

HINDERED INTERNAL ROTATION IN CARBOHYDRATES
CONTAINING NITROGEN IN THE RING

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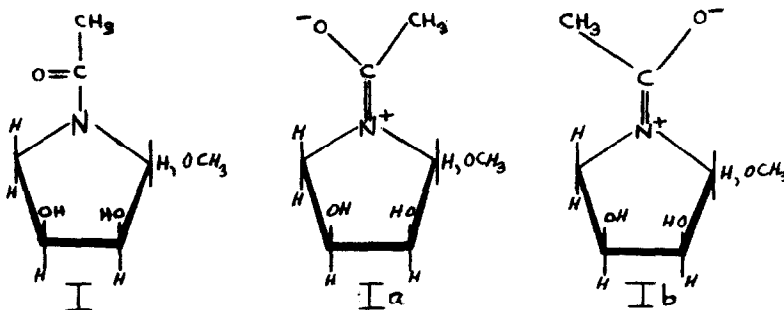
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Recently the synthesis of methyl 4-acetamido-4-deoxy-L-erythrofuranoside (I), the first example of a sugar with nitrogen in a five-membered ring, was reported from this laboratory (1). The n.m.r. spectrum of I was unusually complex and it was suggested that either the compound possesses internal hindered rotation or the substance may be an approximately 1:1 mixture of α - and β - anomers. We now present evidence that substantiates the former hypothesis. Restricted rotation has also been demonstrated in two nitrogen-containing pyranose sugars.

N.M.R. spectroscopy has proved to be an extremely useful tool for the study of hindered internal rotation in compounds in which the rate of interconversion between two rotational conformers is slow enough to allow a chemical shift difference between signals arising from the two conformers (2). The n.m.r. spectrum of I (Fig. 1) in deuterium oxide at room temperature shows two doublets at 4.95 and 5.04 p.p.m. in the general region characteristic of anomeric protons (3). In addition there are two peaks

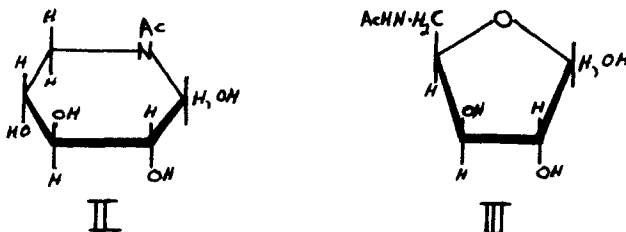
at 3.36 and 3.41 p.p.m. which may be assigned to the methoxyl protons, and peaks at 2.08 and 2.12 p.p.m. which may be assigned to the protons of the N-acetyl group. At an elevated temperature (80°) the two anomeric resonances have broadened and the O-methyl and N-acetyl absorptions have collapsed to single peaks (Fig. 2). The doublet pattern is restored on cooling to room temperature. This behavior is analogous to that of several N-methylamides (4,5). The twin peaks arise from resonance conjugation between the p-orbital on nitrogen and the p-orbital of the Π -electron system resulting in the two dipolar structures Ia and Ib.



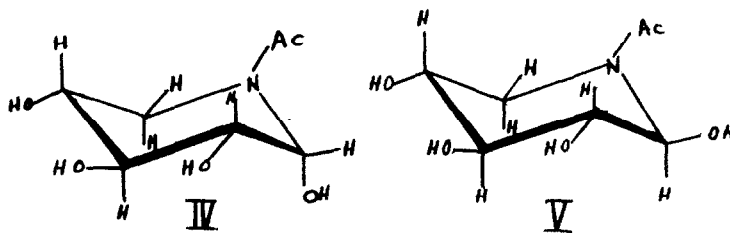
The n.m.r. spectrum at room temperature is the result of a superposition of the peaks arising from the rotational conformers Ia and Ib.

The synthesis of 5-acetamido-5-deoxy-D-xylopyranose (II) and the isomeric furanose form containing oxygen in the ring (III) has been achieved independently by Paulsen (6), Jones and Szarek (7), and Hanessian and Haskell (8). The last group of workers report that aqueous solutions of II and III did not mutarotate at room temperature in the course of seventy-

two hours. A change in optical rotation was observed only when the solutions were acidified or basified. Paper chromatography of the equilibrated solutions then revealed the presence of II and III.



The n.m.r. spectrum of II in deuterium oxide at room temperature, reported by Hanessian and Haskell (8), showed two distinct peaks at 2.63 and 2.67 p.p.m. which these workers attributed to the N-acetyl methyl groups of 5-acetamido-5-deoxy- α -D-xylopyranose (IV) and 5-acetamido-5-deoxy- β -D-xylopyranose (V). The presence of IV and V was suggested by two doublets at 6.05 and 6.45 p.p.m. These were attributed to the C-1 axial hydrogen in V and the C-1 equatorial hydrogen in IV, respectively. The mutarotation studies (*vide supra*) do not, however, indicate the formation of IV and V in aqueous solution.



The n.m.r. spectrum of 5-acetamido-5-deoxy-D-xylopyranose (II) in deuterium oxide at room temperature, determined in our laboratory, is presented in Fig. 3. The spectrum shows two doublets at 5.54 and 5.98 p.p.m. attributable to anomeric protons, and two peaks at 2.15 and 2.18 p.p.m. which may be assigned to the protons of the N-acetyl group. At 80° the two anomeric resonances have merged and the two N-acetyl signals have collapsed to a single peak (Fig. 4). Clearly, this evidence suggests that 5-acetamido-5-deoxy-D-xylopyranose exists as two rotational isomers due to restricted rotation about the CO-N bond and not as a mixture of anomers as suggested by Hanessian and Haskell (8).

Methyl 5-acetamido-5-deoxy-D-xylopyranoside (7) has been shown also to possess internal hindered rotation. The n.m.r. spectra of this compound at room temperature (Fig. 5) and at elevated temperature (Fig. 6) exhibit behavior entirely analogous to that shown by the spectra of the compounds discussed above.

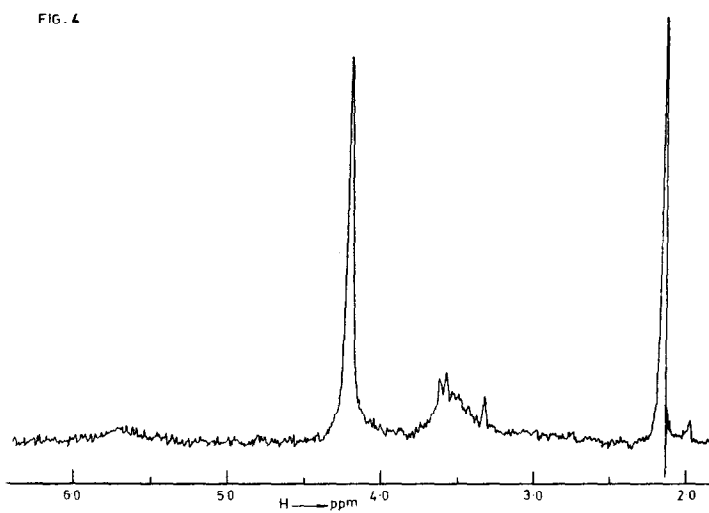
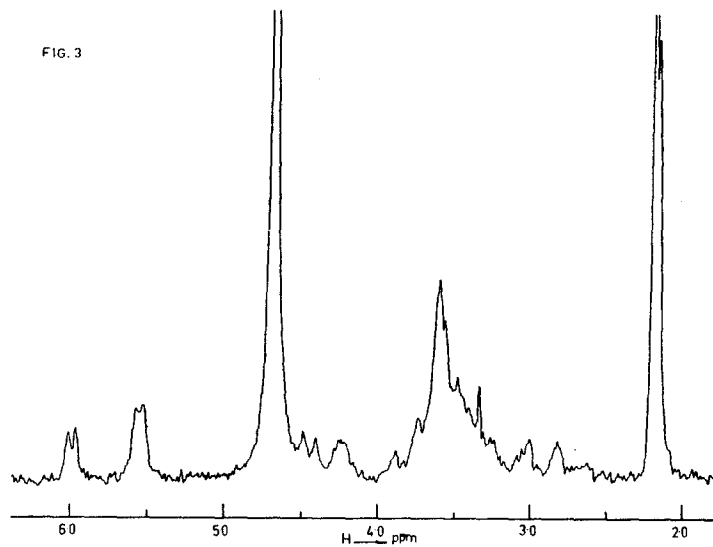


FIG 1

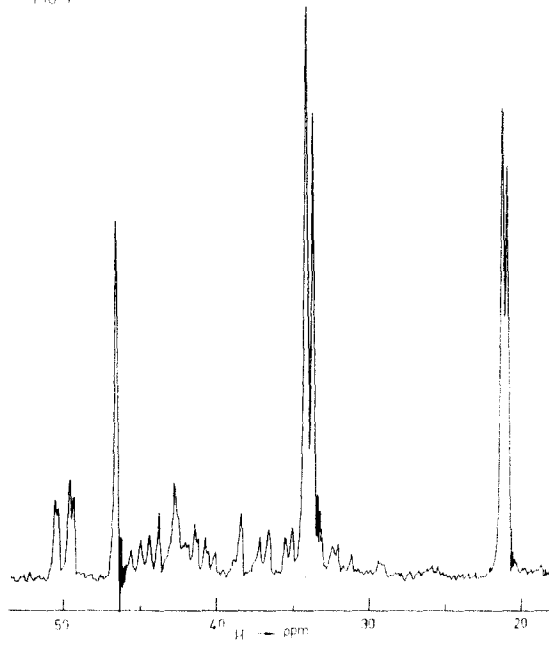


FIG 2

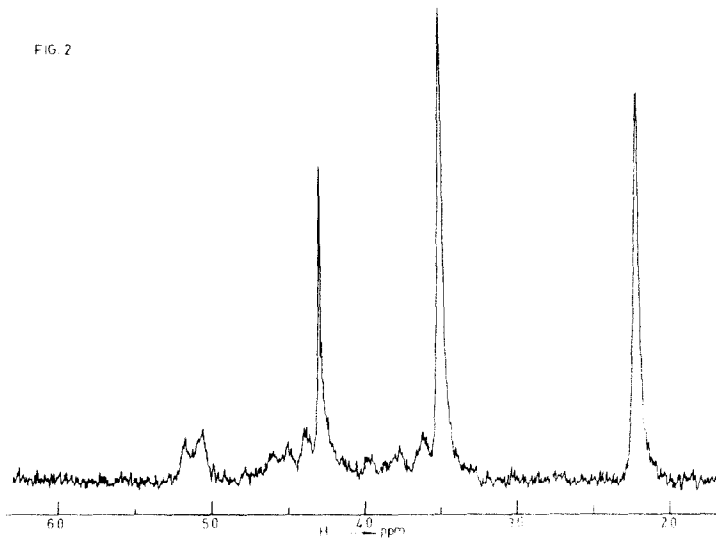


FIG. 5

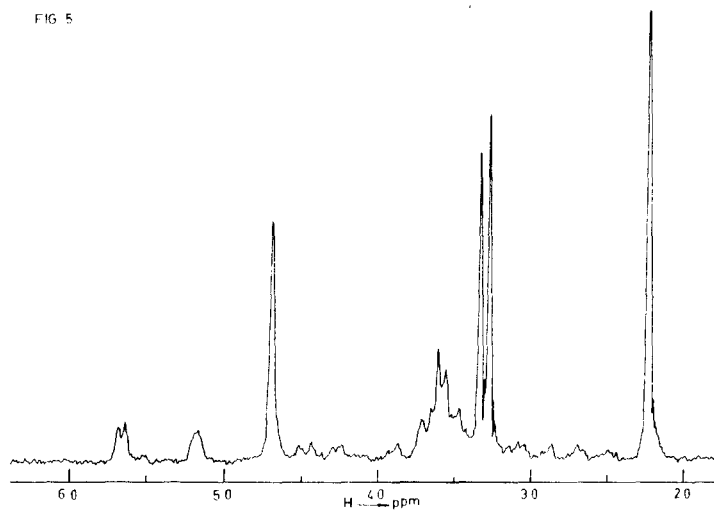
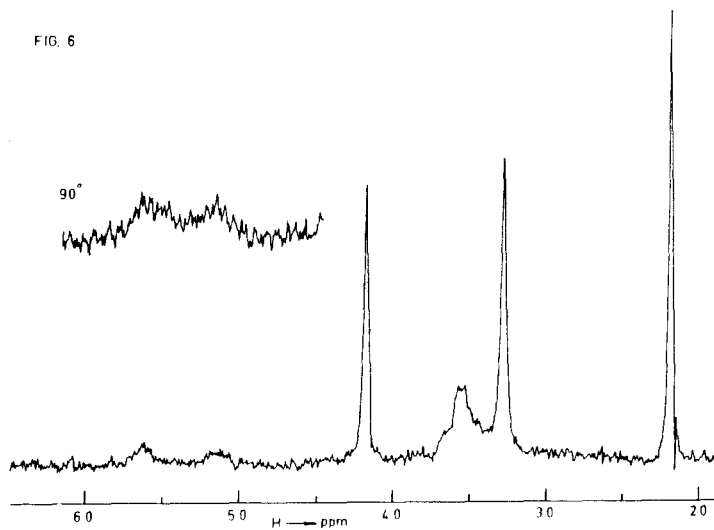


FIG. 6



The n.m.r. spectra reported in this publication were determined at 60 Mc/s with a Varian A-60 n.m.r. spectrometer using approximately 10% by weight solutions in deuterium oxide; chemical shifts were determined as p.p.m. downfield from tetramethylsilane as an external standard.

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