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VII. PHYSICO-CHEMICAL STUDY OF MODELS OF INDOLE ALKALOIDS (1)

CONFIRMATION OF THE ASSIGNMENT OF THE GEOMETRY OF THE TWO ISOMERIC 3-ETHYLIDENE-1-AZABICYCLO [2,2,2] OCTANE BY THE STUDY OF THE NUCLEAR OVERHAUSER EFFECT (NOE).

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It has been shown that the consideration of the intramolecular spin-spin relaxation path for the various protons in a molecule can lead to valuable information on its stereochemistry, particularly when the molecule has a rigid framework 2).

We wish to report the application of the Nuclear Overhauser Effect3) to the confirmation of the assignment of the geometry of the ethylidene side-chain in 3-ethylidene-1-azabicyclo [2,2,2] octane (3-ethylidenequinuclidine)[1].

Both spectroscopic and chemical evidences for the existence of two isomers (C_9- C_{10} bond <u>cis</u> [1a] or <u>trans</u> [1b] with respect to the C_4- H bond) have been given previously as well as first order analysises of their N.M.R. spectra at 60 MHz 8,9).

The 100 MHz spectrum (Fig.1) of a mixture of both isomers (1a/1b = 70:30) in $CDCl_3$ + 10 % of CF_3COOH shows the signals of the C_4-H as a quintuplet labelled X for the isomer 1a, Y for the isomer 1b and the signals of the C_9- Me group as a double triplet labelled A for the isomer 1a and B for the isomer 1b. These signals are sufficiently far apart and well resolved to expect unambiguous results.

In compound 1a, the C_9-Me group lies close to the C_4-H whereas in compound 1b this C_9-Me group is far away and should not contribute appreciably to the intramolecular relaxation of H_4. Thus H_4 should be relaxed largely by the protons of the C_9- Me group in isomer 1a only.

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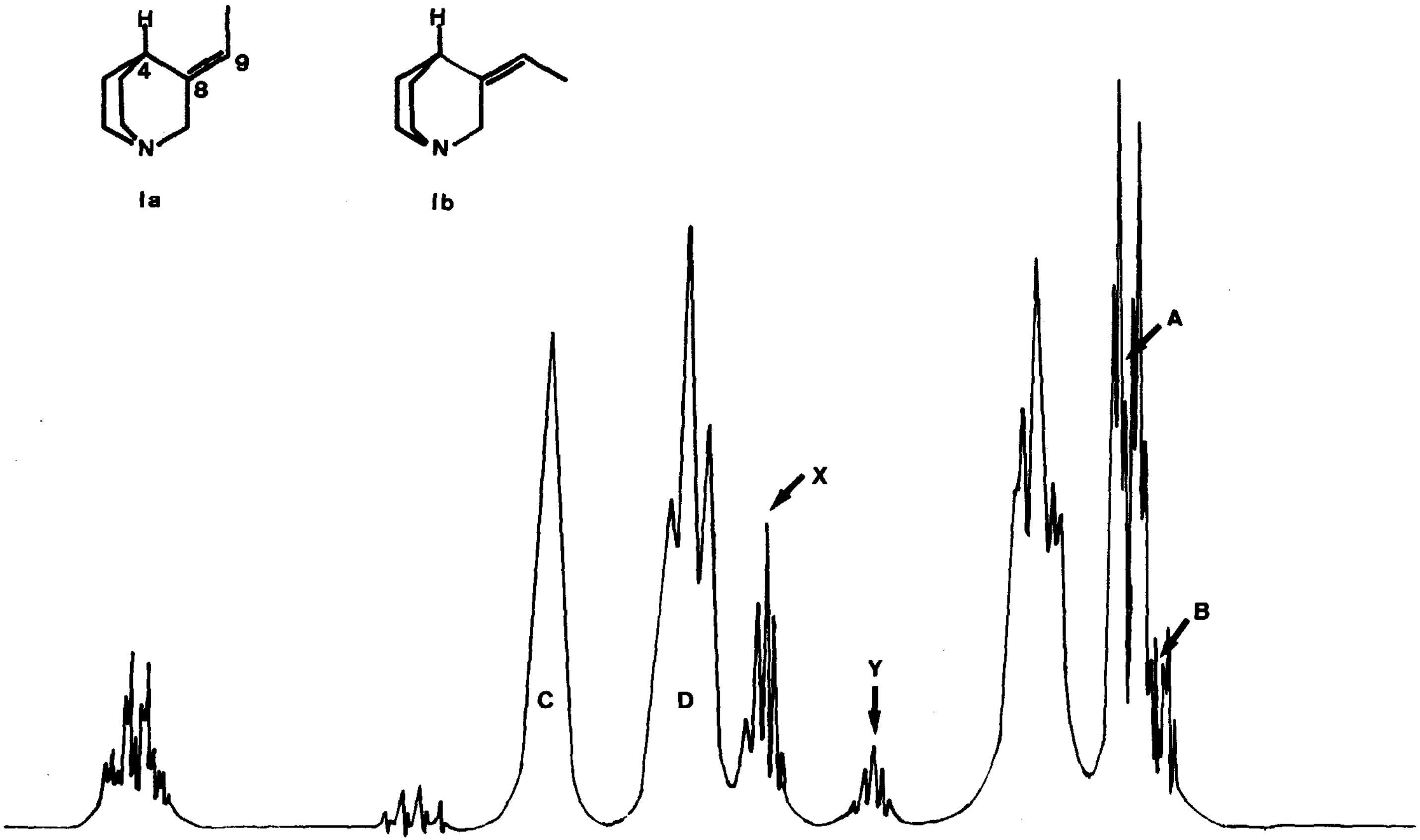

Fig.I 100 MHz NMR Spectrum of 3-ethylidene-1-azabicyclo(2,2,2)octanes (70:30 Mixture of 1a and 1b)

The spectrum of a mixture of 1a + 1b, as a 10 % (v/v) solution in CDCl$_3$ + 10 % (w/w) of CF$_3$COOH* was observed by a frequency sweep method at 100 MHz using a VARIAN H A 100 instrument locking the field on the CF$_3$COO$\underline{\text{H}}$ proton. Special care was taken to avoid paramagnetic impurities and the solution was thoroughly degased.

Irradiation of the B group at the centre of the multiplet resulted in no change of the integrated intensity of the Y group (measured relatively to the sum of the signal strengths of the C and D groups; for explanation see Fig. 1) whereas irradiation of the A group resulted in a positive enhancement of 31 % of the integrated intensity of the X signal leaving the intensity of the Y signal unaltered.

These results are collected in the following table :

Intensity of i) in arbitrary units.	C	D	C+D	X	Y
Undecoupled	264	508	712	100	30
Irradiated at A ii)	256	516	712	131	30
Irradiated at B ii)	258	514	712	100	30

i) These data are the average of four different runs

ii) Data for X and Y calculated by reference to the sum C+D equal to 712.

These results combined ,with an unambiguous assignment of the N.M.R. spectra, confirm the conclusions reached previously 8): the major compound obtained by the Wittig reaction of triphenylethylphosphorane on 3-quinuclidone has the structure 1a (C$_9$-Me, C$_4$-H cis).

This is another interesting example of a deshielding of a proton by a methyl group [$\Delta\delta$ (C$_4$-H in 1a - C$_4$-H in 1b) = 0.42 ppm] when the distance between the carbon atom of the methyl group and the proton is less than 3 Å 10) (2.4 Å as measured on Dreiding models) in spite of the fact that the C-H and the C-CH$_3$ bonds are nearly parallel (the angle between these two bonds is about 11°).

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* Although solvents containing nuclei with high magnetic moments should be avoided in N.O.E. experiments, the use of CF$_3$COOH does not affect the conclusions drawn hereafter. This follows from the fact that the measurements were carried out on a mixture of both isomers in the same solution.

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