The Crystal Structure of 1-Benzyl-4-phenylpiperidine Methobromide: Proof of Preferred Axial Quaternisation of 1-Benzyl-4-phenylpiperidine with Methyl Iodide

By R. BRETTLE, D. R. BROWN, J. MCKENNA,*† and R. MASON
(*Chemistry Department, The University, Sheffield* S3 7HF)

Summary Preferred *axial* quaternisation of 1-benzyl-4-phenylpiperidine with methyl iodide has been demonstrated by *X*-ray crystallographic analysis of the chief reaction product (as bromide).

THE preferred direction of quaternisation of tertiary 4-phenylpiperidines having a primary 1-alkyl group with methyl iodide has been a matter of some controversy.[1] We report unambiguous physical evidence for the preferred axial methylation of 1-benzyl-4-phenylpiperidine.

The chief (80%) quaternisation product of 1-benzyl-4-phenylpiperidine with methyl iodide in acetone or methanol was separated from the minor (20%) diastereomeric product by fractional crystallisation from methanol, progress of the separation being followed by n.m.r. spectroscopy. The pure (major) quaternary bromide was prepared from the iodide by use of an anion-exchange resin, and crystals suitable for *X*-ray analysis were recrystallised slowly from ethanol–ethyl acetate.

The crystals are orthorhombic, space group *Pbca*; $Z = 8$. Relative intensities of 782 independent reflexions were measured by visual methods and used for a structure determination by the standard heavy-atom method. Least-square analysis has reduced R to 0·13; further refinement will be undertaken to reduce the standard deviations of the carbon and nitrogen positional parameters (presently 0·05 Å). The structure of the cation, projected on to (001) is shown in the Figure, and unambiguously establishes the preferred axial methylation of the initial tertiary base. Torsion angles in the piperidine ring approximate quite closely to those of an ideal chair conformation.

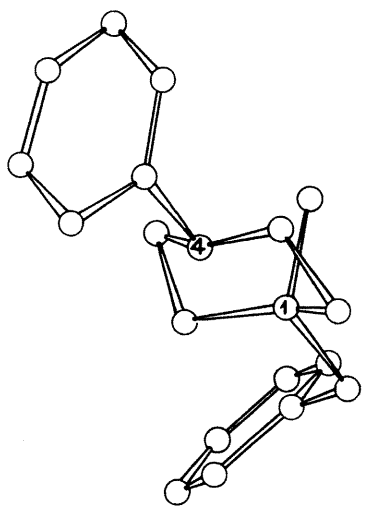

FIGURE. *Major cation from reaction of* 1-*benzyl*-4-*phenylpiperidine with methyl iodide in acetone or methanol.*

(*Received, January* 28*th*, 1969; *Com.* 118.)

† Present address: Department of Chemistry, Mellon Institute, 4400 Fifth Avenue, Pittsburgh, Pennsylvania, 15213, U.S.A.

[1] J. McKenna, J. M. McKenna, A. Tulley, and J. White, *J. Chem. Soc.*, 1965, 1711; J.-L. Imbach, A. R. Katritzky, and R. A. Kolinski, *J. Chem. Soc.* (*B*), 1966, 556; D. R. Brown, B. G. Hutley, J. McKenna, and J. M. McKenna, *Chem. Comm.*, 1966, 719; D. R. Brown, R. Lygo, J. McKenna, J. M. McKenna, and B. G. Hutley, *J. Chem. Soc.* (*B*), 1967, 1184; A. T. Bottini and M. K. O'Rell, *Tetrahedron Letters*, 1967, 423.