Summary

The condensation of 2-pyrrolealdehyde with hippuric acid and acetic anhydride gives rise to two isomeric azlactones. Configurations have been tentatively assigned to these isomers on the basis of an intramolecular condensation which only one of them appears to undergo.

URBANA, ILLINOIS RECEIVED JUNE 27, 1949

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF INDIANA UNIVERSITY]

Comparative Properties of Some Methyl Substituted 8-Quinolinols

BY JOHN P. PHILLIPS[1] AND LYNNE L. MERRITT, JR.

As part of an investigation in this Laboratory of some new analytical reagents of the 8-quinolinol series, the 2- and 4-methyl derivatives were studied.[2,3] Because these derivatives showed some rather interesting differences from each other and from 8-quinolinol, the properties here described were determined and the results compared.

Experimental

Purification of Materials.—The substituted 8-quinolinols were prepared and purified as previously described.[3,4] A further check on the purity of the 8-quinolinol and 2-methyl-8-quinolinol used was obtained through their quantitative bromination[5] with standard potassium bromate, both analyzing better than 99.7%.

Infrared Spectra.—All spectra were obtained with a Beckman IR-2 instrument with automatic recording. The intensity curves for solvent and solution were recorded on the same graph and the ratios of the two curves calculated at corresponding wave lengths in order to get per cent. transmission. The assignment of wave lengths was calculated from the known absorption bands of carbon tetrachloride, carbon dioxide and water vapor with an estimated accuracy of ±0.05μ over most of the range studied.

Approximately saturated solutions in carbon tetrachloride in 0.1 mm. thick salt cells were used throughout.

Ultraviolet Spectra.—Curves were recorded with a Beckman Model DU Quartz Spectrophotometer using 1.00 cm. cells and slit widths from 0.1–2.0 mm. as required. Readings were made every one millimicron in the vicinity of an absorption maximum and at somewhat wider intervals elsewhere. All compounds obeyed Beer's law satisfactorily in the concentration range studied. Molecular extinctions are considered accurate to two significant figures.

Powder Diffraction Lines.—The finely powdered samples, mounted on a rotating hard glass fiber coated with vaseline, were exposed for five hours to filtered copper X-ray radiation. The "*d*" values, calculated in the usual way, are the average values from two or more photographs for each compound. Relative intensities were estimated visually.

Quantitative Precipitations of Metals.—The procedure was the same as previously described[2] except that, owing to coprecipitation of the excess substituted quinolinol, it was usually necessary to ignite the precipitates to the oxides for weighing.

The standard solutions of Cu^{++}, Zn^{++}, Mg^{++}, Co^{++}, Mn^{++}, Fe^{+++} and Al^{+++} were prepared by standard methods from weighed quantities of reagent grade chemicals and further analyzed by precipitation with 8-quinolinol. Determinations were made at 0.2 *p*H unit intervals to obtain the *p*H values at which precipitation begins and is complete.

Reactions with Diazomethane.—A 100–200% excess of an ether solution of diazomethane was added to an ether solution of the substituted 8-quinolinol. Red precipitates formed with 8-quinolinol, 4-methyl-8-quinolinol and 5,7-dibromo-8-quinolinol but did not form with 2-methyl- or 2,4-dimethyl-8-quinolinol. The red products were filtered and recrystallized from benzene; they had indefinite decomposition points and were, therefore, characterized by their ultraviolet and visible absorption spectra. Nitrogen analyses on the product from 8-quinolinol (7.20%) do not conform to that calculated (8.80%) from the structure proposed by Schenkel-Rudin.[6]

Results and Discussion

The infrared absorption spectra (Figs. 1–4) from 2–11μ of these four quinolinols in approximately saturated solutions show several bands that can be correlated with known structural features of all the compounds, but few characteristics capable of distinguishing the compounds from each other. (It is evident from the graphs that 4-methyl-8-quinolinol has a low solubility in carbon tetrachloride compared to its 2-methyl isomer.)

The absorption band at 2.8μ is evidently the O–H stretching band; it is completely absent in the 8-methoxy derivatives of these compounds.[7] The bands at approximately 3.2–3.3μ are due to C–H stretching and vary somewhat in wave length and structure probably because of the different kinds of C–H linkages in the different compounds. (The absence of these bands in 4-methyl-8-quinolinol can be attributed to the low concentration of the solution.) The strong absorption maxima at about 6.35, 6.65 and 6.8μ are fundamental frequencies of the aromatic ring system. The bands at 7.1, 7.3 and 7.5μ are probably due to C–H bending, the one at 7.5μ perhaps being caused by the C–H bond in the active 2-methyl group since it is lacking in 8-quinolinol and 4-methyl-8-quinolinol. Maxima at 7.9–8.1μ are perhaps associated with C–O or C–N stretching vibrations.

No maxima identifiable with a C=O linkage could be found in any of these compounds, although the existence of a considerable proportion of the keto tautomer of 8-quinolinol in non-

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[1] Abstracted from a thesis by John P. Phillips in partial fulfillment of the requirements for the degree Doctor of Philosophy at Indiana University, 1949. Du Pont Fellow for 1948–1949.

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

[3] J. P. Phillips and L. L. Merritt, THIS JOURNAL, **70**, 410 (1948).

[4] J. P. Phillips, R. L. Elbinger and L. L. Merritt, THIS JOURNAL, **71**, 3986 (1949).

[5] M. V. Tsypkin, *Farmatsiya i Farmakol.*, 1937, No. 2, 43.

[6] Schenkel-Rudin, *Helv. Chim. Acta*, **27**, 1456 (1944).

[7] Unpublished observations in this Laboratory.

TABLE I

ABSORPTION MAXIMA IN ULTRAVIOLET SPECTRA OF 8-QUINOLINOLS (WITH MOLECULAR EXTINCTION COEFFICIENTS)

Substituent	Neutral solvent mμ	mμ	mμ	Hydrochloric acid mμ	mμ	Sodium hydroxide mμ	mμ
None[e]	242(42000)	320(2400)[a]	250(40000)	318–9(1700)	358 (1700)	253(32000)	345[d](2700)
CH_2N_2 addn. prod.	260, 280	354, 480[c]	255	323	365–6	238–9, 273	333, 346, 441
4-CH_3–	242(48000)	319(3300)[a]	250(44000)	315–8(1700)	350–3(2400)	253(28000)	343[d](3900)
2-CH_3–[f]	246(53000)	309(2900)[a]	255(44000)	320 (3100)	345 (1700)	255(30000)	335(3000)
2,4-$(CH_3)_2$–	246(50000)	309(3300)[a]	252(48000)	318 (3100)	342 (2400)	255(31000)	337(4200)

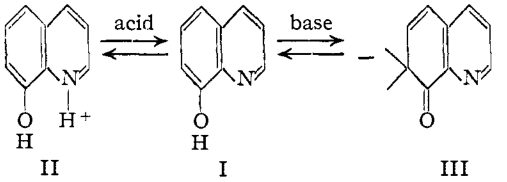
[a] In cyclohexane. [b] In chloroform. [c] In 95% alcohol. [d] Center of a broad band. [e] Copper chelate (in neutral solvent) 262–3(45000), 405–11(4400).[b] [f] Copper chelate (in neutral solvent) 268–9(45000), 392–6(4200).[b]

polar solvents appears probable from other considerations.[8]

The above conclusions should be viewed with caution, however, since overlapping can obscure many absorption maxima and lead to erroneous correlation of structural features with observed spectra.

The maxima in the ultraviolet absorption spectra of these compounds from 225–400 mμ (Table I) furnish additional information about their structure. (It was not considered necessary to graph these spectra since they are all very similar in shape to the curves for 8-quinolinol already recorded in the literature.[9])

The considerable change in the spectra in acidic and basic solvents is probably caused by structure changes of the following sort[10]



The spectra of the copper chelates is of interest because of the complete similarity, except for a large bathochromic shift, of their spectra to those of the parent compounds, which suggests that the role of the copper in the chelate is the same as that of the acidic hydrogen in 8-quinolinol. Similar spectra were observed with the chelates of other divalent metals.

For characterization purposes, the X-ray powder diffraction lines of these compounds and a few derivatives were measured (Table II).

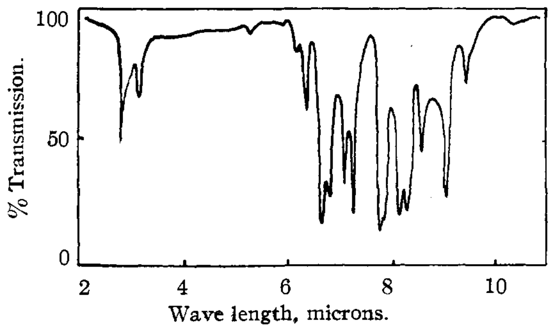


Fig. 1.—Infrared absorption spectrum of 8-quinolinol.

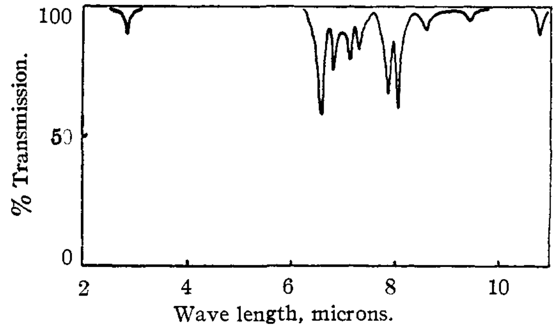


Fig. 2.—Infrared absorption spectrum of 4-methyl-8-quinolinol.

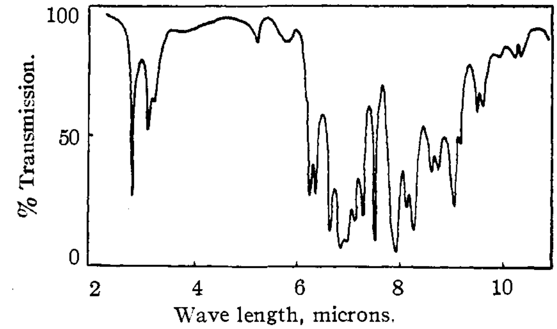


Fig. 3.—Infrared absorption spectrum of 2-methyl-8-quinolinol.

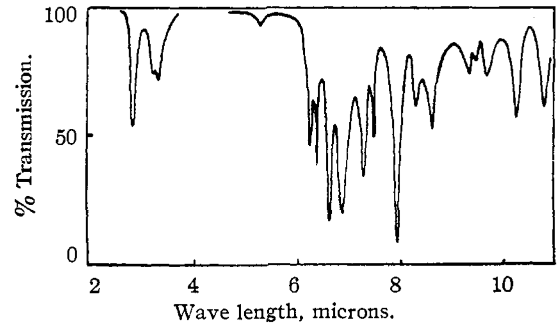


Fig. 4.—Infrared absorption spectrum of 2,4-dimethyl-8-quinolinol.

The analytical behavior of 8-quinolinol is well known; the 2- and 4-methyl derivatives show the

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[8] P. Seguin, *Bull. Soc. Chim.*, **13**, 566 (1946).

[9] Ewing and Steck, THIS JOURNAL, **68**, 2181 (1946).

[10] Stone and Friedman, THIS JOURNAL, **69**, 209 (1947).

TABLE II

"*d*" VALUES OF SUBSTITUTED 8-QUINOLINOLS (IN ORDER OF DECREASING INTENSITY)

Substituent								
None	6.27	3.18	3.82	3.50				
5,7-Br_2-	3.52	3.89	4.06	4.26	3.09	3.20	3.36	6.81
2-CH_3-	3.92	3.67	3.13	5.45	5.93	2.07	5.00	7.94
5,7-Br_2-2-CH_3-	3.52	4.64	3.78	3.10				
4-CH_3-	3.30	6.01	7.29					
2,4-$(CH_3)_2$-	7.14	3.55	3.98	4.50	3.24			
5,7-Br_2-2,4-$(CH_3)_2$-	4.03	3.42	4.31					

same properties with the important exception that 2-methyl- and 2,4-dimethyl-8-quinolinol will not form insoluble chelate compounds with aluminum, the smallest ion of the group tested. Since 4-methyl-8-quinolinol will precipitate aluminum, it seems probable that the 2-methyl group prevents reaction with aluminum by steric hindrance. Further evidence of steric effects by the 2-methyl group is the observation that 2-methyl- and 2,4-dimethyl-8-quinolinol do not give the red addition products with diazomethane that are obtained from 8-quinolinol and 4-methyl-8-quinolinol under comparable conditions.

Quantitative data on the precipitation behavior of these compounds with metals are presented in Table III; the similar results for 8-quinolinol as determined by Goto[11] are included for comparison.

TABLE III

THE *p*H OF PRECIPITATION OF METAL CHELATES OF SUBSTITUTED 8-QUINOLINOLS

Substituent	None[d]		4-CH_3		2-CH_3		2,4-$(CH_3)_2$	
ion	Start[a]	End[b]	Start	End	Start	End	Start	End
Al^{+3}	2.8	4.2	3.5	...	None	None	None	None
Fe^{+3}	2.4	2.8	2.4	3.6	3.1[c]	5.7[c]	3.0	5.4
Mg^{+2}	6.7	8.2	6.8	8.4	7.6[c]	8.9[c]	8.2	>9.5
Mn^{+2}	4.3	5.9	4.6	6.0	5.0	6.6	5.2	7.0
Co^{+2}	2.8	4.2	3.4	4.6	3.8	5.2	4.2	5.8
Zn^{+2}	2.8	4.4	3.2	5.2	3.4[c]	5.3[c]	3.2	5.2
Cd^{+2}	2.2	2.7	...	3.4	2.9[c]	4.5[c]	2.4	4.8

[a] The highest *p*H without any precipitation. [b] The lowest *p*H at which the metal is wholly precipitated. [c] Previously determined.[2] [d] Previously determined.[11]

It is interesting that the order of increasing *p*H at which a given metal ion is precipitated by these four compounds is roughly the order of decreasing acidity of the substituted 8-quinolinols (the ionization constants have been previously reported[3]).

8-Quinolinol increasing *K*a ↓
4-Methyl-8-quinolinol ↑
2-Methyl-8-quinolinol
2,4-Dimethyl-8-quinolinol increasing *p*H

This is explained by noting that, although the weaker acids should form more stable complexes with metallic ions[12] and should, therefore, form precipitates in more acid solutions, it is necessary to go to more basic solutions in order to obtain comparable amounts of the active chelating ion. The latter effect is apparently the predominant one.

Summary

1. The ultraviolet and infrared absorption spectra of the 2- and 4-methyl derivatives of 8-quinolinol have been measured and their correlation with structure discussed.

2. The precipitation behavior of these compounds with metal ions has been determined and evidence for steric hindrance by the 2-methyl group in such reactions presented.

3. The possible relation of the function of the acidic hydrogen in 8-quinolinol to that of the metal ion in the corresponding chelate, as shown by the relation of K_a to *p*H of precipitation, has been pointed out.

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[11] H. Goto, *J. Chem. Soc. Japan*, **54**, 725 (1933), and later references.

[12] Calvin and Wilson, THIS JOURNAL, **67**, 2003 (1945).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, INDIANA UNIVERSITY]

Preparation of Some Substituted 8-Hydroxy- and 8-Methoxyquinolines

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As a result of the discovery[3] that 8-hydroxyquinaldine differed in its analytical behavior from 8-hydroxyquinoline, the compounds here described were synthesized with the hope of obtaining more selective analytical reagents of the 8-hydroxyquinoline series.

The steric nature of the failure of 8-hydroxyquinaldine to react with aluminum was demonstrated by the observation that all the 8-quinolinols studied having alkyl groups in the 2-position would not react with aluminum while the isomeric compounds with substituents in the 3- and 4-positions would react. With the expectation that larger groups in the 2-position would create greater steric hindrance, perhaps enough to prevent reaction with other metal ions besides aluminum, a series of 2-aryl- and 2-styryl 8-quinolinols was prepared, but qualitative tests with several representative metal ions indicated no improvement in selectivity.

All alkyl substituted 8-hydroxy- and 8-methoxyquinolines (Table I) were made by the Doebner–

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[1] Abstracted in part from theses submitted by Rebecca Leash Elbinger and John P. Phillips in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Indiana University.

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