

THE REVISED STRUCTURE OF VISCOSIN, A PEPTIDE ANTIBIOTIC¹

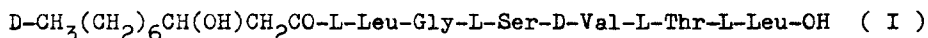
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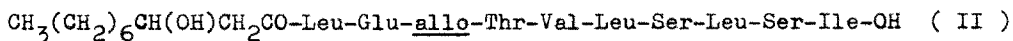
Viscosin, an acidic antibiotic active to tubercle bacillus and virus, was isolated as colorless needles, m.p. 270 - 273°, $[\alpha]_D^{29}$ -168.3 (c 1, EtOH), from Pseudomonas viscosa² and the structure (I) had first been proposed by Ohno et al³.



We have previously reported chemical synthesis of the acyl hexapeptide (I) and found that (I) was not identical with viscosin⁴. The present communication describes the corrected structure (IV) for the antibiotic.

Quantitative amino acid analysis of viscosin revealed the presence of 1 mole each of glutamic acid, allothreonine, valine and isoleucine, 2 moles of serine, and 3 moles of leucine. Saponification of viscosin with a dilute solution of sodium hydroxide in aqueous ethanol followed by acidification yielded colorless crystals, m.p. 170 - 175°, $[\alpha]_D^{20}$ -10.0 (c 1, EtOH), Anal. Found: C, 55.92; H, 8.39; N, 10.83, Calcd. for $\text{C}_{54}\text{H}_{97}\text{N}_9\text{O}_{17}\text{H}_2\text{O}$: C, 55.80; H, 8.59; N, 10.83; it has the same amino acid composition as that of viscosin, however, unlike viscosin, it does not exhibit ester or lactone carbonyl absorption band (1739 cm^{-1}) in its IR spectrum, indicating that the lactone linkage in viscosin was cleaved to form an open chain N-acyl nonapeptide, which was designated as viscosic acid. Titration in 90% methanol with sodium methoxide indicated that viscosin was monobasic and viscosic acid dibasic acid. Permethylation of viscosic acid by methyl iodide and silver oxide in dimethylformamide⁵ gave a product of sufficient volatility for mass spectral analysis⁶. The mass spectrum of permethylated viscosic acid gave a molecular ion at m/e

1353 and peaks due to the loss of methanols at M-32, M-64 and M-96, confirming the expected molecular weight of nona-N-methylviscotic acid dimethyl ester tetra-O-methyl ether. Fragmentations took place principally at the peptide bonds, with accompanying peaks due to the loss of methanols from the corresponding fragment ions (Table I); the resulting peaks determined the entire amino acid sequence of viscotic acid. Both hydrazinolysis⁷ and digestion with carboxypeptidase A⁸ revealed that isoleucine was located in the C terminal of viscotic acid. Thus the above results led unequivocally to the structure (II) for viscotic acid.



Permethylated viscotin gave a mass spectrum very similar to that of the corresponding derivative of viscotic acid, showing that viscotin had the same constituents and sequence as those of viscotic acid. Furthermore the mass spectrum of the perdeuteriomethylated viscotin methyl ester, which was derived

Table I Fragmentation of permethylviscotic acid (i) and perdeuteriomethylviscotin methyl ester (ii)*

(i) Permethylviscotic acid					
Mass units	157	129	113	127	
Dec(OMe)-MeLeu+MeGlu(OMe)+Me <u>allo</u> -Thr(OMe)			-MeVal	-MeLeu	
m/e	280(65.3)	534(2.1)	647(2.2)	774(1.2)	
	312(100)	566(5.0)	679(5.0)	806(2.5)	
	469(44.6)	598(2.5)	711(0.8)	838(1.2)	
	115	127	115	158	
	MeSer(OMe)	-MeLeu+MeSer(OMe)	-MeIle-OMe		
	857(0.3)	984(0.5)	1099(0.2)	1257(0.1)	[M-96]
	889(0.6)	1016(0.9)	1131(0.2)	1289(0.2)	[M-64]
	921(0.5)	1048(0.5)	1163(0.2)	1321(0.2)	[M-32]
	953(0.3)			1353(0.1)	[M]
(ii) Perdeuteriomethylviscotin methyl ester (partial mass spectrum)					
Mass units	160	135	116	130	
Dec(OCD ₃)-CD ₃ Leu+CD ₃ Glu(OMe)+CD ₃ <u>allo</u> -Thr(OCD ₃)			-CD ₃ Val	-CD ₃ Leu	
m/e	283(28.1)	543(2.4)	659(2.0)	789(0.7)	
	318(100)	578(6.0)	694(3.9)	824(1.7)	
	443(7.8)				
	478(28.8)				

* Relative abundances are shown in parentheses

acid, and the structure (IV) to viscosin. The structure (IV) indicates that viscosin is an unusual cyclodepsipeptide containing a remarkable number of D-amino acids, and a β -hydroxy fatty acid moiety which does not participate in the formation of the lactone ring.

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References and Notes

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