[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, INDIANA UNIVERSITY]

Ionization Constants of Some Substituted 8-Hydroxyquinolines

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In the course of other work still in progress, values for the acidic and basic ionization constants of some methyl substituted 8-hydroxyquinolines and their sulfonic acid derivatives were needed. The optical method of Stenstrom and Goldsmith[2] was used to determine these constants.

Experimental

The methyl substituted 8-hydroxyquinolines and 8-methoxyquinaldine were prepared by modification of the Skraup reaction. 8-Hydroxyquinaldine, m.p. 73–73.5°, was made by the Doebner–v. Miller method[3]; 2,4-dimethyl-8-hydroxyquinoline, m.p. 64–64.5°, was prepared according to Bauer and Engler from *o*-aminophenol plus a mixture of paraldehyde and acetone saturated with dry hydrogen chloride[4]; 8-hydroxylepidine, m.p. 140–141°, and 3,4-dimethyl-8-hydroxyquinoline, m.p. 123–124°, were obtained by the analogous reactions of *o*-aminophenol with methylal plus acetone saturated with hydrogen chloride gas and with methylal plus methyl ethyl ketone saturated with hydrogen chloride gas, respectively; 8-methoxyquinaldine, m.p. 123°, was made from *o*-anisidine and crotonaldehyde by the type of procedure used by Campbell and Schaffner to make 4-methylquinolines.[5]

8-Methoxyquinoline,[6] m.p. 45.5–46°, was made from 8-hydroxyquinoline, m.p. 75°, by methylation with dimethyl sulfate.

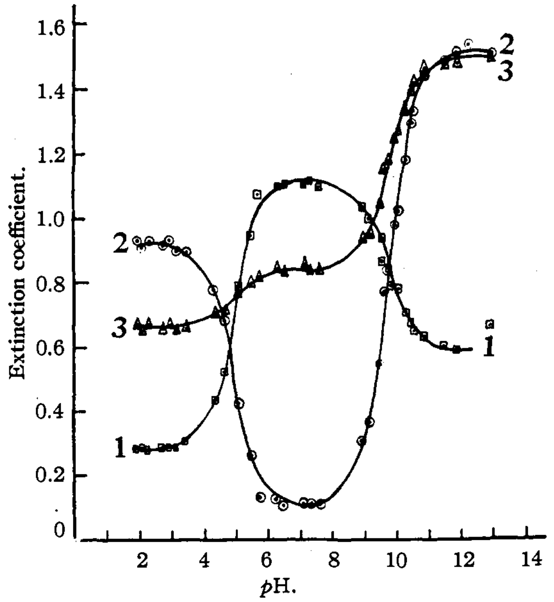

Fig. 1.—8-Hydroxyquinoline, 0.008% in aqueous solution: 1, at 280 mμ; 2, at 330 mμ; 3, at 355 mμ.

The sulfonic acid derivatives of these compounds were formed by direct sulfonation with fuming sulfuric acid at 0–10°.[7]

All compounds were recrystallized until the melting points agreed with those in the literature or, in the case of those compounds whose melting points are not recorded in the literature, until a constant melting point was obtained. The sulfonic acid derivatives melt above 300° and therefore their melting points were not accurately determined.

The ultraviolet absorption spectra of accurately prepared 0.008% aqueous solutions of these compounds (excepting 3,4-dimethyl-8-hydroxyquinoline which had to be run in 0.004% solution owing to its low solubility) at varying *p*H values were measured with a Beckman Model DU Quartz Spectrophotometer using 1.0-cm. cells and slit widths from 1.2 to 0.2 mm. as required. The *p*H was adjusted by additions of dilute sodium hydroxide or hydrochloric acid and was determined with a Beckman *p*H meter that had been standardized against a potassium acid phthalate buffer of *p*H 4.01 and also against five known sodium carbonate–hydrochloric acid buffers in the range of *p*H 10.17–11.36. *p*H above 11.36 was calculated approximately by adding known amounts of a standard sodium hydroxide solution.

From thirty to forty solutions of *p*H between 2 and 13 were measured for each compound, and extinction values at two different wave lengths (280 mμ and 355 mμ in most cases) were used in the calculations. A typical plot of extinction against *p*H at three wave length values for 8-hydroxyquinoline is shown in Fig. 1.

Results

The phenolic ionization constants were obtained by a graphical determination of the *p*H at which the extinction was halfway between its values in alkaline and in neutral solution. (The average values at two wave lengths were used; in no case did the *pKa* determined at one wave length differ by more than about 0.1 unit from the *pKa* at the other wave length.) According to Stenstrom and Goldsmith,[2] at the mid-point *p*H = *pKa*. By analogy, the graphical determination of the *p*OH at which the extinction was halfway between its neutral and acid values gave *pKb*.

For 8-methoxyquinoline and 8-methoxyquinaldine, the extinctions in neutral and basic solutions were the same since no acid ionization could occur.

The experimental results are listed in Table I and the constants *Ka* and *Kb* are given in Table II. By *Ka* is meant the dissociation constant for the phenolic group alone.

Discussion

The relative basicities of these compounds agree very well with what would be predicted from the electron-releasing tendencies of methyl groups substituted *o*, *m*, and *p* to the basic nitrogen; methyl groups in *ortho* or *para* position increase the basicity and decrease the acidity of the substituted

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[1] Abstracted from a thesis to be presented to the faculty of the Graduate School of Indiana University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[2] W. Stenstrom and N. Goldsmith, *J. Phys. Chem.*, **30**, 1683 (1926).

[3] L. L. Merritt and J. K. Walker, *Ind. Eng. Chem.*, *Anal. Ed.*, **16**, 387 (1944).

[4] C. Engler and A. Bauer, *Ber.*, **22**, 209 (1889).

[5] K. N. Campbell and I. J. Schaffner, THIS JOURNAL, **67**, 86 (1945).

[6] B. Vargolici and E. Rothlin, *Ber.*, **49**, 581 (1916).

[7] K. Matsumura, THIS JOURNAL, **49**, 810 (1927).

8-hydroxyquinoline; *meta* substitution exerts a relatively slight influence.

TABLE I

pKa AND *pKb* OF 8-HYDROXYQUINOLINE DERIVATIVES

Compound	Wave length mμ	*pKa*	*pKb*
8-Hydroxyquinoline	280	9.70	9.08
	330	9.70	9.10
	355	9.72	9.08
8-Hydroxylepidine	280	10.08	8.50
	330	9.90	..
	355	10.00	8.38
3,4-Dimethyl-8-hydroxyquinoline	280	10.10	8.20
	355	10.00	8.20
8-Hydroxyquinaldine	280	...	8.43
	330	10.33	8.48
	355	10.28	8.45
2,4-Dimethyl-8-hydroxyquinoline	330	10.60	7.77
	355	10.60	7.83
8-Methoxyquinoline	305	...	8.99
8-Methoxyquinaldine	350	...	8.30
8-Hydroxyquinoline-5-sulfonic acid	280	8.85	9.98
	355	8.87	9.87
8-Hydroxyquinaldine-5?-sulfonic acid	290	9.30	9.20
	355	9.30	9.20
8-Hydroxylepidine-7?-sulfonic acid	300	10.00	9.21
	340	10.01	9.24
2,4-Dimethyl-8-hydroxyquinoline-7?-sulfonic acid	340	10.17	8.80
	350	10.10	8.80

TABLE II

ACIDIC AND BASIC IONIZATION CONSTANTS OF 8-HYDROXYQUINOLINE DERIVATIVES

Substance	*Ka* × 10	

Substance	*Ka* $\times 10^{+10}$	*Kb* $\times 10^{+10}$
8-Hydroxyquinoline	1.95	8.32
8-Hydroxylepidine	1.00	36.4
3,4-Dimethyl-8-hydroxyquinoline	0.892	63.1
8-Hydroxyquinaldine	.490	35.5
2,4-Dimethyl-8-hydroxyquinoline	.252	159
8-Methoxyquinoline	....	10.2
8-Methoxyquinaldine	....	50.1
8-Hydroxyquinoline-5-sulfonic acid	13.8	1.20
8-Hydroxyquinaldine-5?-sulfonic acid	5.01	6.30
8-Hydroxylepidine-7?-sulfonic acid	0.976	6.04
2,4-Dimethyl-8-hydroxyquinoline-7?-sulfonic acid	.725	15.9

The fact that the basic dissociation constants of 8-methoxyquinoline and 8-methoxyquinaldine are only slightly larger than those of the corresponding 8-hydroxy compounds suggests that the hydroxyl group in the latter does not have much influence on the basic dissociation, and hence that the 8-hydroxyquinolines are not ampholytes.

It appears probable from its physical and spectral resemblance to 8-hydroxyquinoline-5-sulfonic acid that the sulfonation product of 8-hydroxyquinaldine has the sulfonic acid group in the 5 position. Owing to the physical differences between these two compounds and the sulfonation products of 8-hydroxylepidine and 2,4-dimethyl-8-hydroxyquinoline and also to the marked discrepancy in their phenolic ionization constants, it is likely that the latter compounds sulfonate in the 7-position rather than the 5-position.

Previous measurements of *Ka* for 8-hydroxyquinoline have been made by Fox[8] and by Stone and Friedman.[9] By hydrolysis measurements Fox obtained 0.368×10^{-10} and by solubility and spectroscopic measurements Stone and Friedman obtain the values 0.420×10^{-10} and 0.428×10^{-10}. Our measurements are not in too good agreement with these values, but we feel that the checks obtained by using different wave lengths for measurement and the care in determining *p*H at a large number of values justify this report. Furthermore the ionic strength was not considered in either case. Feldman and Powell[10] by colorimetric means obtain 80×10^{-10} and 0.8×10^{-10}, respectively, for *Ka* and *Kb* for 8-hydroxyquinoline-5-sulfonic acid. These values from visual comparisons are not as precise as spectrophotometric measurements but are of the same order of magnitude as our results.

Summary

The phenolic and basic ionization constants of some methyl substituted 8-hydroxyquinolines and their sulfonic acid derivatives have been determined spectrophotometrically, and have been found to be in good agreement with predictions based on the electron-releasing tendencies of methyl groups.

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[8] J. J. Fox, *J. Chem. Soc.*, **97**, 1119 (1910).

[9] K. G. Stone and L. Friedman, THIS JOURNAL, **69**, 209 (1947).

[10] H. B. Feldman and A. L. Powell, *ibid.*, **62**, 3107 (1940).