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CONFORMATIONAL STRUCTURE OF ACTINAMINE

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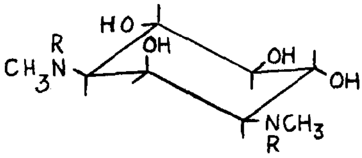
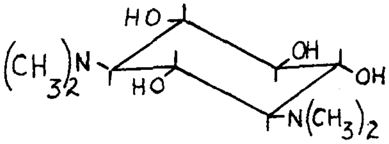
THE isolation of actinamine from the hydrolysis of actinospectacin[1,2] has been reported by Wiley[3]. Nuclear magnetic resonance studies have now shown the complete structure of actinamine to be as in I.



I R = H

II R = CH$_3$



III R = CH$_3$

Several derivatives of actinamine were studied. The spectrum of N, N'-dimethylactinamine[3] (Fig. 1) was the most definitive and was readily factored. It showed in addition to 12 N-methyl hydrogens and some residual HOD, three groups of lines of integrated areas one, two and three. The lowest, a triplet at 301 cps, J = 3 cps, was judged to be the 2-hydrogen of the Wiley structure, since it was between the two positively-charged nitrogen substituents which have a strong deshielding effect. The multiplicity and coupling constant indicated identical axial-equatorial coupling to two neighbors which were found at 198 cps.

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[1] D.J. Mason, A. Dietz and R.M. Smith, Antibiotics and Chemotherapy 11, 118 (1961).

[2] M.E. Bergy, T.E. Eble and R.R. Herr, Antibiotics and Chemotherapy 11, 661 (1961).

[3] P.F. Wiley, J. Amer. Chem. Soc. 84, 1514 (1962).

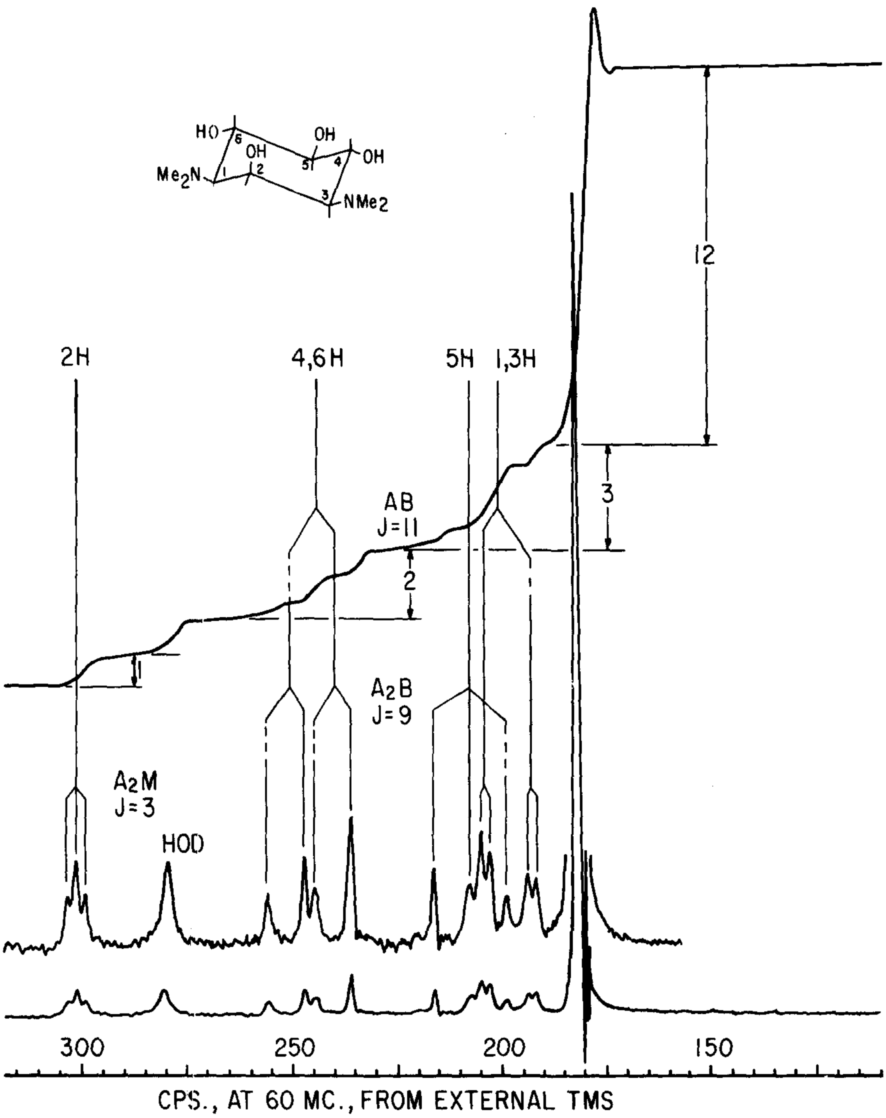

FIG. 1

NMR spectrum of N,N'-dimethylactinamine dihydrochloride, in deuterium oxide, after replacement of six exchangeable hydrogens with deuterium.

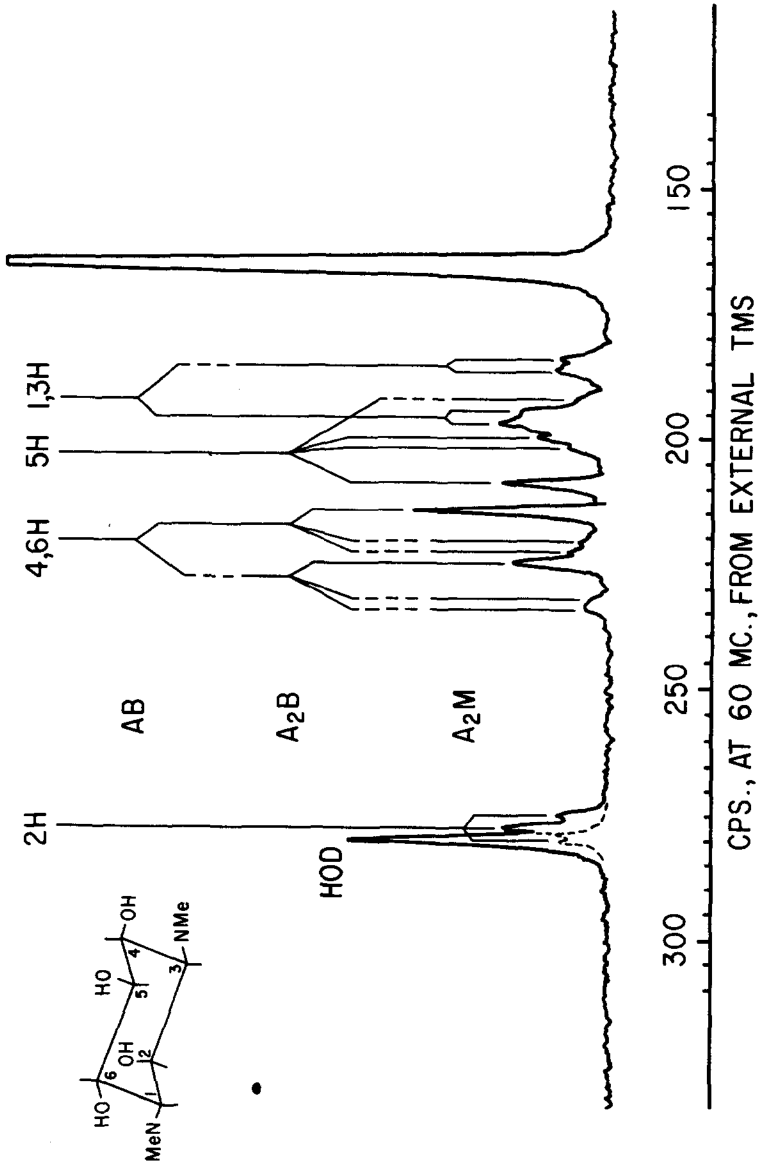

FIG. 2

NMR spectrum of actinamine dihydrochloride, in deuterium oxide, after replacement of eight exchangeable hydrogens with deuterium.

The multiplet at 244 cps was clearly one part of an AB multiplet with its counterpart at 198 cps. Both had one additional split. The areas and shapes of these absorptions indicated they were in fact the absorptions of two identical AB systems. Thus, they had to be the hydrogens at 1, 3, 4 and 6 in the Wiley structure. The magnitude of the AB coupling (11 cps) indicated they were trans-diaxial. The multiplets with total area-3 at about 200 cps were factored into the double-B component of the AB system (described above) at 198 and an asymmetrical triplet of area-1 at 207 cps. The double-B component at 198 was further coupled to the 2-hydrogens in an axial-equatorial arrangement (J = 3) and hence it was assigned to the 1- and 3-hydrogens leaving the 4- and 6-hydrogens for the double-A absorption at 244.

The asymmetrical triplet at 207 was the B-part of an A_2B type system and was diaxially coupled (J = 9) to the two hydrogens absorbing at 244. Hence it was the 5-hydrogen.

Thus, all the hydrogens showed at least one diaxial coupling except the 2-hydrogen which had two equatorial-axial couplings and which was therefore the only equatorial hydrogen on the ring.

The above assignments were confirmed when the spectrum of N, N, N', N'-tetramethylstreptamine[4] (III) was observed. In this all-trans[5] structure the double AB system was the same as in actinamine but the 2-hydrogen had shifted up-field as expected[6] for an equatorial-to-axial modification, absorbing with the 1, 3 and 5 hydrogens in a complex second-order multiplet that was not factored. The spectrum accordingly supported the all-trans

[4] G.F. Holland, R.C. Durant, S.L. Friess and B. Witkop, J. Amer. Chem. Soc. 80, 603 (1958).

[5] M.L. Wolfram, S.M. Olin and W.J. Polglase, J. Amer. Chem. Soc. 72, 1724 (1950); F.W. Lichtenthaler and H.O.L. Fischer, Ibid. 83, 2005 (1961).

[6] R.U. Lemieux, R.K. Kullnig, H.J. Bernstein and W.G. Schneider, J. Amer. Chem. Soc. 79, 1005 (1957).

structure for tetramethylstreptamine too.

The spectrum of actinamine (I) (Fig. 2) was analyzed and it showed the same stereochemical relationships, hence there were no inversions involved on methylation. The A_2B system had a larger $J/\delta\upsilon$ and hence showed more second-order splitting.

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