Stereochemistry and Absolute Configuration of the Antibiotic Spectinomycin: an *X*-Ray Diffraction Study

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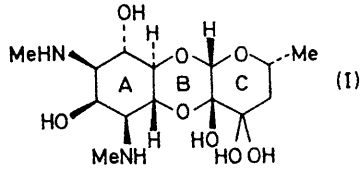
Summary A single crystal *X*-ray diffraction study of spectinomycin dihydrobromide pentahydrate has shown that the molecule has a B/C *cis* ring juncture and exists as a stable ketone hydrate; the absolute configuration of the molecule was determined by anomalous dispersion.

SPECTINOMYCIN (I) is a fused ring aminocyclitol[1] antibiotic currently used in the treatment of gonorrhea. The general structure of the molecule had been determined previously,[2]



(I)

but the details of its stereochemistry were not fully elucidated. The results of the single crystal *X*-ray diffraction study reported here show that the B/C ring juncture is *cis*, with the hydroxy-group axial with respect to ring B, and confirm that the stereochemistry of ring A, is equivalent to that of the C-2 epimer of streptamine.[3] The absolute configuration of the tertiary carbon in the B/C ring juncture was shown to be *S*, and that of the methyl bearing carbon in ring C to be *R*, the same as C-5 of glucose, its suggested biosynthetic precursor.[4]

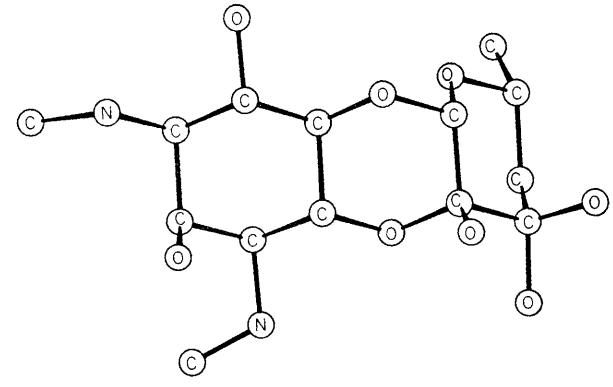


FIGURE. *Perspective view of the spectinomycin di-cation showing the correct absolute configuration.*

In addition it was found that spectinomycin dihydrobromide pentahydrate exists as a ketone hydrate, and not in the carbonyl form. This explains the observation that a carbonyl band at 1735 cm^{-1} is present only in mulls of rigorously dried samples of spectinomycin, and is absent in its crystalline hydrates.[5] Evidence that the ketone hydrate form also predominates in solution is given by the observation that no u.v. absorption[6] or anomalous rotatory dispersion[7] could be detected for the carbonyl chromophore in aqueous solutions of spectinomycin dihydrochloride.

The stability of this unusual ketone hydrate is due, at least in part, to the presence of the four electronegative oxygen atoms bonded to the B/C ring juncture. This stabilization by electron-withdrawing substituents is similar to that found in other carbonyl hydrates, such as chloral hydrate and ninhydrin.

Colourless crystals of spectinomycin dihydrobromide pentahydrate, $C_{14}H_{36}N_2O_{12}Br_2$, were obtained from water–acetone in orthorhombic space group $P2_12_12_1$, $a = 8{\cdot}214$, $b = 18{\cdot}501$, $c = 15{\cdot}020$ Å, $Z = 4$, $D_c = 1{\cdot}70$, D_m (flotation) $= 1{\cdot}69$ g cm^{-3}. Intensity data were collected on a Picker FACS 1 diffractometer using graphite monochromated Cu-K_α radiation to $2\theta = 125°$. The structure was solved by Patterson and Fourier techniques and refined by a full-matrix least-squares procedure, with anisotropic temperature factors for all of the non-hydrogen atoms. Hydrogen atoms were not included in the calculations and no absorption corrections were applied. The final R value was 0·075 for 2078 independent observed reflections. The absolute configuration was determined by the anomalous dispersion of the bromine atoms, using the procedure of Hamilton and Ibers.[8]

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