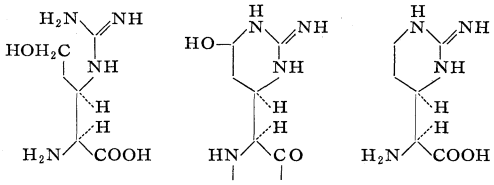
THE STRUCTURE OF DIHYDROVIOMYCIDINE

Sir:

This paper is concerning to revise the structure of dihydroviomycidine as structure I. In a previous communication[1], we gave the structure II for the guanido amino acid moiety of viomycin. The conclusion was derived from the facts that viomycin yielded viomycidine by acid hydrolysis whereas viomycin pretreated with sodium borohydride gave dihydroviomycidine instead of viomycidine.

The properties including analytical and spectral data of dihydroviomycidine were described in the previous report[1]. The structure was deduced as III[1] mainly by interpretation of the n.m.r. spectrum: that is, the presence of unequivalent methylene protons at δ 3.76 ppm could suggest a ring structure.



I II III

Recently BYCROFT *et al.*[2] synthesized capreomycidine* and epi-capreomycidine. They[3] pointed out that neither of them was different from dihydroviomycidine and suggested that dihydroviomycidine would be structure I from our experimental results.

Crystalline dihydroviomycidine monohydrochloride (m. p. 182°C dec.) was dried at 100°C under reduced pressure of 0.004 mm Hg. The constant weight was obtained in three hours. A loss of the hydrate water was 4.09 % (Calcd. for $C_5H_{14}N_4O_3 \cdot \frac{1}{2}H_2O \cdot HCl$; 3.82 %, former formula[1] $C_6H_{12}N_4O_2 \cdot \frac{1}{2}H_2O \cdot HCl$).

O-Acetylation of dihydroviomycidine was tried with acetyl chloride in a mixed solution of 6 N hydrochloric acid and acetic acid (1 : 1 in volume)[4]. Formation of the O-acetyl derivative was confirmed by the IR absorption at 1735 cm^{-1} (KBr) of the monohydrochloride. The n.m.r. spectrum of the dihydrochloride showed acetyl proton at δ 2.13 ppm (3H, singlet) and acetoxymethylene proton at δ 4.2~4.6 ppm (2H, multiplet). The latter proton correspond to methylene proton at δ 3.7~4.0 ppm (2H, multiplet) of dihydroviomycidine dihydrochloride and that at δ 3.76 ppm (2H, multiplet) of dihydroviomycidine monohydrochloride.

These results suggest that the structure of dihydroviomycidine must be revised to L-*threo*-β-guanido-δ-hydroxy-*n*-valine** (I).

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* A guanido amino acid obtained by acid hydrolysis of catalytic-hydrogenated viomycin was also named dihydroviomycidine by BYCROFT *et al.* Their dihydroviomycidine is identical with capreomycidine[3].

** The structure and absolute stereochemistry of viomycidine monohydrobromide were determined by X-ray crystal structure analysis[5]. The result confirmed the validity of the proposed structure[6]. The X-ray analysis has established the absolute configuration at α-carbon as L in the amino acid configurational notation by the use of BIJVOET's anomalous dispersion method. Recently, DYER *et al.*[7] reported the same structure for viomycidine by X-ray analysis.