowed two hours to come to equilibrium for each measurement. The fans and cooling system were turned off momentarily during the measurements to avoid vibration.

The dark current compensation was adjusted with the light beam interrupted just before each measurement and was checked after the measurement. The comparison of the cell transmittances was repeated several times in quick succession, balancing the potentiometer in the standard cell position for the reference absorption cell by varying R4, and then balancing the potentiometer slide wire for the photocurrent from the unknown solution. The repeated comparison was carried out in a systematic way so that the effects of photocell fatigue would be reproducible.

In using the Rubicon colorimeter, the light intensity was first adjusted with no absorption cell in place to an arbitrary value so that a reading of 0.99 would be obtained with a cell containing pure solvent. Two cells were selected which showed identical transmittances with water and with absorbing solutions and duplicate measurements of the solvent and of each solution were made in these cells. Dark current readings were made before and after each series of measurements by turning off the light source. A correction was made using the average of the two dark current readings.

A blank correction was made for the absorption of the buffer solution whenever applicable. This blank was determined either by adding a small amount of hydrochloric acid to the buffer solution immediately after measuring the transmittance or by measuring a buffer solution made up without any indicator. In the former case a small correction was made in the blank for the transmittance of the acid form of the indicator present in the acidified solution.

Preliminary measurements were made of the transmittances of solutions of the complete acid form and the complete basic form of each indicator used. It was found that a single wave length could be used which was suitable for all of the nitrophenols used.

Solutions on the basic and acid forms of each indicator were then measured as a function of concentration. In each case a quantity of sodium hydroxide or hydrochloric acid was added sufficient to ensure a negligible contribution to the absorption from the opposite form of the indicator. Blanks were subtracted for the apparent absorption of the added acid or base where required. In some cases a slight variation of the transmittance with the amount of added base or acid was observed and the value required was obtained by extrapolation to dilute solution, the concentration always being kept high enough to keep the indicator completely in the acid or basic form.

The extinction constant k defined by Beer's law

$$-\log T = kc \qquad (2)$$

was calculated from the measured transmittance T and the concentration c for each indicator in the basic and in the acid form. The extinction constant generally showed small variations with indicator concentration. The measured values of k were plotted against c or against $-\log T$.

The transmittances of buffer solutions of the acids with suitable indicators were then measured for two different buffer ratios differing by a factor of about two and for several different concentrations for each pair of compounds being compared. Each solution contained an amount of indicator sufficient to make the transmittance around 40% which is near to the transmittance at which maximum precision is obtained. The buffer solutions were prepared by adding measured volumes of stock solutions of the indicator and buffer acids and of standard 0.08 N carbonate-free sodium hydroxide.

The calculation of the concentration of the basic and acid forms of the indicator was made by a series of approximations. The absorption of the acid form was first neglected and the approximate concentration of the basic form calculated from the measured transmittance and the previously determined extinction constant for the basic form. The concentration of the acid form was then estimated from the known total concentration and the approximate concentration of the basic form. A correction was then made for the absorption by the acid form and a second approximation for the basic form calculated, etc. The amounts of the basic and acid forms of the buffer acid were calculated from the amount of acid and base added, the amount of indicator converted to the basic form and the amount of hydroxyl or hydrogen ion formed. The hydrogen ion concentration was calculated from the value of the dissociation constant of either the buffer or the indicator acid since one of these constants was known in each case. In calculating the hydrogen ion concentration the activity coefficient was estimated from the Debye-Hückel approximation.

Materials.—The 2,5-dinitrophenol and the 3,4-dinitrophenol were separated from the mixture obtained by the nitration of Eastman Kodak *m*-nitrophenol.[14] The 2,5-dinitrophenol was recrystallized several times from alcohol (m. p. 105.8-106.2°). The 3,4-dinitrophenol was purified by dissolving in aqueous sodium hydroxide solution and precipitating with dilute acid. After two purifications in this manner the product could be recrystallized from dry benzene without forming an oil and was then recrystallized from an alcohol-water mixture (m. p. 134.6-135.1°). No 2,3-dinitrophenol could be isolated from this nitration mixture.

m-Nitromesitol was prepared from mesitylene.[15] Dinitromesitylene prepared from Eastman Kodak Co. mesitylene[16] was reduced with ammonium acid sulfide in a bomb,[17] and the resulting nitromesidine was diazotized and nitromesitol obtained by boiling the diazonium sulfate solution with sulfuric acid solution.[17,18] The product was precipitated from sodium carbonate solution with acid, recrystallized from alcohol and finally purified by vacuum sublimation (m. p. 63.4–63.9°). Attempts to prepare *m*-nitromesitol by nitration of mesitol were unsuccessful.

The *o*-nitrophenol (m. p. 44.9-45.3°) and *m*-nitrophenol (m. p. 96.6-96.8°) were Eastman Kodak Co. products recrystallized several times from alcohol-water mixtures. The *o*-nitrophenol was first steam distilled. The *p*-nitrophenol was a Kahlbaum product recrystallized from water (m. p. 113.1-113.8°).

The phenol was a J. T. Baker product purified by fractional distillation (b. p. 182.0-182.5°; m. p. 39.8-39.9°). The *p*-chlorophenol was a Paragon Testing Laboratory product, purified by fractional distillation (b. p. 219-220°; m. p. 43.2-43.7°). The *m*-chlorophenol (b. p. 216.7°, m. p. 33.2-33.5°), *o*-chlorophenol (b. p. 176°) and *o*-bromophenol (b. p. 194-195°) were Eastman Kodak Co. products fractionally distilled. The 2,4-dichlorophenol was an Eastman Kodak Co. product purified by fractional sublimation (m. p. 42.0-42.8°).

The *p*-fluorophenol was prepared from Eastman Kodak Co. *p*-fluoroanisole by treatment with aluminum chloride following the procedure described for the preparation of *o*-fluorophenol.[19] The product was purified by fractional distillation (b. p. 185.0-185.5°).

The acetic and benzoic acids were Kahlbaum products used without further purification.

Fractional distillations were carried out in an eleven-ball, lagged, electrically-heated Snyder column at a 10:1 reflux ratio except for the distillations of *m*-chlorophenol

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(14) Holleman and Wilhelmy, *Rec. trav. chim.*, **21**, 432 (1902).

(15) We are indebted to Walter Brooks for the preparation of the *m*-nitromesitol.

(16) Kuster and Stallberg, *Ann.*, **278**, 213 (1894).

(17) Knecht, *ibid.*, **215**, 98 (1882).

(18) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 404.

(19) Bennett, Brooks and Glasstone, *J. Chem. Soc.*, 1821 (1935).

and *p*-fluorophenol which were carried out in a smaller six-ball column. Melting points and boiling points were measured with calibrated thermometers and stem corrections were made throughout. All products were dried over phosphorus pentoxide before use.

The melting points found for *m*-chlorophenol and *p*-chlorophenol are about 5° higher than those listed in Landolt-Börnstein but are in agreement with those recently reported by the Dow Co.[20]

Standard carbonate-free sodium hydroxide was used to make up the buffer solutions. The sodium hydroxide was standardized by comparison with Bureau of Standards benzoic acid and was kept in a bottle coated with Vulcalock cement.[21] All solutions were made up in water which had been redistilled from alkaline permanganate, fractionally condensed and freed of carbon dioxide by long bubbling with nitrogen gas.

The volumetric glassware and the balance weights used had been calibrated according to standard procedures.

Results

A preliminary measurement of each dissociation constant ratio was made with the Rubicon colorimeter in order that optimum values of the buffer ratio could be selected for the final measurements. Because of the length of time required for a set of measurements with the photomultiplier colorimeter, measurements were made with this instrument only for the first six comparisons in Table I which constituted the main series of comparisons relating phenol to acetic acid. The other comparisons, which involved a ratio with one of the compounds in the main series, were made with the Rubicon colorimeter because the accuracy required was not so high in these measurements. The error in the determination of the dissociation constant of an acid, which was ultimately compared to benzoic acid or to phenol, involved the error in each of several of the main series of comparisons but involved not more than one of the comparisons which were made with the Rubicon colorimeter.

TABLE I

MEASURED VALUES OF LOG $K_{A_1B}^\circ$

p-Nitrophenol, acetic acid	$\bar{3}.617 \pm 0.001$
p-Nitrophenol, 2,4-dichlorophenol	$0.710 \pm .005$
m-Nitrophenol, 2,4-dichlorophenol	$\bar{1}.504 \pm .004$
m-Nitrophenol, *p*-chlorophenol	$1.032 \pm .004$
m-Nitromesitol, *p*-chlorophenol	$0.394 \pm .004$
m-Nitromesitol, phenol	$0.967 \pm .001$
2,5-Dinitrophenol, acetic acid	$\bar{1}.541 \pm .003$
3,4-Dinitrophenol, acetic acid	$\bar{1}.333 \pm .002$
m-Nitrophenol, *o*-chlorophenol	$0.131 \pm .002$
m-Nitrophenol, *o*-bromophenol	$0.079 \pm .004$
m-Nitrophenol, *m*-chlorophenol	$0.678 \pm .002$
m-Nitromesitol, *p*-fluorophenol	$0.826 \pm .013$
o-Nitrophenol, 2,4-dichlorophenol	$0.616 \pm .006$

The measured value of K_{A_1B} was plotted against the ionic strength and the thermodynamic constant $K_{A_1B}^\circ$ was determined by extrapolation to zero concentration using the method of least squares. Where the plot showed no distinct trend the data were averaged without extrapolation. $K_{A_1B}^\circ$ was calculated separately for the two different buffer ratios used and the two values were averaged.

The accepted values of log $K_{A_1B}^\circ$ are shown in Table I with the calculated probable error. The dissociation constants of the various acids were calculated from these data using the value 1.751×10^{-5} for the dissociation constant of acetic acid, calculated on a molarity basis from the average of the electromotive force[22] and conductance[23] values. In Table II the logarithm of the dissociation constant K_c° and the logarithm of the ratio of the dissociation constant to that of phenol, $K_{A_xB_0}$, are shown for each acid measured. The constant $K_{A_xB_0}$ is the quantity to be used in the study of the effects of substituents. Values which have been reported in the literature for these compounds are shown in Table III for comparison purposes. These values have been corrected to

TABLE II

MEASURED DISSOCIATION CONSTANTS

Compound	log K_c°	log $K_{A_xB_0}$
Acetic acid	$\bar{5}.243 \pm 0.000$	5.194 ± 0.009
2,5-Dinitrophenol	$\bar{6}.784 \pm .003$	$4.735 \pm .009$
3,4-Dinitrophenol	$\bar{6}.576 \pm .002$	$4.527 \pm .009$
p-Nitrophenol	$\bar{8}.860 \pm .001$	$2.811 \pm .009$
o-Nitrophenol	$\bar{8}.766 \pm .008$	$2.717 \pm .008$
2,4-Dichlorophenol	$\bar{8}.150 \pm .005$	$2.101 \pm .007$
m-Nitrophenol	$\bar{9}.654 \pm .006$	$1.605 \pm .006$
o-Bromophenol	$\bar{9}.575 \pm .007$	$1.526 \pm .007$
o-Chlorophenol	$\bar{9}.523 \pm .006$	$1.474 \pm .006$
m-Nitromesitol	$\bar{9}.016 \pm .008$	$0.967 \pm .001$
m-Chlorophenol	$\overline{10}.977 \pm .006$	$.928 \pm .006$
p-Chlorophenol	$\overline{10}.622 \pm .007$	$.573 \pm .004$
p-Fluorophenol	$\overline{10}.190 \pm .015$	$.141 \pm .013$
Phenol	$\overline{10}.049 \pm .008$	$.000 \pm .000$

TABLE III

DISSOCIATION CONSTANTS FROM LITERATURE

Compound	$-\log K_0^\circ$					
Phenol	9.95^a	9.81^b	9.83^c	9.90^d	9.94^e	10.01
o-Nitrophenol	7.23^a	7.17^g	7.23^h			
m-Nitrophenol	8.35^a	8.00^g	8.28^f	8.17^i	8.25^j	8.41^m
p-Nitrophenol	7.14^a	6.91^i	7.09^k	7.15^m	$7.16^{l,h}$	7.19^g
2,5-Dinitrophenol	5.22^a	5.10^i	5.11^j	5.15^n		
3,4-Dinitrophenol	5.42^a	5.35^j	5.37^g	5.43^n		
o-Chlorophenol	8.48^a	8.11^d	8.50^b			
m-Chlorophenol	9.02^a	8.79^d	8.85^b	9.07^o		
p-Chlorophenol	9.38^a	9.18^b	9.20^d	9.43^c		
2,4-Dichlorophenol	7.85^a	7.75^b	7.89^p			
o-Bromophenol	8.42^a	8.39^d				
p-Fluorophenol	9.81^a	9.95^q				

[a] This investigation. [b] Murray and Gordon, THIS JOURNAL, **57**, 110 (1935). [c] Mizutani, *Z. physik. Chem.*, **118**, 318, 327 (1925). [d] Ref. 28. [e] Boyd, *J. Chem. Soc.*, **107**, 1538 (1915). [f] Ref. 24a. [g] Ref. 14. [h] Euler and Bolin, *Z. physik. Chem.*, **66**, 71 (1909). [i] Kolthoff, *Pharm. Weekblad*, **60**, 949 (1923). [j] Ref. 24c. [k] Ref. 24d. [l] Ref. 24b. [m] Brönsted and Wynne-Jones, *Trans. Faraday Soc.*, **25**, 59 (1929). [n] Ref. 27. [o] Hodgson and Smith, *J. Chem. Soc.*, 263 (1929). [p] Ref. 24e. [q] Ref. 29.

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(20) Stull, *Ind. Eng. Chem.*, **39**, 523 (1947).

(21) Soule, *Ind. Eng. Chem., Anal. Ed.*, **1**, 109 (1929).

(22) Harned and Ehlers, THIS JOURNAL, **54**, 1350 (1932).

(23) MacInnes and Shedlovsky, *ibid.*, **54**, 1429 (1932).

25° using temperature coefficients from the literature.[24]

Discussion

Extrapolation.—Reasonably good extrapolation lines were obtained by plotting log K_{A_iB} against the ionic strength u. Actually it was found that, over the small range of concentrations involved, the extrapolation could just as well be made by plotting K_{A_iB} instead of log K_{A_iB}. The extrapolation against the ionic strength is based on the equation[25] for the variation in the activity coefficient with ionic strength.

In two different experiments it was found, unexpectedly, that the data for the different buffer ratios formed distinctly separate lines extrapolating to the same value of $K_{A_iB}°$. That is, the extrapolation depended on c_A as well as on c_B which is nearly equal to μ.

Kortüm[26] has studied the variation in the extinction coefficient of nitrophenols with varying concentration of electrolyte and non-electrolyte. He found particularly marked changes in the extinction of 2,4-dinitrophenolate caused by the addition of phenol. With these experiments by Kortüm in mind an equation was developed for the extrapolation of the measured K_{A_iB} assuming that the major effect was a change in extinction constant which was linear with c_A. The equation obtained was

$$K_{A_iB}° = K_{A_iB} + \frac{K_{A_iB}c_A(c_{B_i} + c_{A_i})\delta}{kc_{A_i}} \qquad (3)$$

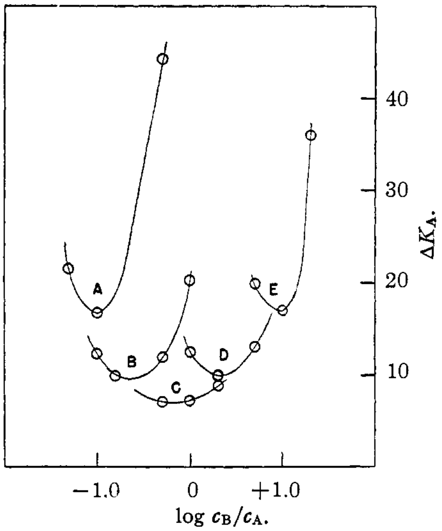

Fig. 2.—Relative error in K_{A_iB}: A, K_{A_iB} = 50; B, K_{A_iB} = 10; C, K_{A_iB} = 1; D, K_{A_iB} = 0.1; E, K_{A_iB} = 0.01: horizontal axis, log c_B/c_A; vertical axis, $(\Delta K_{A_iB}/K_{A_iB})/(\Delta c/c)$.

where δ is a proportionality constant for the change of k with c_A. It can be shown that the last term on the right is approximately proportional to c_B for relatively large values of c_{B_i}/c_{A_i} so that an extrapolation according to equation (3) will differ appreciably from an extrapolation against μ or c_B only for experiments using relatively low values of c_{B_i}/c_{A_i}. In all of the experiments involving low values of the indicator ratio it happened that K_{A_iB} was nearly independent of concentration so that the fit of the data to equation (3) was no better and no worse than an extrapolation against μ. Further consideration of the problem suggested that if the extinction coefficient varied markedly with c_A the activity coefficient might also vary with c_A as well as with μ. In any case if the activity or extinction coefficient depends on c_A the extrapolation against concentration will give separate lines for different values of the buffer ratio.

Precision.—The relative error in measuring indicator concentrations colorimetrically can be calculated by differentiating equation (2). With the Rubicon colorimeter, having a constant absolute error in the transmittance, the error in measuring concentration is lowest at about 37% transmittance. With the photomultiplier colorimeter the relative error in transmittance can be kept constant over a considerable concentration range and the error of the measurement continues to decrease slightly at transmittances below 37%. As it was not convenient to use high indicator concentrations, all measurements were made with concentrations selected to give a transmittance of about 40%.

The selection of the buffer ratio to be used was more complicated. Using rather arbitrary assumptions about the sources of error the curves shown in Fig. 2 were obtained for the relative error in the measured K_{A_iB} as a function of K_{A_iB} and c_B/c_A. In any case it can be shown that the error in measuring a given value of K_{A_iB} will have a minimum value at some intermediate buffer ratio and will increase at very high and very low values of c_B/c_A and that the optimum point will be at lower buffer ratios for high values of K_{A_iB}. The buffer ratios used were selected from the curves of Fig. 2 to give approximately the minimum errors.

Measurements were made at two different buffer ratios for each experiment in order to reduce the possibility of errors. Although it is not immediately obvious, a detailed examination shows that it is possible for a mixture of two indicators with different dissociation constants but with comparable extinction constants to give rise to an intermediate K_{A_iB} value which appears to be nearly constant over a range of buffer ratios. The evidence for the purity of the indicators must then rest on other grounds than the constancy of K_{A_iB} with changing buffer ratio.

If significant quantities of carbon dioxide were present in the solutions, an error would be caused

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(24) (a) Lunden, *Z. physik. Chem.*, **70**, 249 (1910); (b) Lunden, *J. chem. phys.*, **5**, 574 (1907); (c) Michaelis and Kruger, *Biochem. Z.*, **119**, 307 (1921); (d) Michaelis and Gyemant, *ibid.*, **109**, 165 (1920); (e) Hantzsch, *Ber.*, **32**, 3066 (1899).

(25) Harned and Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold Publishing Corp., New York, N. Y., 1943, p. 387, eq. 12-6-3.

(26) Kortüm, *Z. physik. Chem.*, **30**, 317 (1935).

in the buffer ratio. If the amount of carbon dioxide can be assumed constant in solutions with decreasing buffer concentration, a distinct curvature would be introduced into the extrapolation line. The absence of such curvature in the data obtained was taken as evidence that the precautions taken to keep out carbon dioxide were sufficient.

Some measurements were made at temperatures other than 25° to estimate the temperature coefficients of the dissociation constants and of the extinction constants. It was concluded that 0.1° regulation was satisfactory for an accuracy of 0.2% in the measured K_{A_1B}.

Comparison with Literature.—The dissociation constant of *m*-nitromesitol has not been measured previously. The values measured for the other nitrophenols are in reasonably good agreement with the values given in Table III except for the value given by Holleman and Wilhelmy for *m*-nitrophenol which is apparently in error. The visual colorimetric values of Kolthoff and of Michaelis seem also to be consistently lower than the values obtained in other ways. The values reported by Bader[27] for the mononitrophenols are not shown in Table III as they are entirely out of line with all later measurements.

The agreement for the chlorophenols is only fair. Abichandani and Jatkar[28] measured the complete set of chloro-, bromo- and iodophenols and reported that the dissociation constants of the bromo- and iodophenols were somewhat lower than those for the chlorophenols, particularly for the ortho compounds. The measurement of *o*-bromophenol in the present investigation was made to check this point, failing to show a difference comparable with the 0.28 log unit difference reported by Abichandani and Jatkar. Bennett, Brooks and Glasstone[29] also reported from measurements in ethanol–water mixtures that the fluorophenols were distinctly weaker than the chlorophenols, the largest difference being observed for the para isomer. The present measurement of *p*-fluorophenol verifies the marked difference between this compound and *p*-chlorophenol.

Summary

A photoelectric colorimeter has been constructed and used for precise measurements of the ratio K_{A_1B} between the dissociation constant in aqueous solution at 25° for a nitrophenol indicator and the constant for another substituted phenol. A detailed study has been given to the sources of error in measurements by this method. The thermodynamic dissociation constant and the ratio $K_{A_xB_0}$ between the dissociation constant of the substituted phenol and the constant for phenol have been calculated from these data for twelve substituted phenols. The values obtained have been compared with the results of previous measurements.

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[27] Bader, *Z. physik. Chem.*, **6**, 289 (1890).

[28] Abichandani and Jatkar, *J. Ind. Inst. Sci.*, **3**, 99 (1940).

[29] Bennett, Brooks and Glasstone, *J. Chem. Soc.*, 1821 (1935).

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The Effects of Substituents on the Dissociation Constants of Substituted Phenols. II. Calculations from the Electrostatic Theory[1]

BY CHARLES M. JUDSON[2,3] AND MARTIN KILPATRICK[4]

Measurement of the dissociation constants of some substituted phenols have been described in the preceding paper.[5] The equation developed by Sarmousakis[6] using electrostatic theory to calculate the ratio $K_{A_xB_0}$ between the dissociation constant for a substituted acid and the constant for the unsubstituted acid has been applied in this paper to the substituted phenols. The conventions used to determine the variable parameters in the equation were changed slightly from those used by Sarmousakis. The calculated values have been compared with the observed values from the previous paper and from the literature. The test of the agreement between the calculated and observed values was made more rigorous by making the comparison for both the phenols and the benzoic acids using a consistent method of calculation.

The equation developed by Sarmousakis is a modification of the equation used by Kirkwood and Westheimer[7] for the electrostatic interaction between a substituent dipole and a dissociating proton. It can be readily shown from a simple treatment that this equation should have the general form

$$-2.3 \log K_{A_xB_0} = \frac{e\mu \cos \theta}{r^2 D_E k T} \qquad (1)$$

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[1] Taken from the dissertation presented by Charles M. Judson to the Faculty of the Graduate School of the University of Pennsylvania in partial fulfilment of the requirements for the degree of Doctor of Philosophy, August, 1947. Presented before the 112th meeting of the American Chemical Society held in New York, N. Y., September, 1947.

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[5] Judson and Kilpatrick, THIS JOURNAL, **71**, 3110 (1949).

[6] Sarmousakis, *J. Chem. Phys.*, **12**, 277 (1944).

[7] Kirkwood and Westheimer, *ibid.*, **6**, 506 (1938); Westheimer and Kirkwood, *ibid.*, **6**, 513 (1938); Westheimer and Shookhoff, THIS JOURNAL, **61**, 555 (1939); Westheimer, *ibid.*, **61**, 1977 (1939).