THE STRUCTURE, STEREO-CHEMISTRY AND REACTIONS
OF THE GUANIDINE
MOIETY OF VIOMYCIN

Sir:
Recently we presented evidence to sug-
gest that the tuberculostatic antibiotic vio-
mycin contains the unit I. More recently
several papers have lent support to this
proposal and we present here the evidence
allowing a complete stereochemical assign-
ment, together with a summary of the
remarkable chemical reactivity of this unit.

Ion exchange chromatography (Dowex
50 W×8) of the acid hydrolysate (10 N
hydrochloric acid, reflux for 24 hours) of
viomycin afforded two basic amino acids,
viomycidine and a small amount of a com-
 pound which we have termed viocidic acid.

Viomycidine was characterised as its crystal-
lone monohydrochloride m. p. 200~204°C and
our spectral and chemical data were in
accord with the structure II proposed by
Buchi and Raleigh. Viomycidine and a small amount of a compound which we have termed viocidic acid. Viomycidine was characterised as its crystalline monohydrochloride m. p. 200~204°C and our spectral and chemical data were in accord with the structure II proposed by Buchi and Raleigh. Viomycidine and a small amount of a compound which we have termed viocidic acid. Viomycidine was characterised as its crystalline monohydrochloride m. p. 200~204°C and our spectral and chemical data were in accord with the structure II proposed by Buchi and Raleigh. Viomycidine and a small amount of a compound which we have termed viocidic acid. Viomycidine was characterised as its crystalline monohydrochloride m. p. 200~204°C and our spectral and chemical data were in accord with the structure II proposed by Buchi and Raleigh. Violociacid was characterised as its dipicrate m. p. 173~175°C. Found: C 35.2, H 2.7, N 22.8. C₄H₁₃N₅O₄·

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viomycidine but instead capreomycidine IV isolated as the free base m.p. 195°C (decomp.) \([\alpha]_D^{25} -22.7^\circ \) (c 0.17, in H2O) identical (i.r., n.m.r., t.l.c. and o.r.d.) with an authentic sample isolated from the acid hydrolysate of capreomycin7). We have in addition confirmed the gross structure of capreomycidine by total synthesis45 and the above correlation with viomycidine establishes the absolute chirality.

In a recent communication Maeda and Takita3) reported the isolation of a 'dihydroviomycidine' from the acid hydrolysate of the sodium borohydride reduction product of viomycin which they claimed to be epi-capreomycidine. Their spectral and chromatographic data for this compound were not in accord with those observed for our synthetic epi-capreomycidine4) and on the basis of their evidence we suggested the alternative formulation V. More recently they have presented further results corroborating this structure8).

The above observation together with the fact that viomycin gives a positive Sakaguchi reaction provide evidence that the unit I in solution is in equilibrium with the corresponding aldehyde form. This allows an assignment of the chirality of the guanidine carbinol centre in I since the molecule can be expected to adopt the most favourable configuration at this centre, i.e. the hydroxyl group in a pseudo-equatorial position.

Mild base hydrolysis of viomycin with 0.1 N NaOH at 100°C for 20 hours gave on ether extraction a good yield of 2-amino-pyrimidine m. p. 127~128°C completely identical with an authentic sample. Since viomycidine was not present in the total hydrolysate of the resultant peptides it followed that the 2-aminopyrimidine must have been dried from the guanidine moiety.

It is evident that methylviomycin, formed by heating viomycin with methanol, is an O-methyl derivative of the guanidine-carbinol system (Ia, chirality at the carbinol centre not defined). The extraordinary reactivity of I is paralleled in the properties of the neurotoxin, tetrodotoxin9) VI, the only other known naturally occurring compound possessing this unit.

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References