Tetrahedron Letters No. 24, pp. 1103-1106, 1962. Pergamon Press Ltd.
Printed in Great Britain.

CONFIGURATIONS OF CYCLIC QUATERNARY AMMONIUM SALTS BY N.M.R. SPECTROSCOPY

J. K. Becconsall
Imperial Chemical Industries Ltd., Dyestuffs Division,
Hexagon House, Blackley, Manchester, 9

and Richard A. Y. Jones
Department of Chemistry, The University, Sheffield, 10

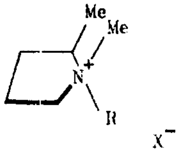
(Received 13 August 1962)

N.M.R. is a valuable technique for configurational and conformational analysis of cyclic systems, and its use for the investigation of the configurations of quaternary salts of cyclic amines has been described[1,2,3].

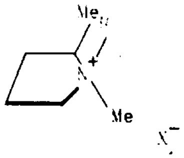
We have used N.M.R. for the structural analysis of the products of the quaternisation reactions described in the previous communication[4], and also, in some cases, to assist in determining the proportions of configurational isomers produced. The approach is basically that of Closs[1]. If the hydrochloride of a tertiary methylamine can exist in two configurations (e.g. 1,2-dimethylpyrrolidine hydrochloride [1 and 2; R = H, X = Cl]) one frequently observes two separate signals in the N.M.R. spectrum, arising from the two differently situated (and differently shielded) $N-CH_3$ groups. One of these signals is likely

---

1. Closs, J. Amer. Chem. Soc. (1959) **81**, 5456.
2. Moynehan, Schofield, Jones and Katritzky, J. Chem. Soc. (1962) 2637.
3. Shamma and Moss, J. Amer. Chem. Soc. (1962) **84**, 1739.
4. McKenna, White and Tulley, preceding communication.



(1)



(2)

to be considerably more intense than the other, reflecting the greater stability of one configuration. For 1,2-dimethylpyrrolidine hydrochloride the more intense signal is at 6.97[*] and the weaker at 7.27. The isomer with methyl groups trans to each other is expected to be the more stable, so that the differential shielding in this series of compounds is such that a trans-1-methyl group absorbs at lower field than a cis-1-methyl group.

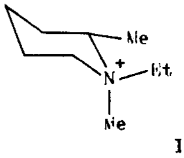
The pyrrolidine quaternary iodides (1 and 2; R = alkyl, X = I) all show N-CH_3 signals at ca. 6.7 or ca. 7.0 or both. If the argument can be transferred from the hydrochlorides to the quaternary salts the 7.0 signal is due to isomer (1) and that at 6.7 to isomer (2). The relative intensities give a measure of the relative amounts of the two configurations.

For 2-methylpiperidine hydrochloride the more intense of the two N-CH_3 signals (7.19 and 7.27) is at lower field, and presumably corresponds to the salt with both methyl groups equatorial.

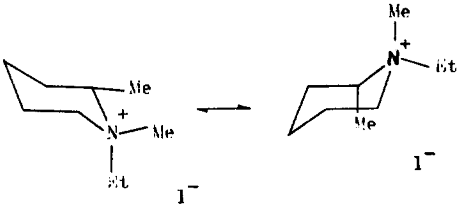
---

[*] Positions of peaks are reported as τ-values. Internal references were $(CH_3)_4Si$ (chloroform solutions, pyrrolidine and camphidine series) and dioxan (aqueous solutions, piperidine and tropane series). In the latter case the τ-value for dioxan was taken as 6.30.

1-Ethyl-2-methylpiperidine methiodide* has a signal at 7.13; 1,2-dimethylpiperidine ethiodide* shows two peaks of similar intensity at 6.91 and 7.09. This suggests that the methiodide is conformationally pure and has N-CH_3 axial (3), while the ethiodide is a mixture of the two conformations (4 and 5).



(3)



(4) (5)

Tropane hydrochloride has the more intense of its two N-CH_3 signals (7.09 and 7.29) at higher field. Tropane ethochloride (6.96) and N-ethylnortropane methochloride (7.09) presumably have axial and equatorial N-CH_3 groups, respectively, as expected^5, although assignments are somewhat confused by impurity peaks in this series because only crude reaction products have been examined. These spectra are very similar to those obtained by Closs^1 from the pseudo-tropines.

The hydrochlorides of 1-methyl-4-phenylpiperidine and 1-methyl-*trans*-decahydroquinoline exhibit only single N-CH_3 signals so that structural assignments for the quaternary salts cannot be based on N.M.R. However, the relative intensities of the N-CH_3 signals are valuable for determining isomer proportions.

---

[5] Fodor, *Tetrahedron* (1957) **1**, 82; *Chem. and Ind.* (1961) 1500.

---

* For nomenclature see preceding communication.

In quaternary iodides derived from camphidine the N-CH_3 signal is either superimposed on the highest N-CH_2- signal or is some 0.2/0.3 p.p.m. to higher field. The hydrochloride shows the high field signal which is accordingly assigned to the equatorial N-CH_3. If the piperidine ring of camphidine quaternary salts (but not of the hydrochloride) existed in a twisted boat conformation[6], our configurational assignments[4] might no longer retain their absolute significance, though they would still be relatively correct. However, the general similarity of the spectrum of the hydrochloride with those of the quaternary salts indicates that such a conformational change probably does not occur.

---

6. Trojánek, Komrsová, Pospíšek and Čekan, Coll. Czech. Chem. Comm. (1961) 26, 2921.