sodium iodide and 1500 ml. of acetone were refluxed for 24 hours. The resulting solid was collected, washed with water then acetone, and dried. The resulting product, a red-orange powder, 134 g. (83%), melted at 194–196° dec.

Anal. Calcd. for $C_{16}H_{11}Cl_2I_2N$: I^-, 23.40. Found: I^-, 23.73.

5-Chloro-1-(2-chlorobenzyl)-4-iodoquinolinium iodide was prepared in the same manner as the corresponding 7-chloro derivative (64%), m.p. 201–202° dec.

Anal. Calcd. for $C_{16}H_{11}Cl_2I_2N$: C, 35.45; H, 2.04. Found: C, 35.28; H, 2.30.

Acknowledgment.—We are indebted to Mr. M. E. Auerbach and Mr. K. D. Fleischer and staffs for the analytical data and corrected melting points and to Dr. J. O. Hoppe, Mr. H. E. Lape and Miss D. J. Fort for the pharmacological screening.

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[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE]

Intramolecular Hydrogen Bonding in 7-Chloro-4-diethylaminoethylaminoquinoline

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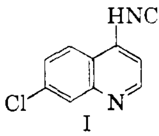
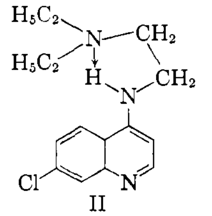
Evidence for intramolecular hydrogen bonding in 7-chloro-4-(2-diethylaminoethylamino)-quinoline is presented.

The results of studies dealing with the reaction of some substituted 4-aminoquinolines with 2-chlorobenzyl chloride as well as with the products obtained therefrom[1] suggested the presence of intramolecular N···H—N bonding in some of the compounds.

The present investigation was undertaken to determine whether experimental evidence could be obtained to support this view. Thus, 7-chloro-4-butylaminoquinoline (I) in which no intramolecular hydrogen bonding is possible was compared with 7-chloro-4-(2-diethylaminoethylamino)-quinoline (II) in terms of infrared absorption spectra, dipole moments and nuclear magnetic resonance.



I



II

The infrared spectra were measured in the 2.5 to 3.5μ region in CS_2 solution using a Perkin-Elmer model 21 instrument with NaCl optics and NaCl cells.

The fundamentals of the NH region of the infrared spectra are shown in Fig. 1. At 0.05 molar concentration and 4 mm. path length, the butyl compound shows a pronounced double peak at 2.903 and 3.055μ. The long wave peak disappears upon dilution. However, the diethylaminoethylamino compound shows a single peak at 2.971 μ. The conclusion which must be drawn is that the shortest wave length belongs to the unimpeded N–H oscillator, the next higher wave length to the intramolecular N—H···H bond and the longest wave length to the intermolecular bond, presumed on account of sterical crowding to be a dimer or higher polymeric association complex.

According to Short[2] very little is apparently known regarding N—H···N bonds. He demonstrated the existence of intramolecular hydrogen bonding in 4-aminoacridine and 8-aminoquinoline with a five-membered system and a N—H···N bond angle of less than 180°.

The influence of dilution on "washing out" intermolecular hydrogen bonding has been pointed out for the OH ··· O system by Smith and Creitz,[3] for the N—H···O system by Gore,[4] and for the N—H···N system by Fuson and co-workers.[5]

The influence of dilution affecting the intermolecular hydrogen bonds of I but not interfering with the intramolecular hydrogen bonds of II is shown in Fig. 2 where the constant $c \times l$ technique was employed. The left-hand side shows the butyl derivative I with the loss of the band at B′, the right hand side the diethylaminoethyl derivative II. In both instances the upper curves show the respective absorption spectra of 0.05 *M* solution in a 1-mm. path cell, the lower curves 0.012 *M* solutions in a 4-mm. path cell. In case II, the curves are superimposable, while in I the intermolecular bonding (B′) is apparent in the more concentrated solution.

Dipole moment measurements carried out on I and II in dioxane tend to confirm the assignment of the spatial orientation of the diethylaminoethylamino side chain of compound II the values being 5.70 and 5.90 D.(±0.05).

Nuclear magnetic resonance spectra were obtained for both compounds.[6] The traces show different band width, the broader spike being characteristic for the N-*n*-butyl compound while the N-diethylaminoethyl derivative has a narrower band.

The latter behavior is believed to reflect a greater symmetry of the molecule as would result from

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[1] A. R. Surrey, *et al.*, THIS JOURNAL, **81**, 2887 (1959).

[2] L. N. Short, *J. Chem. Soc.*, 4584 (1952).

[3] F. A. Smith and E. C. Creitz, *J. Research Bur. Stand.*, **46**, 145 (1951).

[4] R. C. Gore and E. S. Waight, "Determination of Organic Structures by Physical Methods," E. A. Braude and F. C. Nachod, eds., Academic Press, Inc., New York, N. Y., 1955, p. 216.

[5] N. Fuson, M. L. Josien, R. L. Powell and E. Utterback, *J. Chem. Phys.*, **20**, 145 (1952); R. N. Jones and C. Sandorfy, "Technique of Organic Chemistry," A. Weissberger, ed., Vol. IX, Interscience Publishers, Inc., New York, N. Y., 1956, p. 512.

[6] The authors are indebted to Mr. Carl Westbom formerly of Nuclear Magnetics Corporation for obtaining the spectra and to Professor H. S. Gutowsky of the University of Illinois for the interpretation of the experimental data.

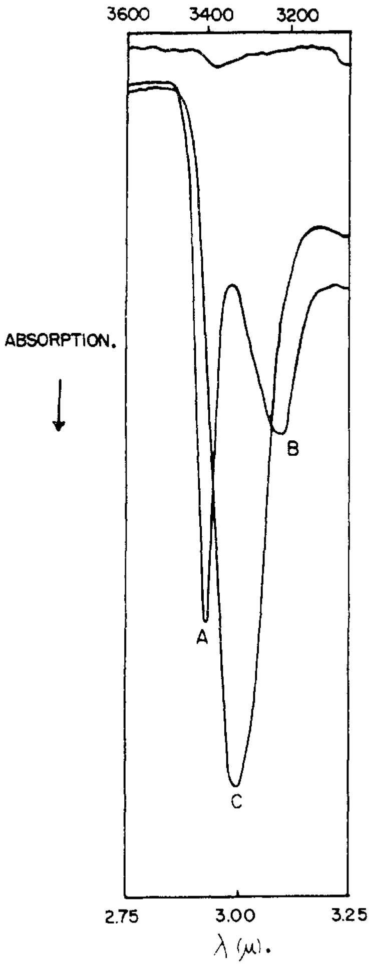

Fig. 1.—The curve AB is the spectrum for 7-chloro-4-butylaminoquinoline in CS_2 solution showing unbonded NH (A) and intermolecular hydrogen bonding (B). The curve C shows intramolecular bonding in the case of 7-chloro-4-(2-diethylaminoethylamino)-quinoline.

intramolecular hydrogen bonding. While the n.m.r. data are not confirmatory evidence *per se*, they support the configuration assignment.

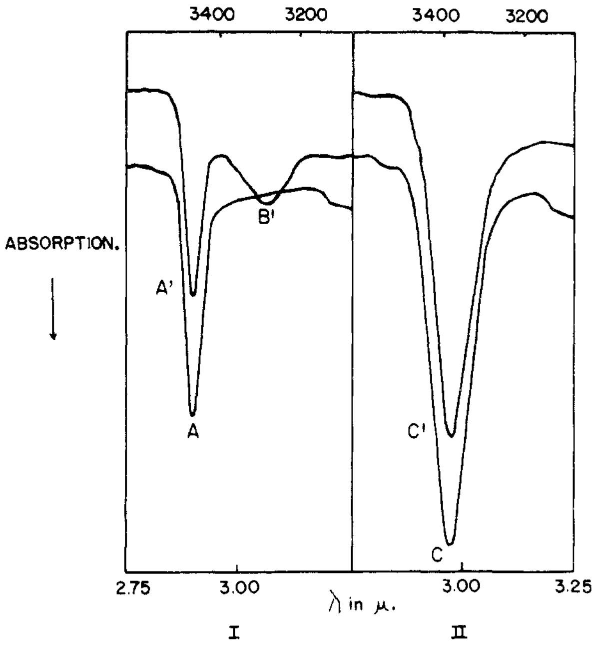

Fig. 2.—(Left) Intermolecular bonding (B') present in 7-chloro-4-N-*n*-butylaminoquinoline at 0.05 *M* solution, 1-mm. path cell, is lost in 0.0125 *M* solution, 4-mm. path cell. (Right) Intramolecular hydrogen bonding in the case of 7-chloro-4-(2-diethylaminoethylamino)-quinoline is not affected by dilution.

We believe that if intramolecular bonding is possible for the molecule at the expense of 2.5-3 kcal./mole (Δ of 79 wave numbers),[7] it forms a stable configuration and maintains it independent of dilution. If there is no additional nitrogen in the system, a concentration dependent association with a lowering of energy of 5–6 kcal./mole (Δ of 172 wave numbers) of the N–H group takes place.

Acknowledgment.—The experimental assistance of Mrs. M. Becker is gratefully recorded.

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[7] As an extrapolation of the Badger–Bauer rule [R. M. Badger and S. H. Bauer, *J. Chem. Phys.*, **5**, 839 (1937)], a shift of 35 wave numbers is taken to be equivalent to 1 kcal./mole.