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SYNTHESIS OF ANOMERIC METHYL 6-O-(L-MYCAROSYL)-β-D-GLUCOSAMINIDES

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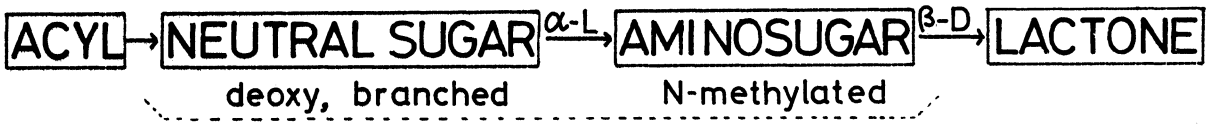
Anomeric isomers of methyl 2-amino-2-deoxy-6-O-(2,6-dideoxy-3-C-methyl-L-ribo-hexopyranosyl)-β-D-glucopyranoside (VI) were synthesized by the condensation of methyl 2-deoxy-2-(2,4-dinitroanilino)-β-D-glucopyranoside with 3,4-O-carbonyl-2,6-dideoxy-L-ribo-hexopyranosyl chloride (III), and subsequent removal of blocking groups.

In the course of chemical studies of the macrolide antibiotics, anomeric isomers of methyl 6-O-(L-mycarosyl)-β-D-glucosaminide (VI) were synthesized as a model glycoside[1]. This synthesis is the first example of the synthesis of the disaccharide in which a branched-chain, neutral sugar is attached glycosidically to a basic amino-sugar; this type of glycoside has frequently been found in the form of N-methyl derivative as the constituent of some macrolide antibiotics[2].



Methyl 3,4-O-carbonyl-α-L-mycaroside (Ia)[3] was hydrolyzed with dil. hydrochloric acid in dioxane and was subsequently treated with p-nitrobenzoyl chloride in pyridine to give 3,4-O-carbonyl-1-O-p-nitrobenzoyl-β-L-mycarose (II) [$\delta^{TMS}_{CDCl_3}$ (ppm): 6.30 (1H, quartet; anomeric H, $J_{1,2e}$= 4.0 Hz, $J_{1,2a}$= 8.0 Hz)]. II was treated with hydrogen chloride in dichloromethane at 10°C for 30 min to generate 3,4-O-carbonyl-L-mycarosyl chloride (III), which was methanolyzed in the presence of Ag_2O to afford an anomeric mixture of methyl 3,4-O-carbonyl-L-mycarosides (α : β = 2 : 3).

The intact III was immediately subjected to the condensation reaction with methyl N-2,4-dinitrophenyl-β-D-glucosaminide[4] (1.3 molar equiv.) in nitromethane in the presence of A: $Hg(CN)_2$ or B: 2,6-lutidine. The main product (A: 19%, B: 14%), obtained by chromatographic separation [$\delta^{TMS}_{CDCl_3}$ (ppm): 4.96 (1H, quasitriplet; 1'-H, $J_{1,2e}$= $J_{1,2a}$= 5.5 Hz)], was crystallized as the fully benzoylated derivative (IVa). The shift toward the lower field of the methine protons in glucosamine moiety in PMR spectrum of IVa showed that mycarosyl group was attached to the oxygen on the C-6 of glucosamine. IVa was treated with dil. methanolic sodium methoxide furnished N-dinitrophenyl mycaroside (Va), which was subsequently treated with Dowex 1X2 (OH type) in moist acetone to give

a ninhydrin-positive free base (VIa); the value of optical rotation of VIa as well as the PMR spectrum of VIa indicated the α-configuration of mycarosyl moiety in the main product.

On the other hand, the minor product (A: 8.1%, B: 7.8%) [$\delta^{TMS}_{CDCl_3}$ (ppm): 4.88 (1H, quartet; 1'-H, $J_{1,2e}$= 4.5 Hz, $J_{1,2a}$= 10.5 Hz)] was converted into crystalline O-benzoyl derivative (IVb): the location of glycoside linkage was confirmed by means of PMR spectrum of IVb. IVb was subjected to the analogous sequence of reactions as mentioned above to result β-anomer of the titled glycoside (VIb).

Thus, the ratios of formation between the both anomers were (A) 7 : 3 and (B) 5 : 3.

The details of this investigation will be published in due course.

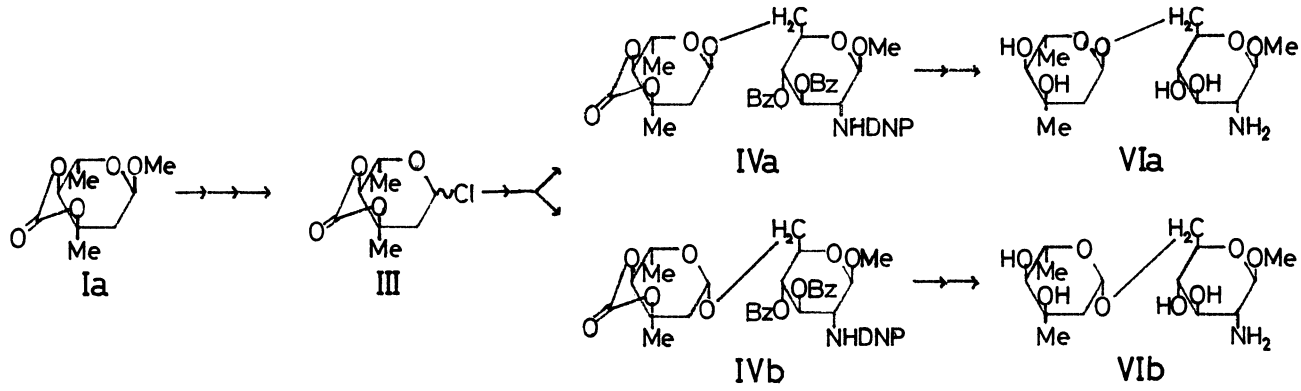


TABLE PHYSICAL DATA

Compounds	mp (°C)	$[\alpha]_D^{25}$ (%, solvent)
II	153—154	7.6° (2.6, chloroform)
IVa	123—124	-13.5° (0.9, chloroform)
IVb	118—120	16.4° (0.9, chloroform)
Va	116—118	-13.4° (1.3, chloroform)
Vb	114—116	-3.8° (0.7, chloroform)
VIa	hygroscopic	-91.0° (1.1, water)
VIb	hygroscopic	-19.0° (0.4, water)

References

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