The Monohalogenation of 8-Quinolinols

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In the course of a study of the kinetics of bromination of the chromium(III) chelate of 8-quinolinol by a coulometric method, it was observed that the metal chelate brominated much faster than the free ligand under identical conditions. The same result was obtained with the cobalt(III), aluminum(III), and copper(II) chelates of 8-quinolinol. Although the reaction rates of the metal chelates were too fast to measure by our method,[1] the stoichiometry of the reaction was readily obtained. One mole of bromine reacted rapidly with every mole of 8-quinolinol present in the metal chelate. Further reaction of the metal chelate with bromine did occur, but at a much slower rate. This behavior of the chelated 8-quinolinol is in direct contrast with that of the free ligand, since each mole of 8-quinolinol is known to react quite rapidly with 2 moles of bromine to form the 5,7-dibromo-8-quinolinol.[1] Attempts to monohalogenate 8-quinolinol directly result in low yields and extensive contamination by the dihalo product.

On a preparative scale, halogenation of the metal chelate, rather than of the ligand itself, with 1 mole of halogen/mole of the 8-quinolinol in the metal chelate and subsequent rupture of the metal chelate with acid should give the monohalogenated derivative in good yields and free of dihalogenated products. N-halosuccinimides were used as halogenating agents since they did not release hydrogen ions that can cause rupture of the metal chelate during the course of the reaction. A further means of avoiding chelate dissociation is the use of an organic solvent as reaction medium. If these conditions are met, then it would not be necessary to use inert chelates such as those of Co(III) and Cr(III) which may by their resistance to dissociation present problems in metal ion removal.

The monochloro, monobromo, and monoiodo derivatives of 8-quinolinol, 2-methyl-8-quinolinol, and 4-methyl-8-quinolinol were synthesized by halogenating the copper(II) chelate with N-halosuccinimde (1 mole/mole of the 8-quinolinol in the chelate). Halogenation of the lithium salt under identical conditions always gave the 5,7-dihalo derivative.

An investigation of the effect of the metal ion on the yield of monobromo-8-quinolinol obtained by this method showed that the maximum yield was obtained with the cobalt(II) chelate (69%) followed by the aluminum(III) chelate (66%), the cobalt(III) chelate (52%), and the copper(II) chelate (50%). The similarity of these results indicate that specific metal ion effects are minimal. It was deduced that halogenation occurred in 5-position in all cases by a comparison of the infrared and proton magnetic resonance spectra of the halogenated compounds that were synthesized with available authentic samples of 5-halo-8-quinolinols.

Experimental

5-Bromo-8-Quinolinol.—The copper(II) chelate of 8-quinolinol[2] (0.43 g.) was dissolved in a minimum volume of chloroform and a chloroform solution of N-bromosuccinimide (0.43 g.) was added. After the reaction mixture was allowed to stand for several hours a precipitate of the copper(II) chelate of 5-bromo-8-quinolinol was formed and separated by filtration. About 80% of the copper(II) chelate was recovered in this step. The chelate was dissolved in 50 ml. of 6 *M* HCl and the copper(II) was precipitated by the addition of excess thioacetamide. The solution containing the copper(II) sulfide was filtered and the filtrate was neutralized with $NaHCO_3$ solution. The 5-bromo-8-quinolinol which precipitated was washed with water, recrystallized from ethanol, and finally vacuum sublimed: yield 0.31 g., m.p. 124° (lit.[2] m.p. 124°).

An alternative method that was used for the separation of copper(II) from the 5-bromo-8-quinolinol was as follows. The copper(II) chelate of 5-bromo-8-quinolinol (0.85 g.) was dissolved in 1:1 HCl and a solution containing 1.13 g. of EDTA was added. When the pH of the solution was raised to 4 with ammonium acetate, a yellowish precipitate was formed. The mixture was extracted with 100 ml. of chloroform, the solid obtained by evaporation of the chloroform layer was redissolved in 1:1 HCl, and a solution containing 1.13 g. of EDTA was added. On raising the pH of the solution to 5 with ammonium acetate, a pale yellow precipitate was obtained. The mixture was extracted with 75 ml. of chloroform and on evaporation 0.63 g. of 5-bromo-8-quinolinol was obtained.

The copper(II) chelates of 8-quinolinol, 2-methyl- and 4-methyl-8-quinolinol[3] were halogenated in a similar manner to give the corresponding 5-halo derivatives.

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The Structure of the Product from Reaction of the Dimedon Formaldehyde Derivative with Base and Iodine. An Example of Coupling through Five Bonds

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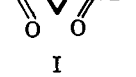
In 1925 and 1927 Radulescu and Georgescu[1,2] proposed the cyclopropane structure I for the product, m.p. 211–212°, obtained by treating iodine with the disodium salt of the dimedon derivative of formaldehyde. Repeating the above authors' procedure we obtained the compound described earlier. However the spectral properties are inconsistent with I and lead to assignment of the isomeric structure II.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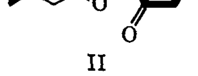
II

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