[CONTRIBUTION FROM THE STERLING-WINTHROP RESEARCH INSTITUTE]

Hypotensive Agents. II. The Preparation of Quaternary Salts of Some 4-Dialkylaminoalkylaminoquinolines

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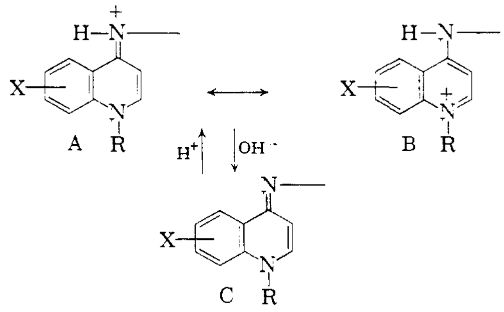
RECEIVED JULY 29, 1958

The preparation of mono- and bis-(2-chlorobenzyl chloride) salts of some 4-dialkylaminoalkylaminoquinoline derivatives is reported. Many of the quaternary salts have been found to possess hypotensive activities when tested in experimental animals.

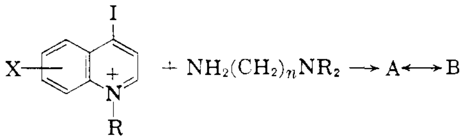
As part of a program in search of potent hypotensive agents we have prepared a variety of mono- and bis-(2-chlorobenzyl chloride) salts of 4-dialkylaminoalkylaminoquinoline derivatives. Many of the products prepared for this study have been found to possess interesting hypotensive activities.

The quinoline bases required as starting materials for the present work were prepared in the usual manner from the appropriate 4-chloroquinoline and dialkylaminoalkylamine in phenol.[1] Some of the bases (Table I) were obtained as crystalline solids, others were isolated as hydrochlorides or phosphates.

The reaction of many of these bases with one equivalent of 2-chlorobenzyl chloride yielded 1-(2-chlorobenzyl)-quinoline derivatives.[2] These compounds have been designated as salts of the 1-(2-chlorobenzyl)-4-imino-1,4-dihydroquinolines since they are readily converted to the 4-imino bases. It is understood, however, that this structure represents only one of the contributing species to the resonance hydrid A ⟷ B as



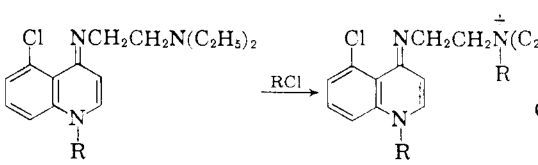
Another method employed for the preparation of these 4-imino-1,4-dihydroquinolines (or, alternatively, they may be named as 4-amino-1-(2-chlorobenzyl)-quinolinium salts) was the reaction of 4-iodo-1-(2-chlorobenzyl) quinolinium iodide with the appropriate primary-tertiary diamine. Treatment of the product with potassium hydroxide yielded the imino base C which could be reconverted to a salt with the desired acid.



Most of the bis-quaternary salts listed in Table III were prepared directly from the 4-amino bases (Table I) using a large excess of 2-chlorobenzyl chloride in acetonitrile solution. Many of these salts retained water of crystallization which could not readily be removed even by prolonged heating *in vacuo*. The products could also be prepared from the imino salts (Table II) by reaction with 2-chlorobenzyl chloride.

Neither of these two procedures were successful for the preparation of the bis-2-chlorobenzyl-chlorides of 5-chloro-4-(2-morpholinoethylamino)-quinoline and 5-chloro-4-(2-diethylaminoethylamino)-quinoline. This is undoubtedly due to the marked steric hindrance associated with the terminal nitrogen atom in the side chain in these compounds.[2]

The imino-base, 5-chloro-1-(2-chlorobenzyl)-4-(2-diethylaminoethylimino)-1,4-dihydroquinoline, does react with 2-chlorobenzyl chloride to give the iminoquaternary, 5-chloro-1-(2-chlorobenzyl)-4-(2-diethylaminoethylimino)-1,4-dihydroquinoline ω-2-chlorobenzylchloride[3] which on treatment with hydrogen chloride yields the desired bis-quaternary compound.



Most of the compounds in the present series have been examined in several species of animals for their pharmacological activity. They have been found to possess hypotensive activity which appears to be primarily central in origin. This was measured by the serial carotid occulsion procedure in dogs anesthetized with sodium barbital or morphine–chloralose and by the cross-circulation technique in dogs; by administration intravenously or orally in unanesthetized dogs; and by the renal hypotensive rat test. These compounds were found to have relatively low ganglionic blocking activity as measured by the nictitating membrane test in cats. Details of this work will be reported elsewhere.[4]

Experimental[5]

The general procedures employed in the preparation of the 4-imino-1,4-dihydroquinolines and their salts (Table II) are illustrated by the following examples.

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[1] J. A. Wiesner and C. E. Kwartler, *Ind. Eng. Chem.*, **41**, 654 (1949).

[2] See discussion in previous paper, part I THIS JOURNAL, **81**, 2887 (1959).

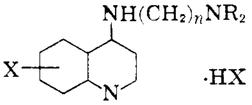
[3] ω-Designates attachment of the 2-chlorobenzyl radical and chloride ion at the terminal nitrogen atom of the basic side-chain attached to the 4-position of the quinoline ring.

[4] H. E. Lape, D. J. Fort and J. O. Hoppe.

[5] All melting points are corrected unless otherwise indicated.

TABLE I

4-DIALKYLAMINOALKYLAMINOQUINOLINES

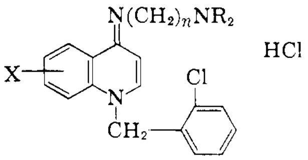


X	n	R	HX	M.p., °C.	Formula (base)	Analyses, % Calcd.	Analyses, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
7-Cl	2	CH_3	.....	121.0–122.8[a]	$C_{13}H_{16}ClN_3$	Cl, 14.19	14.14	11.22	11.19
7-Cl	2	C_2H_5	2·HCl	279.4-283.0[b]	$C_{15}H_{20}ClN_3$	Cl^-, 20.22	19.92	11.98	11.80
5-Cl	2	CH_3	2·H_3PO_4[c]	252.4	$C_{13}H_{16}ClN_3$	H_3PO_4, 44.00	44.30	9.43	9.24
5-Cl	2	C_2H_5	2·H_3PO_4	226.4–228.6	$C_{15}H_{20}ClN_3$	C, 38.00	37.90	8.87	8.99
						H, 5.53	5.55		
5-Cl	3	CH_3	2·H_3PO_4	233.6–236.2	$C_{14}H_{18}ClN_3$	H_3PO_4, 42.60	42.40	9.14	8.76
5-Cl	3	C_2H_5	2·H_3PO_4	244.6–247.4	$C_{16}H_{22}ClN_3$	H_3PO_4, 40.20	40.80	8.62	8.49
5-Cl	2	C_4H_9	2·H_3PO_4	214.6–217.0	$C_{19}H_{28}ClN_3$	H_3PO_4, 37.00	37.40	7.93	7.76
3-Cl	2	C_2H_5	2·HCl	219.0–226.4	$C_{15}H_{20}ClN_3$	Cl^-, 20.22	19.91	11.98	11.67
3,7-Cl_2	2	C_2H_5	.....	67.2–73.4	$C_{15}H_{19}Cl_2N_3$	Cl, 22.71	22.53	13.46	13.33
6,7-Cl_2	2	C_2H_5	.....	116.5–118.0	$C_{16}H_{19}Cl_2N_3$	Cl, 22.71	22.51	13.46	13.42
6-OCH_3	2	C_2H_5	.....	94.8-98.8	$C_{16}H_{23}N_3O$	C, 70.29	70.34		
						H, 8.48	8.35	10.25	10.20
8-OCH_3	2	C_2H_5	.....	126.2-128.8	$C_{16}H_{23}N_3O$	C, 70.29	70.27	10.25	10.19
						H, 8.48	8.74		
H	2	CH_3	2·HCl	224.8–227.0	$C_{13}H_{17}N_3$	Cl^-, 24.60	24.20	14.58	14.44
H	2	C_2H_5	2·HCl	135.6–138.8	$C_{15}H_{21}N_3$[d]	Cl^-, 21.20	21.28	12.56	12.69
						H_2O, 5.40	5.36		
3-CH_3	2	C_2H_5	2·H_3PO_4	241.0–247.8	$C_{16}H_{23}N_3$	C, 42.39	42.39	9.27	9.19
						H, 6.45	6.30		
3,8-$(CH_3)_2$	2	C_2H_5	2·H_3PO_4	249.6–251.8	$C_{17}H_{25}N_3$	H_3PO_4, 42.32	42.40	8.89	8.89

[a] Reported by D. S. Tarbell, N. Shakespeare, C. J. Claus and J. F. Bunnett, THIS JOURNAL, **68**, 1217 (1946). [b] Reported by A. R. Surrey and H. F. Hammer, *ibid.*, **68**, 113 (1946). [c] Base melts at 94–101°; calcd. NAP, 11.24. Found: NAP, 11.01. [d] Monohydrate.

TABLE II

1-(2-CHLOROBENZYL)-4-DIALKYLAMINOALKYLIMINO-1,4-DIHYDROQUINOLINES



X	n	R	Yield, %	M.p., °C.	Formula (base)	Chloride, % Calcd.	Chloride, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
H	2	C_2H_5	54	162.0–164.6	$C_{22}H_{26}ClN_3$	8.77	8.82	10.39	10.23
5-Cl	2	C_2H_5	70	206.0-208.0	$C_{22}H_{25}Cl_2N_3$	8.08	7.96[a]	9.58	9.50[a]
5-Cl	2	C_4H_9	62	206.8–207.7	$C_{26}H_{33}Cl_2N_3$	21.49[c]	21.36	8.49	8.20
5-Cl	2	C_4H_8O[d]	82	215.6–221.4	$C_{22}H_{23}Cl_2N_3O$	7.83	7.72	9.28	9.02
7-Cl	2	CH_3	34	253.8–255.4[e]	$C_{20}H_{21}Cl_2N_3$[e]	27.96[c]	27.90[f]	8.28	8.50[f]
7-Cl	2	C_2H_5	92[b]	106.0–107.6[b]	$C_{22}H_{25}Cl_2N_3$	17.63[c]	17.46	10.44	10.27
7-Cl	2	C_2H_5	58	200.8–204.8	$C_{22}H_{25}Cl_2N_3$	8.08	7.77	9.58	9.63
7-Cl	2	C_4H_9	62	179.2–183.2	$C_{26}H_{33}Cl_2N_3$	7.17	7.13	21.49[c]	21.03[c]
7-Cl	2	C_4H_8O[d]	85	238.2–241.2	$C_{22}H_{23}Cl_2N_3O$	7.83	7.80	9.28	9.12
7-Cl	2	[g]	59	199.8–201.4	$C_{27}H_{26}Cl_3N_3$	26.45[c]	26.37	7.85	7.92
7-Cl	3	CH_3	56[h]	241.8–246.8[i]	$C_{21}H_{23}Cl_2N_3$	15.37	15.11	9.11	8.89
7-Cl	4	C_2H_5	79[h]	216.8–226.4	$C_{24}H_{29}Cl_2N_3$	7.60	7.52	9.00	8.90
7-Cl	5	C_2H_5	20[h]	231.8–235.4[i]	$C_{25}H_{31}Cl_2N_3$	13.62	13.70[k]	8.28	8.13[k]
7-Cl	6	C_2H_5	24[h]	87.0–88.2[l]	$C_{26}H_{33}Cl_2N_3$	6.12[m]	6.01	9.18	9.03
6-OCH_3	2	C_2H_6	59	223.8–228.4	$C_{23}H_{28}ClN_3O$	8.16	8.00	9.67	9.64
8-OCH_3	2	C_2H_5	53	127–130[n]	$C_{23}H_{28}ClN_3O$			7.04[m]	7.07

[a] Found: H_2O, 3.64%. [b] Base prepared from hydrochloride salt which melted at 237–239° (uncor.). *Anal.* Calcd.: Cl^-, 14.92. Found: Cl^-, 14.93. [c] Total chlorine. [d] Morpholino. [e] 2 HCl·*i*-C_3H_7OH. [f] Found: H_2O, 1.30%. [g] R_2 = $(C_2H_5)(2\text{-}ClC_6H_4CH_2)$. [h] Prepared from 7-chloro-4-iodoquinolinium chloride. [i] 2HCl. [k] Found: C_2H_5OH, 5.49%. [l] Base. [m] Basic nitrogen. [n] Uncorrected.

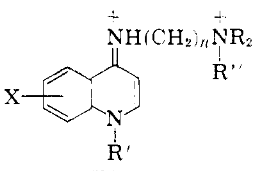
7-Chloro-1-(2-chlorobenzyl)-4-(2-diethylaminoethylimino)-1,4-dihydroquinoline.—A solution containing 5 g. of 7-chloro-4-(2-diethylaminoethylamino)-quinoline, 2.9 g. of 2-chlorobenzyl chloride and 25 ml. of acetonitrile was refluxed for 5 hours and then cooled to about 6° and allowed to stand 48 hours. The precipitate was collected and recrystallized from acetonitrile to yield 3.4 g. of the product, 7-chloro-1-(2-chlorobenzyl)-4-(2-diethylaminoethylimino)-1,4-dihydroquinoline hydrochloride, m.p. 194.0–207.6°.

Three grams of this product was dissolved in 40 ml. of warm water and the solution was made basic by the slow addition of 7.4 ml. of 10% aqueous sodium hydroxide solution. The oil which separated solidified on cooling and triturating. The solid was recrystallized from *n*-hexane to yield 2.29 g. of the product melting at 106.0–107.6°.

Anal. Calcd. for $C_{22}H_{25}Cl_2N_3$: Cl, 17.63; N, 10.44. Found: Cl, 17.46; N, 10.27.

TABLE III

BIS-QUATERNARY SALTS OF 4-DIALKYLAMINOALKYLAMINOQUINOLINES



·2 Cl⁻

X	n	R	R'[a]	R''[a]	Yield, %	M.p., °C.	Formula	Chloride, % Calcd.	Chloride, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
H	2	C_2H_5	A	A	10	202.4–203.2	$C_{29}H_{35}Cl_2N_3$	14.28	14.12	8.46	8.25
5-Cl	2	C_2H_5	A	A	23	206.0–208.0	$C_{29}H_{34}Cl_3N_3$	13.36	13.17	7.92	7.99
7-Cl	2	CH_3	B	CH_3	93	247.8–249.8	$C_{21}H_{25}Cl_4N_3$	15.37	15.20[b]	9.11	9.17[b]
7-Cl	2	C_2H_5	B	CH_3	78	210.0–210.4	$C_{23}H_{29}Cl_4N_3$[c]	12.91	12.93	[d]	
7-Cl	3	CH_3	B	CH_3	67	243.2–247.2	$C_{22}H_{27}Cl_4N_3$	14.93	14.85[e]	8.85	8.63[e]
5-Cl	2	CH_3	B	B	92	200.8–201.8	$C_{27}H_{28}Cl_5N_3$	12.40	11.75[f]	7.35	7.30[f]
5-Cl	3	C_2H_5	B	B	43	131.4–136.2	$C_{30}H_{34}Cl_5N_3$	11.55	11.53[g]	6.84	6.94[g]
7-Cl	2	CH_3	B	B	95	185.0–188.2	$C_{27}H_{28}Cl_5N_3$[h]	12.40	12.12[h]	7.35	6.95[h]
7-Cl	2	C_2H_5	B	B	74	172.2–174.2	$C_{29}H_{32}Cl_5N_3$	11.82	11.59[i]	7.01	6.88[i]
7-Cl	3	C_2H_5	B	B	96	192.4–195.4	$C_{30}H_{34}Cl_5N_3$	11.55	11.31	6.84	6.84
7-Cl	3	C_2H_5	B	B	7	194.2–205.4	$C_{30}H_{34}Cl_3I_2N_3$	31.9[j]	31.9[k]	5.28	5.44[k]
7-Cl	4	C_2H_5	B	B	85	187.0–190.0	$C_{31}H_{36}Cl_5N_3$	11.29	11.22	6.69	6.83
7-Cl	5	C_2H_5	B	B	97	172.4–184.2	$C_{32}H_{38}Cl_5N_3$	11.03	10.75[l]	6.55	6.38[l]
7-Cl	2	C_2H_5	C	C	57	149.4–153.2	$C_{29}H_{30}Cl_7N_3$	10.60	10.91	6.28	6.49
5-Cl	2	C_2H_5	B	B	..	172.0–173.0[m]	$C_{29}H_{32}Cl_5N_3$	11.82	11.96		
3-CH_3	2	C_2H_5	B	B	80	163.4–165.2	$C_{30}H_{35}Cl_4N_4$	12.24	12.40[n]	7.25	7.44[n]

[a] A = benzyl; B = 2-chlorobenzyl; C = 2,4-dichlorobenzyl. [b] H_2O, 2.89%. [c] Contained 1 mole of isopropyl alcohol. [d] Calcd.: C, 56.84; H, 6.74. Found: C, 57.04; H, 6.48. [e] H_2O, 1.80%. [f] H_2O, 3.46%. [g] H_2O, 7.01%. [h] H_2O, 3.24%. [i] H_2O, 3.63%. [j] Compound is bis-iodide salt. [k] H_2O, 2.59%. [l] H_2O, 2.08%. [m] Uncorrected; prepared from imino-quaternary salt. [n] H_2O, 3.48.

7-Chloro-1-(2-chlorobenzyl)-4-(2-dimethylaminoethylimino)-1,4-dihydroquinoline Dihydrochloride.—A solution containing 5.28 g. of 2-dimethylaminoethylamine in 50 ml. of absolute ethanol was heated and treated portionwise with stirring with 11 g. of 7-chloro-1-(2-chlorobenzyl)-4-iodoquinolinium iodide. When a clear solution had resulted, it was cooled. The resulting precipitate was collected and recrystallized from ethanol–water to yield 7.5 g. of 7-chloro-1-(2-chlorobenzyl)-4-(2-dimethylaminoethylimino)-1,4-dihydroquinoline hydroiodide, m.p. 230–231° (uncor.).

Anal. Calcd. for $C_{20}H_{22}Cl_2IN_3$: I^-, 25.26. Found: I^-, 24.91.

This hydriodide salt was converted to the corresponding imino base by dissolving 3.5 g. of it in ethanol–water and treating the resulting solution with excess 5% aqueous sodium hydroxide solution. Addition of water yielded 2.7 g. of 7-chloro-1-(2-chlorobenzyl)-4-(2-dimethylaminoethylimino)-1,4-dihydroquinoline melting at 144–145° (uncor.).

The imino compound was dissolved in isopropyl alcohol and treated with ethanolic hydrogen chloride until the solution was acidic. The solution was cooled and the resulting precipitate was collected and recrystallized from isopropyl alcohol to yield 2.3 g. of product which contained 1 mole of isopropyl alcohol and melted at 253.8–255.4°.

The preparation of the bis-quaternary salts listed in Table III is illustrated by the following general procedures.

7-Chloro-1-(2-chlorobenzyl)-4-(2-diethylaminoethylimino)-1,4-dihydroquinoline-ω-(2-chlorobenzyl Chloride) Hydrochloride. A.—A mixture containing 3 g. of 7-chloro-4-(2-diethylaminoethylamino)-quinoline, 4.03 g. of 2-chlorobenzyl chloride and 50 ml. of acetonitrile was refluxed with stirring for 24 hours on a steam-bath. The solvent was removed by distilling *in vacuo*, and the residue was triturated with acetone to yield 5 g. of solid melting at 163–171° (uncor.). Several recrystallizations from isopropyl alcohol–ethyl acetate gave the purified product melting at 172.2–174.2°.

In many instances the product separated as a crystalline solid from the reaction mixture and was filtered off and purified by recrystallization.

B.—A mixture of 5 g. of 7-chloro-1-(2-chlorobenzyl)-4-(2-diethylaminoethylimino)-1,4-dihydroquinoline hydrochloride, 7.35 g. of 2-chlorobenzyl chloride and 40 ml. of acetonitrile was refluxed for 24 hours. The solvent was removed by distilling *in vacuo* and the residue was triturated with ether to yield a solid, which was collected and recrystallized from acetonitrile to yield 3 g. of product melting at 167.5–168.5° (uncor.).

7-Chloro-1-(2-chlorobenzyl)-4-(2-diethylaminoethylimino)-1,4-dihydroquinoline-ω-(2-chlorobenzyl Chloride).—The following procedure illustrates the general method employed for preparing the 4-imino-1,4-dihydroquinoline-ω-(quaternary salts).

To a solution of 3 g. of 7-chloro-1-(2-chlorobenzyl)-4-(2-diethylaminoethylimino)-1,4-dihydroquinoline-ω-(2-chlorobenzyl chloride) hydrochloride in 10 ml. of methanol was added a solution of 0.3 g. of potassium hydroxide in 5 ml. of methanol. There was an immediate separation of potassium chloride (0.35 g.) which was removed by filtration. The methanol was removed *in vacuo* from the filtrate and the residue, which solidified, was recrystallized from isopropyl alcohol–ether to yield the product melting at 154–157° (uncor.).

7-Chloro-1-(2-chlorobenzyl)-4-(2-dimethylaminoethylimino)-1,4-dihydroquinoline-ω-(methochloride) Hydrochloride.—A reaction mixture containing 7 g. of 7-chloro-1-(2-chlorobenzyl)-4-(2-dimethylaminoethylimino)-1,4-dihydroquinoline hydriodide, 10 g. of methyl iodide and 50 ml. of absolute ethanol was allowed to stand overnight at room temperature. There was thus obtained 8.5 g. of 7-chloro-1-(2-chlorobenzyl)-4-(2-dimethylaminoethylimino)-1,4-dihydroquinoline-ω-methiodide hydriodide which melted at 266–267° (uncor.) with decomposition.

This product was dissolved in hot ethyl alcohol and passed through a column containing 13 g. of ion-exchange resin (Amberlite IRA-400). The resulting solution was concentrated *in vacuo* to give a solid which after recrystallization from ethanol–ether melted at 247.8–249.8° dec.

Anal. Calcd. for $C_{21}H_{24}Cl_3N_3 \cdot HCl$. Cl^-, 15.37; N, 9.11. Found: Cl^-, 15.20 (D.B.); N, 9.17 (D.B.); H_2O, 2.89.

1-(2-Chlorobenzyl)-4,7-dichloroquinolinium Chloride.—Equivalent amounts of 4,7-dichloroquinoline and 2-chlorobenzyl chloride were heated on the steam-bath for two days. Trituration with ether gave a small amount of solid that melted at 192–194° after recrystallization from isopropyl alcohol.

Anal. Calcd. for $C_{16}H_{12}Cl_3N$: Cl_{DC}, 32.80. Found: Cl_{DC}, 32.47.

7-Chloro-1-(2-chlorobenzyl)-4-Iodoquinolinium Iodide.—A mixture of 69 g. (0.3 mole) of 4,7-dichloroquinoline, 97 g. (0.6 mole) of 2-chlorobenzyl chloride, 277 g. (1.8 mole) of 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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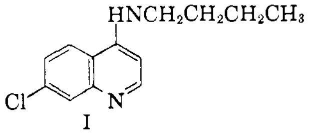
RECEIVED JULY 29, 1958

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.



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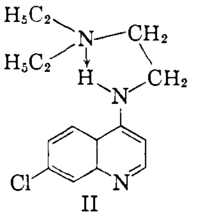

II

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.