562. *The Dissociation Constants of* 8-*Hydroxyquinoline.*

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New values for the acidic and basic dissociation constants of 8-hydroxyquinoline, obtained from solubility and from spectrophotometric measurements, are compared with published data.

IN aqueous solution 8-hydroxyquinoline (" oxine "; HOx) is in equilibrium with hydroxonium ions (H_3O^+), with 8-hydroxyquinolinium ions (H_2Ox^+) and with oxinate ions (Ox^-), and reliable values for the thermodynamic dissociation constants K_1 and K_2 of the acidic species H_2Ox^+ and HOx were required in connection with studies of partition equilibria involved in the determination of various trace metals with this analytical reagent. By two different methods Stone and Friedman (*J. Amer. Chem. Soc.*, 1947, **69**, 209) obtained concordant data which agreed with earlier measurements by Fox (*J.*, 1910, **1119**), but the marked discrepancies between their values and those reported by Kolthoff (*Chem. Weekblad*, 1927, **24**, 606) and Lacroix (*Anal. Chim. Acta*, 1947, **1**, 260) pointed to the need for a redetermination (cf. Table I).

TABLE I.

Ref.	$K_b \times 10^{10}$.	pK_1'.	$K_a \times 10^{10}$.	pK'_2.	Method.
1	2·3	4·5	2	9·7	Colorimetric at 18°; no details given.
2 (*b*)	3·9	4·8	0·44	10·36	Salt hydrolysis and partition measurements.
3	—	—	0·420	10·38	Solubility of oxine in alkaline buffers at 25°.
3	—	—	0·428	10·37	Spectrophotometry at room temperature.
4 (*c*)	11	5·23	2·0	9·70	Potentiometric titration at 20°.

1, Kolthoff. 2, Fox. 3, Stone and Friedman. 4, Lacroix, *locc. cit.*

(*a*) We reserve the symbol K for thermodynamic constants, and K' for the Brønsted acidity constants (*Chem. Reviews*, 1928, **5**, 293) defined by $K_1' = \{H^+\}[HOx]/[H_2Ox^+]$ and $K_2' = \{H^+\}[Ox']/[HOx]$. These are related to each other and to the acid and basic ionisation constants K_a and K_b often quoted in the literature by the equations: $K_1' = K_w/K_b$; $K_2' = K_a$; $K_1 = K_1' \cdot f_{HOx}/f_{H_2Ox^-}$; $K_2 = K_2' \cdot f_{Ox^-}/f_{HOx}$.

(*b*) Stone and Friedman calculate $K_a = 3{\cdot}68 \times 10^{-11}$ from the same data.

(*c*) Calculated for an ionic strength $\mu = 0{\cdot}1$ from $pK_1 = 5{\cdot}07$ and $pK_2 = 9{\cdot}84$ (*q.v.*).

Two methods were employed.

(a) *Spectrophotometric Measurements* [with J. T. WILSON].—Solutions of oxine are yellow in both acid and alkaline media, for, though the neutral molecule does not absorb strongly in the visual region, the ions H_2Ox^+ and Ox^- have absorption bands in the visual violet; since, further, their absorption spectra over the range 2900 to 3100 A. are almost identical, change of pH does not produce such marked changes in the absorption spectrum of oxine as is commonly the case in acid–base systems. Indeed, the marked similarity between the absorption spectra of oxine in buffers of pH 4 and 10 led Stone and Friedman (*loc. cit.*) to state " thus nearly the same species must be present in both solutions "; in fact, about 90% of the acid solution consists of H_2Ox^+, with 10% HOx and extremely little Ox^-, whilst the alkaline buffer contains 60% as Ox^-, 40% as HOx, and practically no H_2Ox^+.

At any fixed wave-length, if E_i represents the optical density of a solution of oxine in an aqueous buffer at the isoelectric point where $pH = \frac{1}{2}(pK_1' + pK_2')$, and E_b is the optical density in a sufficiently alkaline solution where $pH \gg pK_2$ so that $[Ox^-] \gg [HOx] \gg [H_2Ox^+]$, and E_a is the corresponding limiting value in a solution where $pH \ll pK_1'$, it can be shown that the optical density in a solution where $pH = pK_1'$ is given rigorously by

$$E_{pK_1'} = [E_i + E_a + E_bK_2'/K_1' + (2E_i - E_a - E_b)\sqrt{(K_2'/K_1')}]/[2 + (K_2'/K_1')] \quad . \quad (1)$$

with a similar expression for $E_{pK_2'}$. Naturally the constant total amount of oxine employed in every experiment must be such that the optical density is a linear function of concentration for each of the three absorbing species. Since, for oxine, K_2'/K_1' is $<10^{-4}$, we may obtain approximate values for the acid exponents from the simple equations $E_{pK_1'} = \frac{1}{2}(E_i + E_a)$ and $E_{pK_2'} = \frac{1}{2}(E_i + E_b)$, and more accurate values from equation (1) by successive approximation.

Optical densities of oxine of concentration $3{\cdot}45 \times 10^{-5}$ g.-mol./l. in sixteen buffer solutions covering the range pH 2—12 were measured in a 5-cm. silica cell at room temperature (20° ± 3°) over a wide range of wave-lengths. Values for pK_1' calculated from measurements at fourteen wave-lengths differed by less than 0·05 unit from the average pK_1' (5·02). Similar, but less concordant, measurements of pK_2' gave the average value 9·75. Now all the buffer solutions were made up to have the same ionic strength, 0·1 M. Since f_{HOx} will not differ appreciably from unity, on the assumption that $f_{H_2Ox^+}$ (or f_{Ox^-}) is equal to the mean activity coefficient of a typical univalent ion at the same ionic strength and that the radius of these ions is approximately 1·5 A. we obtain $\log f_{\pm} = -0{\cdot}137$ whence the thermodynamic dissociation constants of H_2Ox^+ and HOx are given by $pK_1 = 4{\cdot}88$ and $pK_2 = 9{\cdot}89$.

(b) *Solubility Measurements* [with J. A. D. EWART].—If S g.-mol./l. is the measured solubility of oxine in an aqueous buffer in which the hydrogen ion activity is α_{H^+}, then

$$S = [HOx] + [H_2Ox^+] + [Ox^-] = [HOx]\{1 + \alpha_{H^+}/K_1' + K_2'/\alpha_{H^+}\}$$

Writing S_0 for the (hypothetical) solubility of the single species HOx in pure water and rearranging (cf. Krebs and Speakman, *J.*, 1945, 593), we have

$$(S - S_0)/S_0 = (\alpha_{H^+}/K_1')(1 + K_1'K_2'/\alpha_{H^+}{}^2) = (K_2'/\alpha_{H^+})(1 + \alpha_{H^+}{}^2/K_1'K_2')$$

whence

$$pK_1' - pH = \log(S - S_0)/S_0 - \log[1 + (K_1'K_2'/\alpha_{H^+}{}^2)]$$

and

$$pH - pK_2' = \log(S - S_0)/S_0 - \log[1 + (\alpha_{H^+}{}^2/K_1'K_2')] \quad . \quad . \quad . \quad . \quad (2)$$

As they stand these equations are insoluble since the value of S_0 is not accessible to direct measurement: its graphical evaluation from solubility in various alkaline (or acid) media by plotting S against $1/\alpha_{H^+}$ (or against α_{H^+}) may involve a long and unsatisfactory extrapolation (see below). However the solubility of an ampholyte reaches a minimum value, S_i, at the isoelectric point where $\alpha_{H^+} = \sqrt{K_1'K_2'}$, and if its magnitude is such as to permit of accurate measurement it is legitimate to use this value in place of S_0 in plotting equations (2), omitting in each case the second term on the right-hand side. Lines of roughly unit slope should result, and the values of the abscissæ when S equals $2S_i$ will give approximate values for pK_1' and pK_2' from which the required solubility of oxine in pure water can be calculated from the expression $S_0 = S_i/(1 + 2\sqrt{K_2'/K_1'})$. By use of this first approximation to the value of S_0 and the tentative values for K_1' and K_2' the equations (2) can be plotted to give a pair of lines of unit slope intersecting at the isoelectric point. Values of the acid exponents obtained from this graph can be refined by successive approximation where this is justified by the accuracy of the experimental data. Measurements at 20° ± 0·05° of the solubility of purified oxine in aqueous buffers covering the range pH 4—11 and of constant ionic strength gave values of 5·27 and 9·68 for the Brønsted acidity exponents, whence $pK_1 = 5{\cdot}13$ and $pK_2 = 9{\cdot}82$.

(c) *Discussion.*—After this work had been completed, Phillips and Merritt (*J. Amer. Chem. Soc.*, 1948, **70**, 410) reported spectrophotometric measurements leading to $pK_a = 9{\cdot}71$ and $pK_b = 9{\cdot}08$. Neither the ionic strength nor the temperature of measurement was specified but assuming that the latter was 20° with μ 0·1 we obtain $pK_1 = 4{\cdot}95$ and $pK_2 = 9{\cdot}85$, in satisfactory agreement with our own measurements. In calculating dissociation constants from his potentiometric measurements at 20° where oxine precipitates and saturates the solution before the point of half-neutralisation, Lacroix (*loc. cit.*) used the solubility of oxine at 18°. Use of the correct data for 20° changes his results but slightly, to give $pK_1 = 5{\cdot}07$ and $pK_2 = 9{\cdot}84$. The excellent agreement between the four recent and independent values for pK_2 confirms the early colorimetric measurements of Kolthoff (*loc. cit.*) but is incompatible with those of Stone and Friedman. Though the solubility measurements by Stone and Friedman were made at 25° (the temperature of their spectrophotometric measurements is not recorded) it seems improbable than an increase of 5° could change pK_2 by as much as 0·5 unit. However of the four solubility measurements which they record, their extrapolated value of K_s (our S_0), $6{\cdot}12 \times 10^{-3}$, can be obtained only by omitting the measurement at pH 9·6: the remaining observations then lead to pK_2' 10·44 (not 10·38 as they state). It seemed possible that the pH values they quote might refer to the buffer solutions *before* saturation with oxine. With the same buffers (Kolthoff and Vleeschouwer, *Biochem. Z.*, 1927, **189**, 191) our own measurements at 25° ± 0·05° gave a significantly lower value for S_0 of $4{\cdot}75 \times 10^{-3}$ g.-mol./l. with pK_2' (25°) = 9·80.

An error of 0·02 unit in pK may arise from a 1% error in solubility measurements, whilst the accuracy of dissociation constants derived spectrophotometrically depends on the accuracy with which the graph of optical density as a function of pH can be plotted and interpolated. Pending a more accurate determination by an independent method we favour the values $pK_1 = 5{\cdot}00 \pm 0{\cdot}10$ and $pK_2 = 9{\cdot}85 \pm 0{\cdot}05$.

EXPERIMENTAL.

8-Hydroxyquinoline was purified by steam-distillation from acid solution, followed by recrystallisation from metal-free water and from alcohol. During making up of solutions for spectrophotometric measurements the presence of alcohol (which causes erratic readings in the ultra-violet; cf. Stone and Friedman, *loc. cit.*) was avoided. Since the reagent dissolves rather slowly in water it was generally dissolved in 25 ml. 0·2N-sodium hydroxide, diluted with distilled water, and exactly neutralised with 0·2N-hydrochloric acid before being made up to the desired volume. Buffer solutions for use below pH 2 were prepared from mixtures of hydrochloric acid and sodium chloride. For more alkaline media conventional buffers compounded of partly neutralised acetic, phosphoric, and boric acid were employed, sufficient sodium chloride being added in each case to give an ionic strength of 0·1M. at the dilution finally employed for measurements.

Optical absorptions were measured with a Beckman Model DU Spectrophotometer with a 5·001-cm. silica cell. The slit widths varied according to the wave-length used but a maximum of 1·5 A. was used over the range 2650—3300 A. Preliminary measurements showed that Beer's law was obeyed for solutions of oxine up to a concentration of at least 10 mg./l., but all the buffer solutions employed were made up to contain a smaller total concentration, *viz.*, 5·0 mg./l. The appropriate buffer solution containing no oxine was used in the " solvent " or comparison cell. Measurements of the pH were made to 0·01 unit with a Cambridge pH Meter.

Solubility measurements were carried out by stirring excess of oxine with the appropriate buffer in a thermostat controlled to ±0·05°. To facilitate saturation it was advantageous to obtain a crop of fine crystals by heating to some 10° above the desired final temperature and then chilling rapidly. That no appreciable supersaturation persisted was shown by data agreeing to within 1—2% after 24 hours' stirring in experiments where equilibrium was approached from both lower and higher temperatures. After 24—40 hours the excess of oxine was allowed to settle and the concentration of aliquots of the saturated solution after filtration through sintered glass or cotton-wool plugs was determined bromometrically (Berg, *Pharm. Zeitung*, 1926, **71**, 1542). The pH of the solutions were, of course, measured *after* saturation, for where the solubility was considerable the acidity of the original buffer was significantly altered; the effect was most marked with the hydrochloric acid–sodium chloride mixtures and with others of low buffer capacity. Solubility measurements at 20·0° gave the following results, each value being the mean of at least three concordant determinations :

pH	3·92	4·03	4·29	4·38	4·65	4·75	5·83	6·36
Solubility in g./l.	72·2	14·64	5·50	5·28	3·396	2·093	0·653	0·585

pH	7·01	7·75	8·55	9·76	9·95	10·25	11·07
Solubility in g./l.	0·556	0·555	0·594	1·102	1·608	2·525	14·59

Taking S_i as 0·555 g./l. ($3{\cdot}82 \times 10^{-3}$ g.-mol./l.) we obtain from the plot of $\log(S - S_i)/S$ against pH the values $\mathrm{p}K_1' = 5{\cdot}2$ and $\mathrm{p}K_2' = 9{\cdot}7$, whence $S_0 = 3{\cdot}78$ g.-mol./l. Successive applications of equation (2) give $\mathrm{p}K_1'$ 5·28, $\mathrm{p}K_2'$ 9·67, $S_0 = 3{\cdot}775$, and finally $\mathrm{p}K_1'$ 5·27 and $\mathrm{p}K_2'$ 9·68. The isoelectric point is at pH 7·48.

Solubility measurements at 25° with the alkali–glycine buffers used by Stone and Friedman (*loc. cit.*) gave the following mean values :

pH	9·57	9·70	9·83	10·01
Solubility in g./l.	1·099	1·222	1·405	1·841

Eight measurements in a borax–boric acid buffer of pH 7·60 gave $S_i = 0{\cdot}694 \pm 0{\cdot}003$. Assuming the previous values for K_1' and K_2' we calculate $S_0 = 4{\cdot}75 \times 10^{-3}$, whence $\mathrm{p}K_2'$ (25°) = 9·80.

In an extended series of measurements at 25° in a buffer of initial pH 11·4 it was noted that the solubility of oxine rose to a steady value of $12{\cdot}7 \times 10^{-3}$ g.-mol./l. during 24 hours but subsequently decreased to 12·6, 12·3, and 12·2 on successive days, whilst the corresponding pH values fell to 9·96, 9·95, and 9·91.

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