Crystal Structure of Streptolidine, a Guanidine-containing Amino-acid

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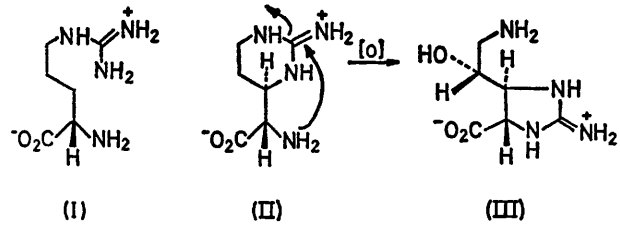
Summary The structure and chirality of the amino-acid streptolidine have been determined by *X*-ray techniques and the possible relationship of this amino acid to other guanidine-containing amino acids is discussed.

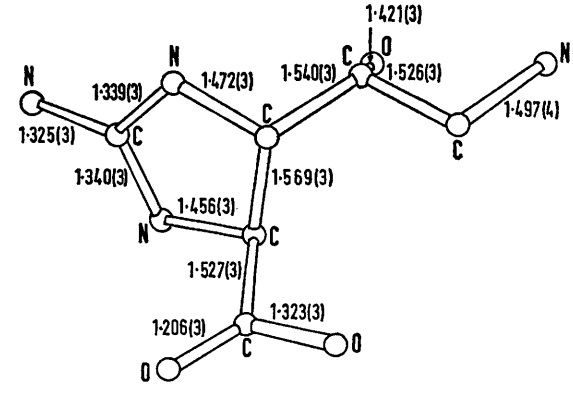
THE strongly basic amino-acid streptolidine,[1] isolated on hydrolysis of the antibiotics streptolin and streptothricin, is identical with geamine[2] from geomycin and roseonine[3] from roseothricin and racemomycin. This important guanidine amino-acid has been isolated from a considerable number of other closely related antibiotics of this general



(I) (II) (III)

family[4] and its structure has been the subject of considerable controversy. The generally accepted structure (III, stereochemistry defined only at the α and β centres) is that proposed by Carter[5] and we now report a complete *X*-ray crystallographic analysis of streptolidine dihydrochloride which confirms this assignment as well as establishing the complete chirality.

Streptolidine dihydrochloride ($C_6H_{12}N_4O_3,2HCl$) crystallised as orthorhombic prisms for which oscillation and equi-inclination Weissenberg photographs established the space group $P2_12_12_1$. The final cell parameters, after refinement on a Hilger and Watts linear diffractometer, were a = 11·43-



FIGURE

(3), b = 11·81(3), c = 8·41(2) Å. Intensity measurements were made using Mo-K_α *X*-radiation and 1580 observed

reflexions were counted. The chloride ions were located from a three-dimensional Patterson synthesis and a subsequent Fourier synthesis phased on these ions revealed the molecular structure shown in the Figure. Refinement was carried out by block-diagonal least-squares and in the final stages all nonhydrogen atoms were treated anisotropically and all hydrogen atoms (located from a difference map) were included but their positions not refined. The final conventional R factor was 0·03.

Structure-factor calculations, taking into account the anomalous scattering of the chloride anion, were made at several stages during the refinement and these consistently supported the absolute configuration [Figure and (III)] with a significance level[6] better than 0·005.

The primary amino-acid arginine (I) has not been observed in microbial peptide antibiotics, but capreomycidine[7] (II) and several related derivatives[8] have been isolated from their hydrolysates. Recently we established the structure and absolute stereochemistry of capreomycidine and viomycidine[9] and suggested that this group of amino-acids was derived from arginine *via* an $\alpha\beta$-dehydro-arginine intermediate.[10] This proposal has received some support from biosynthetic experiments[11] and we now suggest that streptolidine is also derived from arginine *via* an intermediate capreomycidine derivative as illustrated, although the precise sequence of events is not defined. In this respect, it is of interest that the relative and absolute stereochemistry at the α and β centres of streptolidine corresponds with those observed in capreomycidine.

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