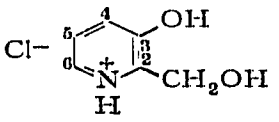
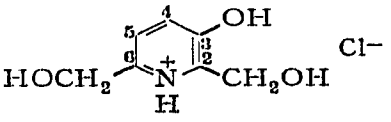
Structure elucidation of mono-(hydroxymethyl)- and di-(hydroxymethyl)-3-hydroxypyridines*

In the previous article, the isolation of mono-(hydroxymethyl)- and di-(hydroxymethyl)-3-hydroxypyridines is described. The plausible structures I and II, respectively, indicated by analysis, equivalent weight and pK values, are established in detail by the n.m.r. spectra of the products as outlined in this accompanying note.



(I)



(II)

The structure of the monosubstituted product is available from its n.m.r. spectra in trifluoroacetic acid and deuterium oxide solutions. In the latter solvent all active hydrogens (OH, NH) are replaced by deuterium; three resonances due to aromatic protons appear in the spectrum, centred at $\delta = 8.31$ p.p.m. (quartet, with splittings of 5 c/s and 2 c/s), $\delta = 8.00$ p.p.m. (perturbed quartet with splittings of 2 c/s and 9 c/s) and $\delta = 7.83$ p.p.m. (perturbed quartet with splittings of $\sim$5 c/s and $\sim$ 9 c/s). These resonances are assigned to H-6, H-4 and H-5 respectively. In particular, a large splitting of each of these resonances established that all three protons undergo an *ortho*-interaction. Therefore the hydroxymethyl group is located at C-2 (see I). The methylene protons of the hydroxymethyl group resonate as a sharp singlet at $\delta = 5.40$ p.p.m. in trifluoroacetic acid solution.

The structure of the disubstituted product follows from its n.m.r. spectrum in trifluoroacetic acid solution. Two 2-proton resonances occur as singlets at $\delta = 5.32$ p.p.m. and $\delta = 5.38$ p.p.m. and indicate the presence of two hydroxymethyl substituents. In confirmation, only two proton resonances occur (as an AB system with $J =$ 9 c/s) in the aromatic region at $\delta = 7.89$ p.p.m. and $\delta = 8.25$ p.p.m.** The magnitude of the coupling constant (9 c/s) establishes that the second hydroxymethyl substituent is at C-6 and not at C-4 (see II), since $J_{2,3}$ (or $J_{5,6}$) values are smaller ($\sim$5–6 c/s) in pyridines than the corresponding $J_{3,4}$ (or $J_{4,5}$) values ($\sim$8–9 c/s); the characteristic difference in the J values is probably caused by the electronegativity of the nitrogen atom[1].

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1 H. S. GUTOWSKY AND A. L. PORTE, *J. Chem. Phys.*, 35 (1961) 839.

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** The pair of lines centered at $\delta = 7.89$ p.p.m. is broadened slightly, presumably due to allylic coupling between H-5 and the methylene protons of the C-6 hydroxymethyl group (see II).