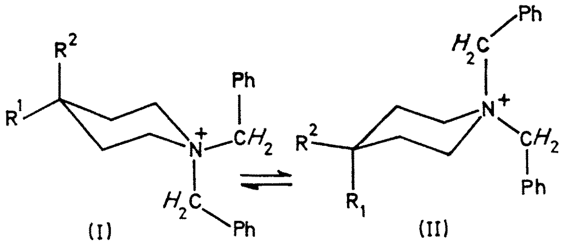
Failure of the Chemical Shift Method of Conformational Analysis in Quaternary Salts from 4-Alkylpiperidines

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

Summary Conformational free-energy values for 4-substituents (or 4,4-geminal pairs) in 1-benzylpiperidine benzobromides cannot be derived from the chemical-shift differences between *ax*- and *eq*-1-benzyl methylene protons.

THE marked chemical-shift differences between *ax*- and *eq*-1-benzyl methylene protons in 1,1-dibenzylpiperidinium salts[1] led us to examine the applicability of the related n.m.r. method of conformational analysis[2] to a range of 4-substituted salts (see Table). With the usual (if questionable) assumption that 4-alkyl substituents do not affect the chemical shifts of protons in 1-substituents, $\Delta\nu°$ for the 4-Bu^t salt should be greater than $\Delta\nu$ for any other salt, the equilibrium constant for (II) $\rightleftharpoons$ (I) (R^1 = alkyl; R^2 = H or alkyl) should be given by $(\Delta\nu° + \Delta\nu)/(\Delta\nu° - \Delta\nu)$, and the mean chemical shift of *ax*- and *eq*-1-benzyl methylene protons should coincide with the value for the corresponding protons in the 4-unalkylated salt in spectra of appropriate mixtures. The ease of synthesis of such a wide range of piperidinium salts makes possible a more critical and comparative assessment of the applicability of the n.m.r. method than has previously been possible in studies with cyclohexane derivatives.



TABLE

Chemical-shift differences ($\Delta\nu$) *between* ax- *and* eq-1-*benzyl methylene protons in* 4-*substituted*-1-*benzyl-piperidine benzobromides, and offsets* (+: *upfield offset*; —: *downfield*) *in mean signal position relative to that for benzyl methylene protons in* 1-*benzylpiperidine benzobromide. Figures are for* 60 *MHz spectra of* $CDCl_3$ *solutions at* 35°, *extrapolated to zero concentration*; *offsets from spectra of mixed salts. Precision* ca. ±0·1 *Hz.*

4-Substituents in 1-benzylpiperidine benzobromide	$\Delta\nu$ (Hz)	Mean offset (Hz)
H,H	0·0	0·0
Me,H	22·2	+0·4
Et,H	22·6	+0·6
Pr^i,H	23·8	+1·4
Bu^t,H	23·4 (=$\Delta\nu°$)	+2·7
Me,Et	7·4	+0·9
Me,Pr^i	17·1	+1·9
Ph,H	27·5	−6·2
Me,Ph	21·2	−0·4
$PhCH_2$,H	33·5	−1·8

---

† Present address: Mellon Institute, 4400 Fifth Avenue, Pittsburgh, Pennsylvania, 15213.

Our results strikingly demonstrate the progressive failure of the method for the 4-alkyl salts, not only from the increasing values for mean offset (3rd column in Table) but also from the fact that $\Delta\nu$ (second column) for Pr^i is greater than for Bu^t. Previous doubts[2] about the utility of the n.m.r. procedure are thus convincingly validated. Deviations are (understandably) more obvious still in salts with aromatic 4-substituents, which were examined for comparison. A plot of the polar substituent constants, σ^*, for (single) 4-substituents against offsets is approximately linear, but we feel that other factors than inductive effects of the 4-substituents are also likely to be important in causing the offsets and deviations in $\Delta\nu$, principally anisotropy effects and ring-distortion.

(*Received, March 24th,* 1969; *Com.* 412.)

---

[1] R. W. Horobin, J. McKenna, and J. M. McKenna, *Tetrahedron*, 1966, Suppl. 7, 35; D. R. Brown, J. McKenna, and J. M. McKenna, *J. Chem. Soc.* (*B*), 1967, 1195.

[2] For recent reviews see E. L. Eliel and R. J. L. Martin, *J. Amer. Chem. Soc.*, 1968, **90**, 682; S. Wolfe and J. R. Campbell, *Chem. Comm.*, 1967, 872.