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THE ELECTROPHILIC SUBSTITUTION OF BENZOQUINUCLIDINE

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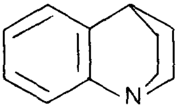
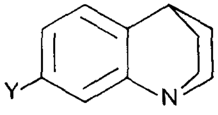
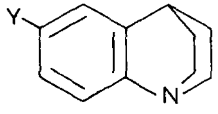


I



II : Y = NO_2
III : Y = SO_2Cl



IV

Benzoquinuclidine (I) differs from the usual N, N-dialkylanilines in that the lone pair on nitrogen is orthogonal to the π-electron system of the benzene ring in I. This is reflected in the pK_a value and the failure to couple with p-nitrobenzene diazonium chloride, demonstrated by Wepster (1). Moreover, bromination of benzoquinuclidine under a variety of conditions (2) yields only a molecular complex ($C_{11}H_{13}N.Br_2$, m. p. 152-153°) or the perbromide ($C_{11}H_{13}N.HBr.Br_2$, m. p. 85-87°) which can be reconverted to benzoquinuclidine under mild conditions.

However, benzoquinuclidine will undergo electrophilic substitution in the benzene ring: thus nitration with mixed acids at -4 to +7° gives a mononitrobenzoquinuclidine (89%, m. p. 117-118°), which forms a methiodide, m. p. 234-235°. Again, sulphonation with chlorosulphonic acid initially at 0° and then at 50° yields a benzoquinuclidinesulphonyl chloride which was characterised as the sulphonamide ($C_{11}H_{14}N_2O_2S$, m. p. 236-238°) and as the sulphon-(N, N-dimethylamide) ($C_{13}H_{16}N_2O_2S$, m. p. 148-150°; methiodide, m. p. 184-185°).

Physical measurements (2) show that these electrophilic substitutions have taken place at the 7-position to yield compounds II and III. The dipole moment of the nitro compound in benzene solution was determined as 5.23 ± 0.01 D and that for quinuclidine as 1.39 ± 0.02 D (3). Vector additions at 60° of the latter value with that of 4.39 D reported (4) for p-nitrotoluene in benzene gives 5.23 D, which strongly indicates structure II, with little mutual interaction between the substituent groups. By contrast, similar vector additions suggest that 5-, 6-, and 8-nitrobenzoquinuclidine should have dipole moments of

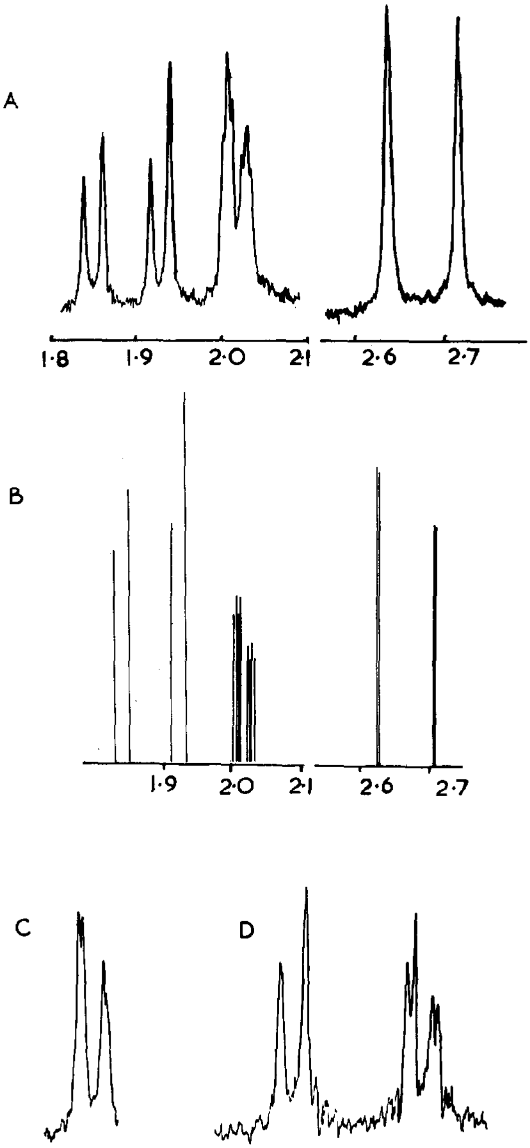
TABLE

NMR Chemical Shifts and Coupling Constants for Benzoquinuclidines [a]

Substituent(s)	Solvent	τ-Values in p. p. m.				J-values in Hz.			
		4	5	6	8	4,8	5,6	5,8	6,8
7-nitro	$CDCl_3$	6.79	2.68	1.89	2.02	0.7	8.1	0.4	2.1
	CD_3OD-D_2O (10:1)		2.55	1.88	2.08				
" (cation)	$CDCl_3-CF_3CO_2H$ (20:1)		2.30	1.56	1.51				
" (methiodide)			2.15	1.50	1.47				
7-dimethylaminosulphonyl	CH_2Cl_2		2.62	2.36	2.50	0.6	8	(<0.5)	2
	CD_3OD-D_2O (10:1)		2.48	2.30	2.49				
" (cation)	$CH_2Cl_2-CF_3CO_2H$ (20:1)		2.37	2.12	1.94				
" (methiodide)			2.16	1.99	2.02				

[a] Except for the 7-nitro compound in $CDCl_3$ (6), all values were obtained at 60 Mc/s, and the spectra were treated by first order analysis.

FIGURE



(A) Undecoupled spectrum; (B) Calculated spectrum of the aromatic region using the assignment of II and LAOCOON III Programme; (C) H_8 observed, H_4 irradiated (322.3 Hz. from TMS); (D) H_6 and H_8 observed, H_5 irradiated (738.2 Hz from TMS).

ca. 2.4, 3.8, and 5.6 D, respectively.

This conclusion is confirmed by N.M.R. spectroscopy. The gross magnitudes of the coupling constants of the nitrobenzoquinuclidine and of the sulphonyl derivatives (see Table) show clearly the presence of a 1,2,4-trisubstituted benzene ring, and thus eliminate the 5- or 8-orientation for the substitution products. The precise assignment of the aromatic signals, allowing a distinction between the 6-(cf. IV) and 7-orientations to be made (II, III), was obtained by two independent methods:

(i) Bicyclic aromatic compounds (such as 1,7-naphthyridine (5)) frequently show a long range coupling of ca. 0.5 Hz. between protons in 5,8-positions. In the substituted benzoquinuclidines such a coupling is observed, and this serves to identify the 8-position proton. Thus, the nitro-compound, which was studied in detail (6) showed in the aromatic region an ABC system with additional coupling of one of the signals to one other proton; the detailed assignment was confirmed by decoupling experiments (see Figure).

(ii) Whereas on protonation or methylation at the cyclic nitrogen atom a general down field shift of all the aromatic protons is expected (and found), the 8-position proton can be identified by its greater down field shift under these conditions and hence it can be shown that the 7-position is substituted as no ortho coupling is found for this 8-proton (see Table).

Conclusions. - All the physical criteria agree that the electrophilic substitution products are formed by reaction at the 7-position, meta to the cyclic nitrogen atom. These results afford further evidence for the absence of resonance interaction between the nitrogen lone pair and the benzene ring in quinuclidine.

REFERENCES

[1] B.M. Wepster, Rec.Trav.Chim., 71, 1159, 1171 (1952).

[2] Details will be given in the full paper, to be published in Khimiya Geterotsiklicheskikh Soedinenii. All new compounds gave satisfactory analyses.

[3] For details of the techniques utilised in the measurements of dipole moments see R.A.Y. Jones, A.R. Katritzky, K.A.F. Record, M. Snarey and R.J. Wyatt, J.Chem. Soc. (B), in preparation.

[4] Recommended value from A.L. McLellan, "Tables of Experimental Dipole Moments," Freeman, San Francisco, 1963.

[5] J. Altman, H. Giboa, D. Ginsburg, A. Loewenstein, Tetrahedron Letters, 1329 (1967).

[6] The N.M.R. spectrum was obtained at 100 MHz. on a Varian HA 100 instrument with decoupling, as 15% w/v solutions in $CDCl_3$ with TMS as internal standard. The spectral parameters were obtained by the LAOCOON III technique. (Spectral parameters for the other compounds are the result of first order analysis).