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Chelating Properties of 8-Quinolinol Mannich Bases

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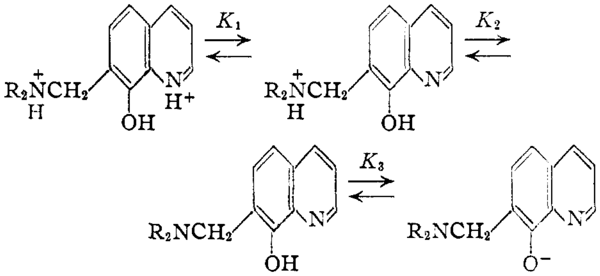
The Mannich reaction of 8-quinolinol with aliphatic secondary amines gives products that are stronger bases than 8-quinolinol. As expected from the high base strength of these substances they form chelate compounds with metal ions only at high *p*H. The chelate compounds of 7,1′-piperidylmethyl-8-quinolinol with cupric, ferric, indium and uranyl ions are similar to the corresponding 8-quinolinolates in most respects except *p*H of precipitation and stability to heat.

Although many substituted 8-quinolinols have been tested as chelating agents for metal ions,[1] none have been much stronger bases than 8-quinolinol. From an investigation of other substituted 8-quinolinols[2] a large increase in base strength was expected to increase the *p*H required for chelate formation with metal ions. Basic substituents were therefore introduced by means of the Mannich reaction. The hydrochlorides of 7-dimethylaminomethyl-, 7-diethylaminomethyl- and 7,1′-piperidylmethyl-8-quinolinol were prepared according to usual methods.[3] The only new compound was 7-diethylaminomethyl-8-quinolinol.

Determination of changes in the absorption spectra of these compounds with changing *p*H confirmed the presence of a basic nitrogen, a weaker quinoline nitrogen and a weakly acidic hydroxyl group. Equilibria for the following structure changes with *p*H were then measured by a spectrophotometric method.[4]



The values of pK_1 obtained for the dimethylamino, diethylamino and piperidyl bases were 2.4, 2.9 and 1.7, respectively; of pK_2, 7.8, 7.2 and 6.6; and of pK_3, 11.0, 11.3 and 10.9. When these figures are compared with a pK_1 of 4.9 and a pK_3 of 9.7 for 8-quinolinol,[4] the new reagents are seen to be much stronger bases, since 8-quinolinol has no equilibrium corresponding to K_2 at all.

Spot tests for common metal ions with the Mannich bases revealed that a very high *p*H relative to that for 8-quinolinol was required to get precipitation. At *p*H 1 color reactions only were observed with cupric, uranyl and ferric ions; at *p*H 4.6 precipitation still did not occur; finally at a *p*H of 10 and above precipitation of these ions as well as most of the others known to chelate with 8-quinolinol could be obtained.

The determination of the sensitivities of the reagents for cupric, uranyl and ferric ions at *p*H 1 and 4.6 by a known procedure[5] led to the conclusion that the piperidine derivative was slightly more sensitive than the other two reagents, and all subsequent tests were therefore performed on the piperidine compound alone. At *p*H 9.0 the minimum amounts of metal ion precipitated, expressed in micrograms per milliliter, were: Fe^{+3}, 1.6; Al^{+3}, 0.5; Cu^{+2}, 2.7; Co^{+2}, 4.0; Cd^{+2}, 1.6; and Mg^{+2}, 0.7. These magnitudes are not notably different from similar data for 8-quinolinol.[4]

As representative examples the cupric, ferric and indium chelate compounds with 7,1′-piperidylmethyl-8-quinolinol were studied in some detail.

Measurement of the *p*H required for quantitative precipitation of the copper chelate compound showed no precipitation up to *p*H 8.0, 53% precipitation at *p*H 8.7 and complete precipitation at *p*H 9 and 10. The absorption spectrum of this chelate compound in chloroform was quite similar to copper 8-quinolinolate[6] except for somewhat higher molecular extinctions.

Ferric ion formed a green soluble complex at low *p*H, the color intensity increasing without precipitation from *p*H 2.1 to 4.6. The determination of the formula of this complex by the molar ratio method[7] gave three moles of reagent per mole of ferric ion in dilute nitric acid, but in acetate buffers ratios from three to six could be obtained depending on the *p*H and the amount of acetate present. The unreliability of these results was probably caused by the presence of other iron complexes involving hydroxide or acetate ion.

The indium chelate compound could be extracted from aqueous solutions with chloroform but only at a *p*H much higher than was employed in a similar method with 8-quinolinol.[8] Quantitative extraction and analysis by measuring the extinction at 400 mμ showed no extraction in the *p*H range 3 to 8, about 60% extraction at *p*H 8.7 and complete extraction from 9.5 to 11.0.

Examination of chelate compounds with other metal ions revealed that none were stable to drying at 110. The compounds with zinc, cadmium, magnesium, indium and aluminum fluoresced yellow under ultraviolet light. An orange soluble complex with uranyl ion was observed in the *p*H range 1 to 4.6; the color intensity increased with increasing *p*H.

From the structures of these Mannich bases it would appear possible for the side chain nitrogen to

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[1] F. J. Welcher, "Organic Analytical Reagents," Vol. I, D. Van Nostrand Co., New York, N. Y., 1947, pp. 262–265.

[2] J. P. Phillips, THIS JOURNAL, **74**, 552 (1952).

[3] J. H. Burckhalter, *et al.*, *ibid.*, **68**, 1894 (1946).

[4] J. P. Phillips and L. L. Merritt, *ibid.*, **70**, 410 (1948).

[5] H. Irving, E. J. Butler and M. F. Ring, *J. Chem. Soc.*, 1489 (1949).

[6] J. P. Phillips, W. H. Huber, J. W. Chung and L. L. Merritt, THIS JOURNAL, **73**, 630 (1951).

[7] A. E. Harvey and D. L. Manning, *ibid.*, **72**, 4488 (1950).

[8] T. Moeller, *Anal. Chem.*, **15**, 270 (1943).

take part in chelate formation in place of the quinoline nitrogen. This apparently did not happen since the chelate compounds actually obtained were so similar in physical appearance and most other properties to the 8-quinolinolates.

Experimental

7,1'-Piperidylmethyl-8-quinolinolyl Hydrochloride.—Paraformaldehyde (0.1 mole) and 8.5 g. (0.1 mole) of piperidine were mixed with cooling and 14.5 g. (0.1 mole) of 8-quinolinol in the minimum volume of ethanol added. After standing for an hour the mixture was refluxed five hours. The ethanol was distilled off and the residue taken up in chloroform. By passing hydrogen chloride through the solution 7,1'-piperidylmethyl-8-quinolinol hydrochloride was precipitated. This was triturated with acetone and ether and then recrystallized from acetone–ethanol mixtures yielding 10.5 g. (35%), m.p. 198°.[9]

Anal. Calcd. for $C_{15}H_{18}N_2O \cdot HCl \cdot H_2O$: N, 9.44; Cl, 11.97. Found: N, 9.55; Cl, 11.9.

The ultraviolet absorption spectrum in 0.1 *N* hydrochloric acid had maxima at 252, 320 and 335 mμ with respective molecular extinctions 20000, 1700 and 1400. In 0.1 *N* sodium hydroxide maxima were at 260 (15000) and 340 (2100) mμ.

The compound was quantitatively monobrominated by 0.1 *N* potassium bromate in acid solution; analyses of five 0.100-g. samples by this method were in error by less than 3%.

7-Dimethylaminomethyl-8-quinolinol Hydrochloride.—The same procedure was used with dimethylamine hydrochloride in place of piperidine so that hydrogen chloride was not needed to precipitate the product; yield 50%, m.p. 192° (literature[3] gives 186°).

Absorption maxima in 0.1 *N* hydrochloric acid were at 255 (34000), 320 (2200) and 355 (2200) mμ.

7-Diethylaminomethyl-8-quinolinol Hydrochloride.—The same procedure as for the piperidine derivative was used; yield 55%, m.p. 205°.

Anal. Calcd. for $C_{14}H_{18}N_2O \cdot HCl \cdot 2H_2O$: N, 9.25; H_2O, 12.05. Found: N, 9.55; H_2O (Karl Fischer), 12.4.

Absorption maxima in 0.1 *N* hydrochloric acid occurred at 256 (22000), 320 (2100) and 352 (1300) mμ.

Equilibrium Constants.—A Beckman DU spectrophotometer with 1.00-cm. silica cells was used. The technique has been described before.[4] Thirty to forty 0.01% solutions for each compound varying in *p*H from 0 to 13 were measured at several wave lengths. Graphical computation of the equilibrium constants was performed at 350 mμ for the piperidine derivative and at 370 mμ for the other compounds. The accuracy of the *pK* values is estimated as ±0.2 unit.

Spot Tests.—Aqueous 1% solutions of the reagents were used. Tests with 1% metal ion solutions on spot plates were conducted at *p*H 1.0, 4.6 (acetate buffer) and 10 (dilute sodium hydroxide). The ions tested were Co^{+2}, Ni^{+2}, Mg^{+2}, Zn^{+2}, Cd^{+2}, Cu^{+2}, Mn^{+2}, Pb^{+2}, Hg^{+2}, Ca^{+2}, Sr^{+2}, Ba^{+2}, UO_2^{+2}, VO^{+2}, ZrO^{+2}, La^{+3}, Cr^{+3}, Al^{+3}, Fe^{+3} and Th^{+4}. At *p*H 1 colors were obtained with Cu^{+2}, UO_2^{+2} and Fe^{+3} only; at *p*H 4.6 only Cd^{+2} precipitated; at *p*H 10 or higher all the ions tested gave precipitates.

Sensitivity Tests.—The minimum concentrations of metal ions capable of reacting with 7,1'-piperidylmethyl-8-quinolinol were determined at several *p*H values according to a known method.[5] Minimum concentrations giving positive reaction, expressed as micrograms per milliliter, were: at *p*H 1.0, Fe^{+3}, 3.2, UO_2^{+2}, 20.0; at *p*H 4.6, Fe^{+3}, 2.4, UO_2^{+2} 4.0, Cu^{+2}, 3.6; at *p*H 12.0, Zn^{+2}, 4.5 and Ni^{+2}, 3.3.

Chelate Compounds of 7,1'-Piperidylmethyl-8-quinolinol.—The cupric, indium and ferric chelates were precipitated by adding a 5% excess of the reagent solution in water to the metal ion and raising the *p*H to 10 by addition of ammonia. After digestion at 50° the precipitates were filtered, washed thoroughly with warm water and dried at room temperature over magnesium perchlorate. The compounds decomposed when dried in the oven at 110°.

By ignition to the oxides the following analyses were obtained. Calcd. for $Cu(C_{15}H_{17}N_2O)_2 \cdot 2H_2O$: Cu, 10.9. Found: Cu, 11.3. Calcd. for $Fe(C_{15}H_{17}N_2O)_3$: Fe, 7.18. Found: Fe, 6.90. Calcd. for $In(C_{15}H_{17}N_2O)_3$: In, 13.7. Found: In, 13.95.

The absorption spectrum of the copper chelate compound in chloroform had maxima (and corresponding log molecular extinctions) at 270 (5.22) and 430 (3.72) mμ. The indium chelate in chloroform had maxima at 330–335 and 395–405 mμ.

The *p*H required to precipitate the copper salt was studied by electro-deposition of the unprecipitated copper. To a solution containing 0.220 g. of cupric ion a 5% excess of reagent solution was added and the *p*H adjusted to the desired value with ammonia. The precipitate was removed by filtration and the filtrate electrolyzed. The weight of copper obtained was subtracted from the initial weight present in order to get the amount precipitated by the reagent.

Formula of Ferric Complex.—The absorption spectrum of the soluble ferric complex had maxima in the visible at 452 and 600 mμ. Attempts to use the molar ratio method of formula determination at 600 mμ gave values between 3 and 6 acetate buffers of *p*H 1.5 to 4.6; a value of three moles of reagent per mole of iron was obtained in nitric acid solutions of *p*H 1.5.

Extraction of Indium Chelate Compound.—A solution of indium chloride containing 0.10 mg. of indium in 25 ml. was treated with an excess of the reagent and extracted with five 5-ml. portions of chloroform. The extract was made up to 50 ml. with chloroform and the extinction at 400 mμ measured. The extinction reached a maximum of 0.350 at *p*H 9.5 and higher, and was negligible when the solution extracted had a *p*H less than 8.0.

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[9] In reference 3 the preparation of the sesquihydrate of this compound has been reported. Footnote *c* of Table VI in this reference apparently should read "anal. for H_2O."