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A ^{13}C-NMR STUDY OF THE CARBOHYDRATE PORTION OF RISTOCETIN A

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Summary A ^{13}C NMR study of the antibiotic ristocetin A establishes two changes which must be made to the structures hitherto accepted for the carbohydrate portion of the antibiotic.

Ristocetin A (1) is a glycopeptide antibiotic (identical to ristomycin A[1]) for which a ψ-aglycone structure has recently been determined.[2] The structure of the carbohydrate moiety has been elucidated by Hungarian and Russian groups,[3] the only points of doubt being the ring size of an arabinose moiety (for which conflicting evidence has been provided[3a, b]), and the anomeric configuration of a monosaccharide unit, mannose. These points have been clarified by the application of ^{13}C NMR. Our conclusions are now presented, and agree fully with those independently reached by Sztaricskai et al.[4]

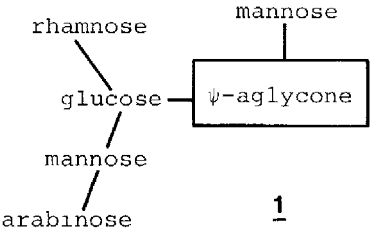
Ristocetin B is identical to ristocetin A (1) except that it lacks a D-arabinosyl-(1→2)-O-α-D-mannopyranosyl residue (which is attached to C-2 of glucose in 1). It is therefore possible to identify the resonances originating from the anomeric carbons of arabinose and the mannose to which it is attached, and of glucose, by comparison of the ^{13}C spectra of ristocetins A and B. Spectra were obtained at 25.2 MHz at 80°C in D_2O on a Varian XL-100 spectrometer, and collected with 8K data points. Using model compounds, and the slower longitudinal relaxation rate of the signal found at 110.3 ppm in ristocetin A and absent in ristocetin B, this signal may be assigned to the arabinose anomeric carbon. This remarkably low field signal can only arise from an α-D-arabinofuranoside, as can be seen by comparison of data for methyl α- and β-D-arabino-furanoside and -pyranoside (Table). In addition, two high-field sugar resonances at 85.3 and 82.1 ppm cannot be assigned to any other sugar residue by chemical shift arguments, and confirm the presence of an α-D-arabinofuranoside.

Chemical shifts (ppm downfield from TMS) found for methyl arabinosides in D_2O at 35°C[5]

Carbon	Methyl α-D-arabinofuranoside	Methyl β-D-arabinofuranoside	Methyl α-D-arabinopyranoside	Methyl β-D-arabinopyranoside
1	109.3	103.2	105.1	101.0
2	81.9	77.5	71.8	69.4
3	77.5	75.7	73.4	69.9
4	84.9	83.1	69.4	70.0
5	62.4	64.2	67.3	63.8

The other anomeric signals may be assigned by off-resonance studies, which show that the anomeric carbon of the monosaccharide mannose unit resonates at 98.2 ppm. This chemical shift may be compared with 101.5 ppm found for α-[p-nitrophenyl]-D-mannopyranoside,[6] and an estimated 103.7 ppm for the β-form, indicating the probability of an α-linkage The α-linkage was confirmed by a $^{1}J_{C1-H}$ of 173 ±2 Hz in agreement with a calculated value of 173 Hz for aryl α-linkages, and quite different from the value of 163 Hz for aryl β-linkages.[7]

Thus, the corrected portion of the structure of ristocetin A is as shown in 2. Complete details of the assignment will be presented elsewhere.



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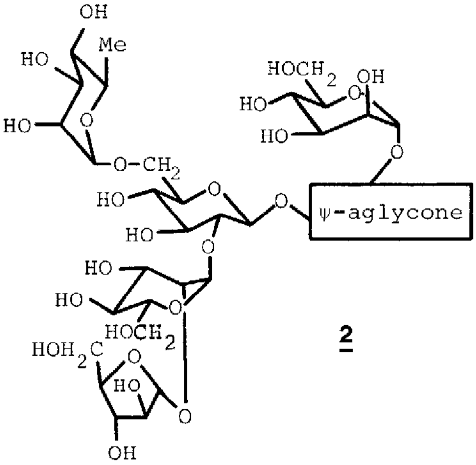

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