Tetrahedron Letters No.47, pp. 5837-5840, 1966. Pergamon Press Ltd.
Printed in Great Britain.

PERIMYCIN: CHEMISTRY OF PEROSAMINE (1)

Chi-Hang Lee and Carl P. Schaffner

Institute of Microbiology

Rutgers, The State University

New Brunswick, New Jersey

(Received 6 September 1966)

Perimycin (2, 3) (syn.: Fungimycin), an antifungal substance isolated from cultures of Streptomyces coelicolor var. aminophilus, belongs to the aromatic subgroup of heptaenic antibiotics (4) and contains an aminosugar, perosamine, shown (2) to be different from mycosamine(5). Perosamine was obtained as its amorphous hydrochloride salt by hydrolysis of perimycin with 2 NHCl--$C_6H_{14}O_4NCl$, $[\alpha]_D^{23} = -20° \rightarrow -13°$ (c 1.3, H_2O), and exhibited a yellow coloration with ninhydrin spray reagent on paper chromatogram (6). In solution the reaction between perosamine and ninhydrin gave rise to a chromophore having λ max at 413 mμ, but with no absorption at 570 mμ as has glucosamine. Perosamine gave a positive Elson-Morgan reaction, even with omission of acetylacetone, and its positive reaction to the Waldron chromatographic spray reagent (7) suggested a 6-deoxy sugar.

N-acetyl perosamine, $C_8H_{15}O_5N$, mp 178-180°, $[\alpha]_D^{23} = +34°$

(c 2.0, H_2O) was prepared from perosamine hydrochloride by the Roseman-Ludowieg method (8). Positive to the Pan-Dutcher spray reagent (9) and thus showing the nitrogen function in perosamine as a primary amine, it consumed two moles of periodate and gave rise to allothreonine after this sequential treatment: periodate oxidation, bromine-water oxidation, and acid hydrolysis. Identification of the amino acid by paper chromatography placed the amino group on C-4 and indicated the relative stereochemistry at C-4 and C-5.

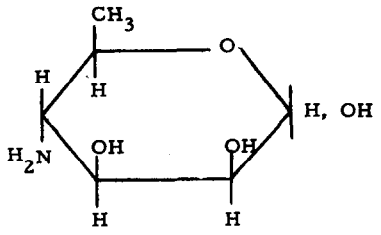
Methanolysis of the antibiotic produced methyl perosaminide, $C_7H_{15}O_4N$, mp 150-151°, $[\alpha]_D^{23}$ = +67° (c 2.0, H_2O) and +80° (c 1.0, MeOH), which consumed two moles of periodate to yield the known D'-methoxy-D-methyl diglycolic aldehyde (10), placing perosamine in the D-series of sugars. Nitrous acid deamination of methyl perosaminide and subsequent hydrolysis led to identification of 6-deoxy-mannose (the acetylated diethyldithioacetal derivative (11) of which had a positive rotation): this identification displayed the anti-relationship between perosamine's C-2 and C-5 substituents -- viewed in the Fischer projection -- since it is unlikely that the C-2 substituent was involved in the deamination of the C-4 amino group.

With configuration for C-2, C-4, and C-5 assigned, only two possibilities remained for the perosamine structure: 4-amino-4,6-dideoxy-D-mannose, or 4-amino-4,6-dideoxy-D-altrose.

Considering the molecular rotation of methyl perosaminide (+11,800°) and the rotations of the corresponding 6-deoxy-α-D-mannoside (+11,100°) and -altroside (+21,000°) derivatives (12),

we concluded that perosamine possesses the manno configuration (I).

Detailed NMR analyses to support the suggested structure will receive subsequent publication.



(I)

Acknowledgments: This study in part was supported by a grant from the National Institute of Allergy and Infectious Diseases (Public Health Service grant AI-02095) and the authors wish to thank Benjamin Schwartz of the Warner-Lambert Research Institute for the generous sample of perimycin.

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