d-**Pinacolyl Alcohol.**—Two crystallizations of brucine pinacolyl phthalate[9] from acetone gave pure brucine *d*-pinacolyl phthalate (m.p. 148–151°). The success of the resolution lay in adding a pure seed crystal to a concentrated solution (about 40%) of the brucine salt in acetone at 25°. This non-equilibrium crystallization is aided by the fact that the brucine salt of the *l*-isomer crystallizes much more slowly than that of the *d*-isomer. After two hours about 80% of the salt of the *d*-isomer had precipitated in nearly pure form. The brucine salt from two such crystallizations gave *d*-pinacolyl alcohol, $[\alpha]^{25}_{5160}$ +7.97° and $[\alpha]^{25}_{5160}$ +9.44° (using 0.81 for the density of *d*-pinacolyl alcohol). This value is somewhat higher than the $[\alpha]^{25}_{5893}$ +7.71° previously reported.[9]

The *l*-pinacolyl alcohol recovered from the filtrate had $[\alpha]^{25}_{5893}$ −4.41°.

Barium *d*-*s*-Butyl Sulfate.—This sulfate was prepared as described.[2] The barium *d*-*s*-butyl sulfate was analyzed after drying at 25° and 1 mm. to constant weight (several hours required).

Anal. Calcd. for $(C_4H_9OSO_3)_2Ba\cdot 3H_2O$: Ba, 27.6. Found: Ba, 27.7.

Barium *d*- and *dl*-Pinacolyl Sulfates.—A mixture of 25 g. (0.157 mole) of pyridine–sulfur trioxide and 20 cc. (16 g., 0.157 mole) of *d*-pinacolyl alcohol ($[\alpha]^{25}_{5893}$ +7.97°) was vigorously shaken in a stoppered flask immediately after mixing. The mixture warmed up to about 70° and nearly liquefied. The vigorous shaking was continued until the contents of the flask solidified (about five minutes). After standing several days, the solid was dissolved in 200 cc. of distilled water and 30 g. of finely ground barium hydroxide octahydrate was slowly added with good stirring. After several hours an additional 10 g. of barium hydroxide octahydrate was added. After 18 hours, excess carbon dioxide was passed in and the mixture decolorized with charcoal (Darco G-60) and filtered with the aid of Super-cel (previously washed with distilled water). The colorless solution was evaporated to dryness in a current of air. The white crystalline residue was dried at 25° and 1 mm. to constant weight (six hours). The barium *d*-pinacolyl sulfate trihydrate weighed 36 g. (83%).

(9) R. H. Pickard and J. Kenyon, *J. Chem. Soc.*, 1120 (1914).

Anal. Calcd. for $(C_6H_{13}OSO_3)_2Ba\cdot 3H_2O$: Ba, 24.8. Found: Ba, 24.8, 24.7, 24.7.

dl-Pinacolyl sulfate was prepared in a manner identical to barium *d*-pinacolyl sulfate. The barium salts of the *d*- and *dl*-sulfates were hydrated to different degrees when dried under the same conditions.

Anal. Calcd. for $(C_6H_{13}OSO_3)_2Ba\cdot 2H_2O$: Ba, 25.7. Found: Ba, 25.6, 25.6, 25.7.

The products varied in stability. Some samples, by the odor of olefins and failure to dissolve completely in water, showed evidence of decomposition within several days.

The following specific rotations were calculated on the basis of *anhydrous* barium *d*-pinacolyl sulfate: $[\alpha]^{25}_{5893}$ +6.39°, $[\alpha]^{25}_{5461}$ +7.63° and $[\alpha]^{25}_{5160}$ +8.68°. It was assumed that no racemization took place in converting the *d*-pinacolyl alcohol ($[\alpha]^{25}_{5893}$ +7.97°) to the sulfate.[10]

Bromine Oxidation of Pinacolyl Alcohol.—To a solution of 0.406 g. of pinacolyl alcohol in 100 cc. of ice-water was added a solution of 0.65 g. of bromine dissolved in 100 cc. of ice water. The solution was allowed to warm up to 25° over one hour and then stand three hours at 25°. An excess of 2,4-dinitrophenylhydrazine dissolved in dilute sulfuric acid was added and the precipitate collected after one hour. The yield was 0.85 g. (75%) m.p. 119–124°. One recrystallization from methanol raised the m.p. to 126.1–126.5° (undepressed when mixed with authentic dinitrophenylhydrazone of pinacolone) with little loss. This was the best way we found for establishing the presence of pinacolyl alcohol in dilute aqueous solution.

The barium pinacolyl sulfate was resistant to the action of bromine water at 25° as well as to alkaline permanganate and dichromate in dilute sulfuric acid.

α-Naphthylurethan of Pinacolyl Alcohol.—The α-naphthylurethan, m.p. 126.8–127.6°, was obtained in 72% yield by heating the components for ten minutes at 100° and crystallizing from 60–70° alkanes.

Anal.[11] Calcd. for $C_{17}H_{21}O_2N$: C, 75.3; H, 7.8. Found: C, 75.5; H, 8.0.

(10) *Cf.* R. L. Burwell, THIS JOURNAL, **71**, 1769 (1949); R. L. Burwell and H. E. Holmquist, *ibid.*, **70**, 878 (1948).

(11) Clark Microanalytical Lab., Urbana, Ill.

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[CONTRIBUTION FROM THE DEPARTMENT OF PHYSIOLOGICAL CHEMISTRY, THE JOHNS HOPKINS UNIVERSITY, SCHOOL OF MEDICINE]

Apparent Ionization Exponents of 4-Hydroxyquinoline, 4-Methoxyquinoline and N-Methyl-4-quinolone; Evaluation of Lactam–Lactim Tautomerism[1]

BY GABRIEL F. TUCKER, JR.,[2] AND J. LOGAN IRVIN[3]

Apparent ionization exponents for 4-hydroxyquinoline (4-quinolone), 4-methoxyquinoline and N-methyl-4-quinolone have been determined by combined spectrophotometry and potentiometry. These data are applied in the calculation of the microscopic ionization constants and of the equilibrium constant for the lactam–lactim tautomerism of 4-hydroxyquinoline. This compound in aqueous solution at *p*H 7 exists predominantly in the lactam form (4-quinolone), and some evidence is presented which suggests that this form also predominates in solvents of low dielectric constant.

Ewing and Steck[4] have presented absorption spectra for 4-hydroxyquinoline in 0.01 *N* hydrochloric acid, 0.01 *N* sodium hydroxide, aqueous buffer at *p*H 7, and 95% ethanol. In comparing the properties of this compound with those of other hydroxyquinolines, these authors suggested that their data and other observations in the literature were consistent with the existence of a 4-quinolinol: 4-quinolone tautomerism, but no quantitative data were presented for the evaluation of the tautomeric equilibrium.

An examination of the spectrophotometric data of Ewing and Steck and a review of the older literature suggested that quantitative data for the ionization exponents of 4-hydroxyquinoline would be particularly useful in evaluating the contributions of tautomerism and resonance to the properties of this compound. In the present paper the ionization exponents of 4-hydroxyquinoline, N-methyl-4-quinolone and 4-methoxyquinoline are reported from spectrophotometric measurements, and from these the status of the 4-hydroxyquinoline:4-quinolone tautomerism is deduced. These studies are of biochemical interest inasmuch as certain derivatives of 4-hydroxyquinoline are products of the metabolism of the amino acid tryptophan. Also any investigation of lactam–lactim tautomerism has biochemical implication

(1) Aided by a grant from the Penrose Fund of the American Philosophical Society.

(2) Henry Strong Denison Scholar for 1949–1950; 1950–1951.

(3) The Department of Biological Chemistry and Nutrition, School of Medicine, University of North Carolina, Chapel Hill, N. C.

(4) G. W. Ewing and E. A. Steck, THIS JOURNAL, **68**, 2181 (1946); **71**, 238 (1949).

in view of the occurrence of such tautomerism in certain purines and pyrimidines.

Formulation of Equilibria

A. Formulation for 4-Hydroxyquinoline.—The two ionization equilibria or proton exchanges exhibited by 4-hydroxyquinoline are represented in Fig. 1 together with the resonance hybrids of the ions and the quinolinol–quinolone tautomerism postulated for this compound. The resonance structures presented are not the only ones that are possible, but they probably are the most important ones. In order to conserve space, only one of the three possible Kekulé structures is shown for each species. Double-headed arrows are used to represent resonance, and the structures comprising the resonance-hybrid are enclosed by brackets. The following symbols are used to represent the various species shown in Fig. 1: Q_E, the non-ionized quinolinol; Q_K, the non-ionized quinolone which is in tautomeric equilibrium with Q_E; Q^+, the cation formed by addition of a proton to Q_E or Q_K; Q^-, the anion formed by removal of a proton from Q_E or Q_K. Ionization equilibria (proton-exchanges) between species are indicated by two single arrows. The lactam–lactim tautomerism between Q_K and Q_E is represented by two broken arrows directly linking these two forms. However, it should be emphasized that this carries no implication regarding the mechanism of the tautomerism. The most probable mechanism involves the ionization steps shown in the upper and lower parts of Fig. 1 with the species Q^- and Q^+ as intermediates.

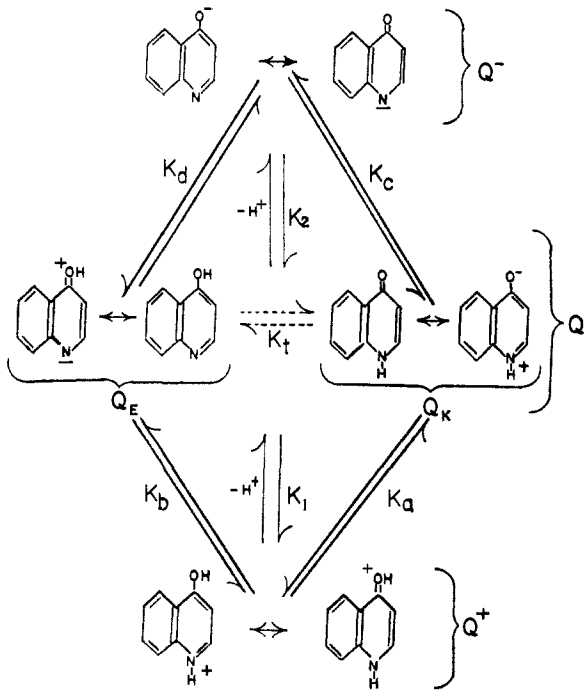

Fig. 1.—Proton-equilibria and lactam–lactim tautomerism of 4-hydroxyquinoline.

The various ionization equilibria can be formulated in terms of the microscopic constants, K_a, K_b, K_c and K_d by the equations in which parentheses represent activities.

$$K_a = \frac{(H^+)(Q_K)}{(Q^+)} \quad (1) \qquad K_c = \frac{(H^+)(Q^-)}{(Q_K)} \quad (3)$$

$$K_b = \frac{(H^+)(Q_E)}{(Q^+)} \quad (2) \qquad K_d = \frac{(H^+)(Q^-)}{(Q_E)} \quad (4)$$

The microscopic constants K_a, K_b, K_c and K_d cannot be determined directly. However, two ionization constants, K_1 and K_2, can be evaluated experimentally by potentiometric titration. In the case of 4-hydroxyquinoline the two ionization steps are widely separated and do not overlap.[5] The constants, K_1 and K_2, are defined and are related to the intrinsic constants as

$$K_1 = \frac{(H^+)(Q_E + Q_K)}{(Q^+)} = K_a + K_b \quad (5)$$

$$K_2 = \frac{(H^+)(Q^-)}{(Q_E) + (Q_K)} = \frac{K_c \times K_d}{K_c + K_d} \quad (6)$$

The tautomeric equilibrium between Q_E and Q_K can be described in terms of the constant K_t

$$K_t = \frac{(Q_K)}{(Q_E)} = \frac{K_a}{K_b} = \frac{K_d}{K_c} \quad (7)$$

The two ionization equilibria involving 4-hydroxyquinoline can be evaluated spectrophotometrically inasmuch as non-ionized 4-hydroxyquinoline and the two ionized species, Q^+ and Q^-, have distinct and characteristic absorption spectra. Presumably the two tautomers, Q_E and Q_K, differ in absorption spectra, but there appears to be no satisfactory procedure for obtaining the characteristic absorption of each individual tautomer since it must be assumed that both are present in an equilibrium mixture at all times. With the postulate that the tautomeric equilibrium between Q_E and Q_K is independent of *p*H, K_t can be assumed to be a true constant. This postulate can be shown to have a sound thermodynamic basis, and experimental evidence of its validity will be discussed later. With the assumption of constancy of K_t at all *p*H values, the spectrophotometric absorption of $Q_E + Q_K$ can be treated as that of a single species. Failure of the validity of this assumption would become apparent in deviation of the experimental data from the theoretical relationships as pointed out later. With such an assumption, apparent ionization constants, K_1', and K_2', can be evaluated at constant temperature and ionic strength by spectrophotometry at selected wave lengths conducted upon buffered solutions of 4-hydroxyquinoline of known *p*H. The apparent ionization constants, K_1' and K_2', have essentially the significance of equations (5) and (6) with the exception that the apparent ionization constants are expressed in terms of *concentrations* of the species Q_E, Q_K, Q^+ and Q^- rather than *activities*. In this paper all constants designated by a prime symbol are *apparent* constants, defined in terms of concentrations rather than activities and restricted to the condition of constant ionic strength. The procedure for evaluating K_1' and K_2' is similar to that

(5) The non-ionized 4-hydroxyquinoline exists in aqueous solution from *p*H 5 to *p*H 8 as a tautomeric equilibrium mixture of Q_E and Q_K, the species Q^+ and Q^- being almost completely absent in this range.

of Clark[6] and of Flexser, *et al.*,[7] as applied by Irvin and Irvin[8] in a study of various aminoquinolines.

The logarithmic equations for the spectrophotometric evaluation of the apparent ionization constants are

$$pH = pK_1' + \log \frac{\epsilon_{Q^+} - \epsilon}{\epsilon - \epsilon_Q} \quad (8)$$

and

$$pH = pK_2' + \log \frac{\epsilon_Q - \epsilon}{\epsilon - \epsilon_{Q^-}} \quad (9)$$

in which ϵ_{Q^+} is the molar absorption coefficient of the compound at a *p*H value sufficiently low to ensure complete transformation into the proton-donor species Q^+, ϵ_{Q^-} is the molar absorption coefficient of the compound at a sufficiently high *p*H value to ensure complete transformation into the proton-acceptor species Q^-, ϵ_Q is the coefficient of the compound at a *p*H value sufficiently distant from and between pK_1' and pK_2' to ensure that the compound is completely in the tautomeric forms Q_E and Q_K, and ϵ is the absorption coefficient for solutions of the compound at a *p*H value at which forms Q_E, Q_K and Q^+ coexist (in evaluating pK_1') or at a *p*H in which forms Q_E, Q_K and Q^- coexist (in evaluating pK_2'). The molar absorption coefficient is defined by the equation, $-\log T = D = \epsilon cl$, in which T is the transmittancy, D is the optical density, c is the concentration of the solution in moles per liter, and l is the length of the light path through the solution in centimeters.

B. Formulation for 4-Methoxyquinoline.—Tautomerism cannot occur in the case of non-ionized 4-methoxyquinoline, and the single proton-exchange exhibited by this compound can be formulated as a simple proton addition at the ring nitrogen. The probable resonance structures of the cationic species are shown in Fig. 2. The ionization constant, K_M, is expressed as

$$K_M = (H^+)(Q_M)/(Q_M^+) \quad (10)$$

Here Q_M represents the non-ionized 4-methoxyquinoline, and Q_M^+ the cation formed by the addition of a proton to Q_M.

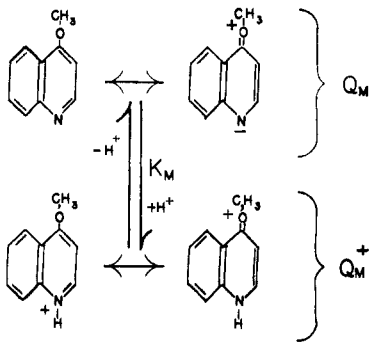

Fig. 2.—Proton-equilibrium involving 4-methoxyquinoline.

C. Formulation for N-Methyl-4-quinolone.—N-Methyl-4-quinolone may be postulated to exist in two tautomeric forms in the ionized state (Fig. 3). In the following formulation Q_N designates the non-ionized N-methyl-4-quinolone, and Q_{NK}^+ and Q_{NE}^+ the ketonic and enolic tautomers of the compound formed by the addition of a proton to Q_N.

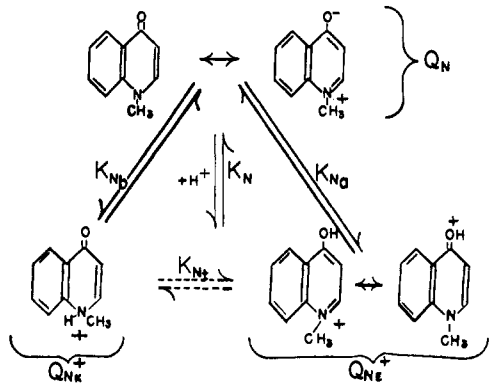

Fig. 3.—Proton-equilibria and tautomerism of N-methyl-4-quinolone.

$$K_{Na} = (H^+)(Q_N)/(Q^+_{NE}) \quad (11)$$

$$K_{Nb} = (H^+)(Q_N)/(Q^+_{NK}) \quad (12)$$

$$1/K_N = \frac{1}{(H^+)(Q_N)/(Q^+_{NE} + Q^+_{NK})} = 1/K_{Na} + 1/K_{Nb} \quad (13)$$

$$K_N = (K_{Na} \times K_{Nb})/(K_{Na} + K_{Nb}) \quad (14)$$

$$K_{Nt} = K_{Na}/K_{Nb} = (Q^+_{NK})/(Q^+_{NE}) \quad (15)$$

Experimental

The sample of 4-hydroxyquinoline which we employed was obtained through the courtesy of Dr. Gerald R. Lappin, m.p. 200–201°. *Anal.* Calcd. for C_9H_7NO: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.19; H, 4.85; N, 9.66.

4-Methoxyquinoline was prepared from 4-chloroquinoline, by refluxing the 4-chloro compound for 2 hours with an excess of metallic sodium in absolute methanol, evaporating the solution to dryness, dissolving the residue with 0.1 *N* NaOH and extracting several times with ether. The combined ether extracts were evaporated under diminished pressure until only an oily residue remained. This residue was dissolved in 2 ml. of 1 *N* HCl, methanol–acetone (1:3) mixture was added, and the solution was evaporated to a small volume under diminished pressure; the hydrochloride crystallized in the form of white needles. The 4-methoxyquinoline hydrochloride was recrystallized from methanol–acetone (1:3) mixture containing a small amount of hydrochloric acid. The hydrochloride melted at 165° with decomposition (reported 164–166° dec.,[9] and 171°).[4] *Anal.* Calcd. for $C_{10}H_{10}NOCl$: C, 61.38; H, 5.152; N, 6.997. Found: C, 61.1; H, 5.11; N, 7.10.

4-Chloroquinoline was prepared by refluxing 4-hydroxyquinoline[10] with $POCl_3$ for 90 minutes. Excess $POCl_3$ was removed under diminished pressure; the residue was dissolved in 0.1 *N* NaOH and was extracted into ethyl ether. The combined ether extracts were re-extracted with 0.1 *N* NaOH, and then the ether was evaporated under diminished pressure in order to obtain the 4-chloroquinoline as the free base. The compound formed a chloroplatinate, m.p. 270° (dec.) (reported 278°).[11]

Synthesis of N-Methyl-4-quinolone.—One hundred milligram of 4-hydroxyquinoline was dissolved in a saturated solution of sodium hydroxide in methanol, an excess of methyl iodide was added and the mixture was refluxed on a water-bath for 3 hours. The reaction mixture was distilled to dryness at 60° under reduced pressure. The residue was dissolved in 3 ml. of 2 *N* NaOH. This solution was ex-

(6) W. M. Clark, "The Determination of Hydrogen Ions," Williams and Wilkins Co., Baltimore, Md., 1928, pp. 152-159.

(7) L. A. Flexser, L. P. Hammett and A. Dingwall, THIS JOURNAL, **57**, 2103 (1935).

(8) J. L. Irvin and E. M. Irvin, *ibid.*, **69**, 1091 (1947); *J. Biol. Chem.*, **174**, 577 (1948).

(9) H. Meyer, *Monatsh.*, **27**, 987 (1906).

(10) O. G. Backeberg, *J. Chem. Soc.*, 618-619 (1933).

(11) F. Wenzel, *Monatsh.*, **15**, 453 (1894).

tracted with four 10-ml. aliquots of chloroform. The combined chloroform extracts were re-extracted with 5 ml. of 0.2 *N* NaOH, and then the chloroform was removed under diminished pressure. The residue was recrystallized as the hydrochloride from a methanol–hydrochloric acid mixture; m.p. 178–182° (reported[12] 176°). *Anal.* of the hydrochloride: Calcd. for $C_{10}H_{10}NOCl$: C, 61.38; H, 5.152; N, 6.997. Found: C, 60.99; H, 5.05; N, 7.13. The chloroplatinate melted at 210° (reported[12] 212°).

The procedure for evaluation of pK_1' and pK' by the spectrophotometric method was similar to that employed in previous studies of various quinoline derivatives. Measurements of *p*H were made with a glass electrode which was standardized against a series of buffer solutions the *p*H values of which were determined with a hydrogen electrode of our design. The hydrogen used in the hydrogen electrode measurements was passed over reduced copper at 600°. The standard of *p*H was "standard acetate" buffer,[13] a solution 0.1 molar with respect both to acetic acid and sodium acetate; it was assigned a *p*H number of 4.64 at 30°. Potentials were measured with a Leeds and Northrup students' potentiometer and were recorded in international volts without correction for liquid junction potentials. All junctions were made with saturated KCl solution. The value[14] of the factor, 2.3026 RT/F was taken as 0.06011 at 30°. For measurements with the glass electrode the null instrument was a number 2420 Leeds and Northrup galvanometer used in conjunction with a Leeds and Northrup thermionic amplifier. This assembly had a sensitivity of 0.003 *p*H unit. The over-all accuracy of *p*H measurements was evaluated as 0.015 *p*H unit in the range from *p*H 1 to *p*H 9 and 0.03 *p*H unit in the range from *p*H 9 to *p*H 12.

Spectrophotometry was carried out with a Beckman photoelectric quartz spectrophotometer, model DU, with 1-cm. fused silica cuvettes. The cuvette compartment was equipped with a channeled plate through which water was circulated from a thermostat, thus maintaining the solutions at 30 ± 0.5°. The nominal spectral interval isolated, evaluated from data for dispersion and slit widths furnished with the Beckman instrument, varied within the range of 1.2 to 2.8 mμ, but was kept at a constant value for any particular wave length for a series of measurements. The absorption spectra obtained at a given *p*H (in the range from *p*H 1 to *p*H 3) were found to be identical in phosphate buffer and in hydrochloric acid–sodium chloride buffer. For evaluation of the apparent ionization exponents, the data for *p*H and the corresponding absorption coefficients at some selected wave length were rectified by the general method of Reed and Berkson[15] with the adaptation of Clark[16] applied essentially as described previously.[8]

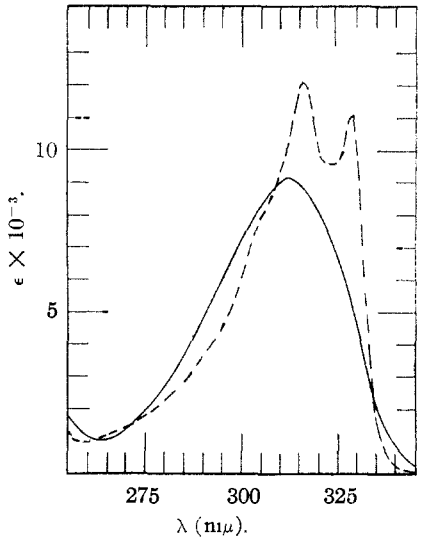

Fig. 4.—Spectrophotometric absorption curves for 4-hydroxyquinoline (4-quinolone) in aqueous solutions: - - -, *p*H 7; —, *p*H 13.

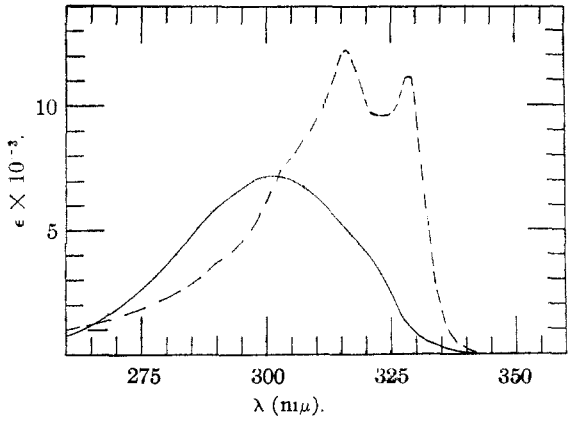

Fig. 5.—Spectrophotometric absorption curves for 4-hydroxyquinoline (4-quinolone) in aqueous solutions: - - -, *p*H 7; —, *p*H 1.08.

Discussion

Absorption spectra for 4-hydroxyquinoline are presented in Figs. 4 and 5. These curves are similar to those reported by Ewing and Steck[4] but differ in certain important respects. The principal discrepancy is in the curves for this compound in aqueous solution at *p*H 7, the molecular absorption coefficient for the peak at 313 mμ reported by Ewing and Steck being about 30% lower than the value which we have determined. The curve reported by Ewing and Steck for 4-hydroxyquinoline in 0.01 *N* hydrochloric acid does not correspond to complete transformation to the species Q^+ but represents the spectrophotometric absorption of a mixture of species consisting principally of Q^+ but containing an appreciable proportion (approximately 30%) of the species Q (Q_E and Q_K) as defined in the present paper. The curve which we are presenting for the compound at *p*H 1.08 corresponds to 5.2% dissociation of Q^+ into Q (as calculated from our value of 2.34 for pK_1') and is more symmetrical than the curve of Ewing and Steck and has an absorption maximum at 302 mμ instead of approximately 312 mμ as shown on the curve of the latter authors.

Isosbestic points[17] were closely maintained at wave length 302.5 mμ throughout the range from *p*H 7 to *p*H 1 and at wave length 309 mμ from *p*H 7 to *p*H 13. The absorption curves reported by Ewing and Steck do not intersect at the points corresponding to our isosbestic points, apparently due to the low values which they have reported for absorption at *p*H 7.

The following values for the apparent ionization

(12) H. Meyer, *Monatsh.*, **27**, 255 (1906).

(13) L. Michaelis, "Die Wasserstoffionenkonzentration," Berlin, 1914; D. A. MacInnes, D. Belcher and T. Shedlovsky, THIS JOURNAL, **60**, 1094 (1938).

(14) W. M. Clark, "The Determination of Hydrogen Ions," Williams and Wilkins Co., Baltimore, Md., 1928, pp. 244-250 and 674. This value of the factor was based on the now discarded use of international volts rather than absolute volts. However, we have used this value of the factor inasmuch as our potentiometer was calibrated in international volts.

(15) L. J. Reed and J. Berkson, *J. Phys. Chem.*, **33**, 760 (1929).

(16) W. M. Clark, J. F. Taylor, T. H. Davies and C. S. Vestling, *J. Biol. Chem.*, **135**, 543 (1940).

(17) The definition and significance of the isosbestic point is discussed by W. M. Clark, "The Determination of Hydrogen Ions," Williams and Wilkins Co., Baltimore, Md., 1928, pp. 152–154.

exponents of 4-hydroxyquinoline at 30° and ionic strength 0.1 were calculated from the spectrophotometric data: $pK_1' = 2.34 \pm 0.03$; $pK_2' = 11.06 \pm 0.04$. In Fig. 6 data for the proton dissociation of the species Q^+ as a function of pH are presented in terms of α, the degree of dissociation of the proton donor, Q^+, into Q and H^+ as calculated from the absorption coefficients. The experimental values of α are averages calculated from data at three wave lengths. The curve is drawn to the theoretical relationship, $p\text{H} = pK_1' + \log [\alpha/(1 - \alpha)]$, for $pK_1' = 2.34$.

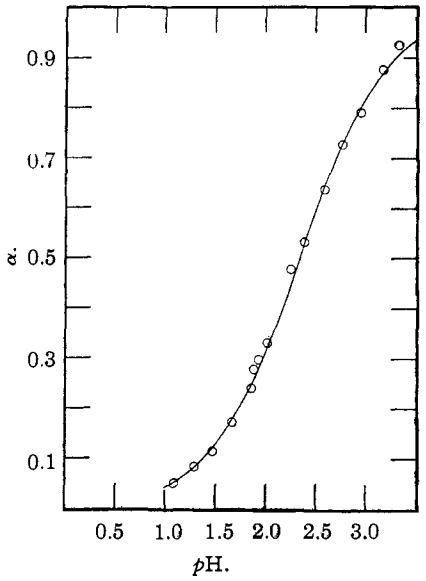

Fig. 6.—Data for the dissociation of a proton from the species Q^+ (see Fig. 1) of 4-hydroxyquinoline. The line is drawn according to the equation: $p\text{H} = pK_1' + \log (\alpha)/(1 - \alpha)$; $pK_1' = 2.34$. α is the degree of dissociation of a proton from the species Q^+. The spectrophotometrically determined values of α are given by the circles.

Constancy of K_t throughout the range of pH examined is a requirement for the spectrophotometric evaluation of pK_1' and pK_2'. The following facts are substantial proof of the constancy of K_t: (1) The constancy of the isosbestic points throughout the ranges of pH in which the proton exchanges occur argue for a constant ratio of Q_K to Q_E such that the non-ionized compound is practically a single species from the spectroscopic standpoint. The probability of maintenance of an isosbestic point if the proportions of *three* species, Q_E, Q_K and Q^+ (or Q^-) were changing simultaneously would be remote. (2) The absorption spectrum of the non-ionized 4-hydroxyquinoline was constant throughout the range of pH 8.5 to 5.0 thus indicating that the ratio of Q_K to Q_E was constant. (3) The values of pK' and pK_1' calculated from data at a number of wave lengths (316, 324, 325 and 328 mμ) were in good agreement. If the ratio of Q_K to Q_E was changing, the values of the ionization exponents calculated at various wave lengths might be expected to differ. (4) Conformity of the experimental data throughout a wide range of pH to the simple relationships derived in equations 1–9 argues for the constancy of K_t since the equations were based upon the assumption of constant K_t.

The absorption spectra of 4-methoxyquinoline under varying conditions of pH are shown in Fig. 7. The apparent ionization exponent was determined as outlined above. The value obtained at 30° and ionic strength 0.1 was $pK_M' = 6.45 \pm 0.03$.

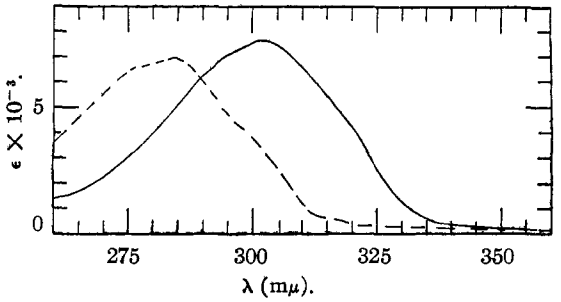

Fig. 7.—Spectrophotometric absorption curves for 4-methoxyquinoline in aqueous solutions: —, pH 1.0; - - -, pH 13.

The absorption spectrum of N-methyl-4-quinolone (Fig. 8) is identical in shape with that of 4-hydroxyquinoline at the same values of pH, the only difference being that the absorption peaks for N-methyl-4-quinolone lie at wave lengths approximately 8 mμ higher than the analogous peaks in the spectra of 4-hydroxyquinoline. The value for pK_N' obtained spectrophotometrically at 30° and ionic strength 0.1 ($pK_N' = 2.36 \pm 0.03$) is identical with the value of pK' for 4-hydroxyquinoline within the limits of error.

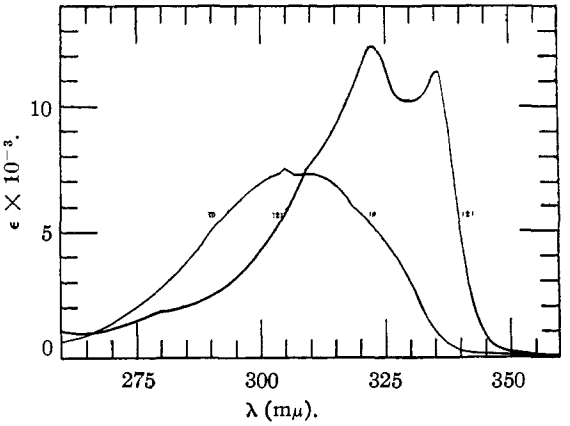

Fig. 8.—Spectrophotometric absorption curves for N-methyl-4-quinolone in aqueous solutions: curve (1), pH 1.0; curve (2), pH 7.0.

Evaluation of K_t' for 4-Hydroxyquinoline.—By use of a procedure similar to that employed by Edsall and Blanchard[18] in studying dipole ions of amino acids, K_t for the 4-quinolone:4-quinolinol tautomerism was evaluated as follows: 4-methoxyquinoline cannot undergo tautomerism and is "fixed" in the lactim configuration. It ionizes in acid solution (evaluated in terms of K_M') but not in alkaline solution. It is reasonable to assume that K_M' for 4-methoxyquinoline would be approximately equal to K_b' for 4-hydroxyquinoline, since

(18) J. T. Edsall and M. H. Blanchard, THIS JOURNAL, **55**, 2337 (1933).

the substitution of a methyl group for a hydrogen atom would have a minor effect. With this assumption and with equations (1), (2) and (7)

$$K_t' = K_a'/K_b' \cong K_a'/K_M' \quad (16)$$

From equation (5)

$$K_a' = K_1' - K_b \cong K_1' - K_M' \quad (17)$$

Substituting the value of K_a' from (17) into (16)

$$K_t' = \frac{K' - K_M'}{K_M'} = \frac{K_1'}{K_M'} - 1 \quad (18)$$

By substitution of the values obtained experimentally for K_1' and K_M', K_t' was calculated to be 1.29×10^4. This value of K_t' indicates that the state of the lactam–lactim tautomeric equilibrium for 4-hydroxyquinoline in aqueous solution is greatly in favor of the lactam species (4-quinolone) and the proportion of the lactim species (the true 4-hydroxyquinoline species) is very small.

The data for pK_1', pK_2', pK_t' and pK_M' permit the calculation of the intrinsic ionization exponents, pK_a', pK_b', pK_c' and pK_d' by application of equations 1–7. The data are summarized in Table I.

TABLE I

APPARENT IONIZATION EXPONENTS FOR 4-HYDROXYQUINOLINE AT 30° AND IONIC STRENGTH, 0.1

pK_1'	2.34	pK_a'	2.34
pK_2'	11.06	pK_b'	6.45
pK_t'	−4.11	pK_c'	11.06
		pK_d'	6.95

The absorption spectrum of 4-hydroxyquinoline in 95% ethanol was found to differ slightly from that exhibited by this compound in aqueous buffers (of *p*H 5 to 8) in two respects: (1) The wave lengths of maximum absorption (316 and 329 mμ) for two of the peaks observed in aqueous solutions were found to be shifted to 317 and 330.5 mμ, respectively, and (3) the relative values of the absorption coefficients at these maxima were found to be reversed for alcoholic solutions of the compound as compared with aqueous solutions (Fig. 9).

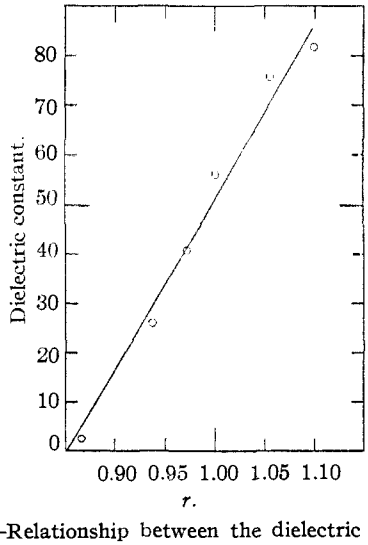

Fig. 9.—Relationship between the dielectric constant of the solvent and the value of r, in which r is the ratio of the absorption coefficient of the peak at 316–318 mμ to the absorption coefficient of the peak at 329–331 mμ.

These changes in the absorption spectrum which accompanied the changes in solvent were at first thought to be suggestive of a possible shift in the tautomeric equilibrium between the lactam and the lactim species inasmuch as such a shift in equilibrium could produce a change in the absorption spectrum of the equilibrium mixture if the two species differed in their absorption of radiant energy. The absorption spectra of 4-hydroxyquinoline in a series of solvents possessed of widely different dielectric constant values were obtained in order to determine whether definite evidence of a shift in lactam–lactim tautomerism could be observed. The solvent of highest dielectric constant in the series was water, and the absorption spectrum of 4-hydroxyquinoline in this solvent must be assumed to be predominantly that of the lactam species in view of the evidence obtained from the analysis of the data for the ionization exponents as presented above. The absorption spectrum of 4-hydroxyquinoline in benzene, the solvent of lowest dielectric constant (2.29) in our series, was very similar to the absorption spectra in water and ethanol and was characterized by a double-peaked band in the 315–335 mμ region of the spectrum, but the absorption coefficient of the peak at the shorter wave length (318 mμ) was less than the absorption coefficient at the higher wave length (331 mμ). This was the reverse of the relative magnitudes of these peaks for the absorption spectrum of aqueous solutions. However, the absorption spectra for solutions in benzene and in ethanol were so similar to that for solutions of the compound in water that it seems reasonable to conclude that the lactam species predominates in each of these solvents. In none of these solvents did the absorption spectrum for 4-hydroxyquinoline (4-quinolone) show a trend in the direction of the absorption spectrum of 4-methoxyquinoline which presumably would be characteristic of the lactim configuration. The changes in the ratio of the absorption coefficients of the two peaks of the bifurcated band at 315–335 mμ with change in dielectric constant is of some interest although we cannot offer an adequate explanation of this effect. In Fig. 9 it can be seen that the ratio of the absorption coefficients for these peaks bears an approximately linear relationship to the dielectric constant of the solvent.[19] The possible significance of this relationship is not known. The small changes in absorption spectrum resulting from changes in the nature of the solvent do not appear to be due to the formation of dimers or higher polymers of 4-hydroxyquinoline of the type discussed by Sheppard.[20] The values of the molar absorption coefficients (ϵ), calculated from optical densities at the wave lengths of the two absorption peaks, for 4-hydroxyquinoline in either ethanol or water were constant over a wide range of concentrations (2×10^{-4} to 4×10^{-7} M).

(19) The solvents of intermediate dielectric constants were mixtures of ethanol and water and the values of the dielectric constants for these mixtures were taken from data presented by H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold Publishing Corp., New York, N. Y., 1943.

(20) S. E. Sheppard, *Rev. Mod. Phys.*, **14**, 304 (1942); THIS JOURNAL, **66**, 1995, 2003 (1944).

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

The Heat of Adsorption of Nitrogen on Titanium Dioxide (Rutile) at 77.3°K.

BY G. L. KINGTON AND J. G. ASTON

Terms in the expression for the isothermal heat of adsorption as given by Hill are shown to be the quantity known to previous authors as the heat of compression. The relationship between the *adiabatic* differential heat of adsorption and the heat of compression is deduced and the isothermal and adiabatic heats of compression related. The relationship between the calorimetric heat and isosteric heat is obtained and is shown to be independent of any assumption of a two-dimensional surface pressure. Differential heat of adsorption data for the system nitrogen on titanium dioxide (rutile) at 77.32°K., have been obtained in a precision adiabatic calorimeter and the data are described. Heat data have been obtained for the same system using the Clausius–Clapeyron relationship. These directly measured experimental values of the isosteric and calorimetric heats of adsorption have been compared and the validity of the theoretical relationship between these two quantities has been verified by the experimental data given. The value of the calorimetric heat of adsorption corrected for the adiabatic heat of compression is shown to agree within ±15 cal./mole (*i.e.*, ±0.9%) with the isosteric heat. There is no basis for considering calorimetric heats as usually measured, as obscure.

The field of adsorption has been obscured for some time due to statements[1,2] that the meaning of calorimetric heats as usually measured is uncertain. It is one of the aims of this paper to investigate the basis of such comments.

Differential heats of adsorption may be determined by three methods. A calorimetric measurement may be made under adiabatic or isothermal conditions, or the heat may be determined using the Clapeyron equation, *i.e.*, by the so-called isosteric method. It is of some importance to understand the significance of the quantities obtained from these three methods and to be able to relate them. Joyner and Emmett[3] have made a comparison of calorimetric and isosteric heats but the comparison is limited by the probable error in the calorimetric values which were determined by Beebe and estimated by him to have an accuracy of ±5%. Nevertheless, these calorimetric values are, in general, higher than the isosteric values. This may be explained by the fact that a correction for the heat of compression (as explained in the present paper) should be applied to the calorimetric values. Furthermore, if these heat quantities are to be of maximum value in helping to determine the state of the adsorbed phase, then calorimetric data must be determined with the highest possible accuracy.

It has been known for a considerable time that the calorimetric differential heat of adsorption includes a heat of compression. This aspect was discussed by Ward.[4] The adiabatic calorimetric heat of adsorption contains a so-called adiabatic heat of compression and the isothermal calorimetric heat of adsorption contains a corresponding isothermal heat of compression. The adiabatic and isothermal heats of compression are naturally different. The only possible uncertainty in a calorimetric measurement of a heat of adsorption is in the extent to which the heat of compression is conveyed to the calorimeter. This paper will show that in the usual type of adiabatic calorimeter the whole of the heat of compression appears in the calorimeter, within the experimental error.

Hill has recently obtained the relationship between the *isothermal* differential heat of adsorption and the isosteric heat. However, in practice the isothermal type of calorimeter is seldom used, since it has the disadvantage of operating at a few fixed temperatures, depending on the choice of the bath material. It is more advantageous to make measurements in a precision type of *adiabatic* calorimeter where the temperature may be controlled at will by electrical means, allowing isotherms, heat capacities and heats of adsorption or change of phase to be measured at any desired temperature. Precision adiabatic calorimeters have been developed for the measurement of heat capacities and this paper describes the use of such a calorimeter for measuring heats of adsorption and the data obtained. In order to interpret the data it has been necessary to investigate the theoretical basis of a heat of adsorption measurement in an adiabatic calorimeter, *i.e.*, the significance of the adiabatic heat of adsorption and the so-called adiabatic heat of compression.

Experimental

The Calorimetric Heat of Adsorption.—The calorimetric differential heat of adsorption of nitrogen on titanium dioxide was measured in the adiabatic calorimeter described by Morrison and Szasz.[5] The titanium dioxide was in the rutile crystalline form and had a surface area, as determined by the B.E.T. method, of 10.4 sq. m./g.

The heat effect accompanying the change in quantity of gas on the surface of a solid may be measured either as an adsorption process or as a desorption process. It is possible to measure an adsorption heat at any coverage of the surface,[6] but the determination of desorption heats is limited to that part of the surface (*i.e.*, above approximately one layer in this case) where the equilibrium gas pressure permits sufficient quantities of gas to be desorbed to give a measurable temperature change.

The majority of runs were made using the adsorption process, and covered the range 0 to 1.5 v/v_m. A smaller number of runs were carried out in desorption in the region 1 to 1.5 v/v_m. The maximum possible error in the calorimet-

(1) Brunauer, "The Absorption of Gases and Vapors—Physical Adsorption," Princeton University Press, Princeton, N. J., 1943, Chapter 8.

(2) Hill, *J. Chem. Phys.*, **17**, 520 (1949).

(3) Joyner and Emmett, THIS JOURNAL, **70**, 2356 (1948).

(4) Ward, *Proc. Roy. Soc.* (*London*), **133A**, 506 (1931).

(5) Morrison and Szasz, *J. Chem. Phys.*, **16**, 280 (1948).

(6) All surface coverages are expressed in terms of v/v_m, where v_m is obtained in the usual manner from the treatment of Brunauer, Emmett and Teller.