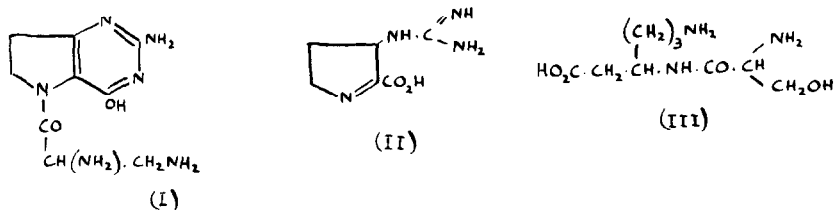


VIOMYCIN

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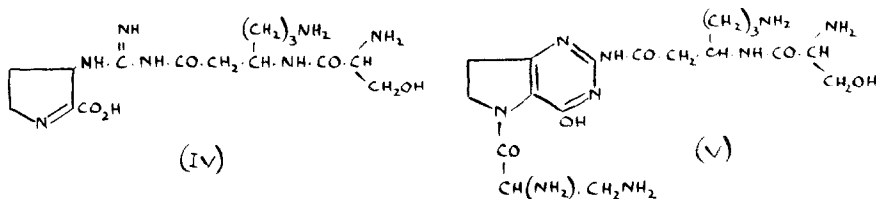
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In a previous note,¹ we presented evidence to suggest that peptide A, a hydrolytic fragment from the antibiotic viomycin should be formulated as (I). Acid hydrolysis of peptide A causes fission to 1,2-diaminopropionic acid and viomycinidine² (II).



The remaining units formed by hydrolysis of viomycin are serine, β -lysine and urea (ratio 2:1:1) and carbon dioxide. Further partial hydrolyses of the antibiotic have given other peptides. Thus peptide B, obtained from acid as well as baryta hydrolyses of the antibiotic gave equimolecular amounts of β -lysine and serine on further hydrolysis, and moreover the bis(2,4-dinitrophenyl) (DNP) derivative of peptide B gave mono- ϵ -DNP- β -lysine and N-DNP-serine on hydrolysis, and hence peptide B is formulated as (III).

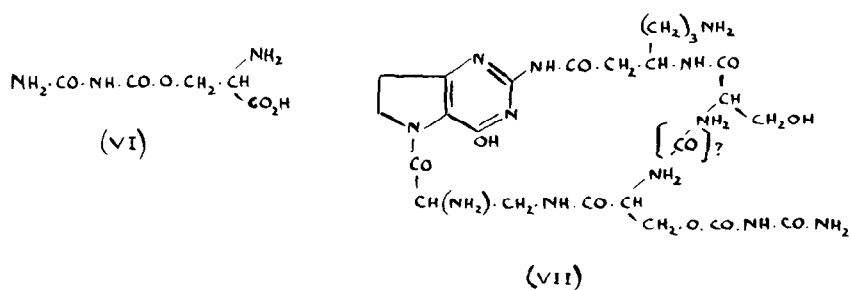
Peptides A and B can be united structurally by consideration of two other peptides, C and D, isolated by hydrolysis of viomycin with $N/10$ lithium hydroxide. Peptide C was obtained only in very small amount but gave equimolecular quantities of viomycin and β -lysine on further hydrolysis. Peptide D, $C_{15}H_{27}N_7O_5$, formed a crystalline tripicrate, and gave approximately (1:1:1) quantities of serine, viomycin and β -lysine on further hydrolysis. The DNP derivative of peptide D gave mono- ϵ -DNP- β -lysine and N-DNP-serine as identifiable hydrolysis products and consequently the probable structure for this tripeptide is (IV), seryl- β -lysyl-viomycin. This structure, when combined with that of peptide A, leads to the partial structure (V) for viomycin, lacking the urea fragment and another serine unit.



The urea and the second serine grouping are contained in the products derived from the permanganate oxidation of viomycin. Using 8 mole. of permanganate an oily product, chromatographically homogeneous, was isolated which gave only equimolecular quantities of L-serine and urea on hydrolysis with 2N hydrochloric acid and consequently is believed to be L-serine allophanate (VI). Another fraction from the oxidation also gave serine and urea, together with 1,2-diaminopropionic acid, all in equimolecular quantities, on hydrolysis.

Yet another fraction gave the above products together with viomycinide as the recognisable hydrolysis products.

Taking into account the observation that hydrolysis of the DNP derivative of viomycin gave, among other products, mono- α -DNP-diaminopropionic acid and mono- ϵ -DNP- β -lysine, it appears that it is the β -amino groups of both 1,2-diaminopropionic acid and β -lysine which are involved in peptide linkages with the serine units. For comparison purposes the α - and β -mono-DNP derivatives of 1,2-diaminopropionic acid and the β - and ϵ -mono-DNP derivatives of β -lysine have been synthesised by unambiguous methods^{cf.3} and direct comparison with the products obtained from degradations of the DNP derivative of viomycin have been carried out. On the above evidence we can expand the partial structure of the antibiotic to (VII), further support being obtained by the isolation, from mild alkaline hydrolyses of viomycin of peptide E which has been shown to contain serine, 1,2-diaminopropionic acid, β -lysine and viomycinide in the ratio of 2:1:1:1 (i.e. lacking the urea grouping.)



It is believed that neither of the serine amino groups are free in the antibiotic itself and it is possible that they might be linked through a carbonyl group but evidence on this point is still being sought.

REFERENCES

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3. A. Kjaer and P. O. Larsen, Acta Chem. Scand., 15, 750 (1961).