Synthesis of 2,4-Diacetamido-2,4,6-trideoxy-D-glucose and its Identification with the Diacetamido-sugar of *Bacillus licheniformis*

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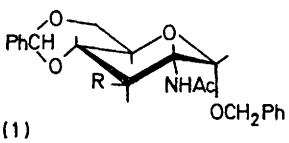
Summary Benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (**1a**) obtained from 2-acetamido-2-deoxy-D-glucose was converted into benzyl 2-acetamido-3-*O*-benzyl-2,6-dideoxy-α-D-glucopyranoside (**2e**); double inversion of configuration at C-4 in (**2e**) with introduction of an amino-group *via* the corresponding azide followed by *N*-acetylation and removal of the benzyl groups gave 2,4-diacetamido-2,4,6-trideoxy-D-glucose (**4**), found to be identical with the diacetamido-sugar of *B. licheniformis*.

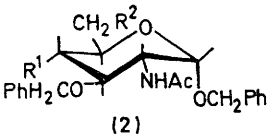
IN 1959 Sharon and Jeanloz[1] reported the isolation from *Bacillus licheniformis*† of the first natural 2,4-diaminohexose. This compound was obtained as the crystalline 4-acetamido-2-amino-2,4,6-trideoxyhexose (*N*-acetylbacillosamine) from an acid hydrolysate of the polysaccharide, and was converted into the crystalline 2,4-diacetamido-2,4,6-trideoxyhexose. Subsequently, 2,4-diaminohexoses were found as constituents of a uridine diphosphate nucleotide synthesized by extracts of *Diplococcus pneumoniae*,[2] a C-substance of *D. pneumoniae*[3] and the antibiotic Kasugomycin.[4]

We have shown[5] that the diacetamido-sugar from *B. licheniformis* possesses the structure of 2,4-diacetamido-2,4,6-trideoxy-D-glucose. Here we report the synthesis of this compound from 2-acetamido-2-deoxy-D-glucose.

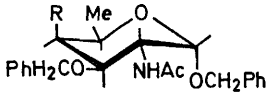
2-Acetamido-2-deoxy-D-glucose was converted into benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside (**1a**) by a modification of the procedure described in the literature.[6] This compound was benzylated with benzyl chloride to yield the 3-*O*-benzyl derivative (**1b**),



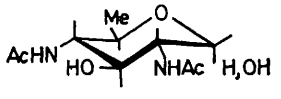
(1)
a; R = OH
b; R = OCH_2Ph



(2)
a; $R^1 = R^2 = OH$
b; $R^1 = OH, R^2 = OTs$
c; $R^1 = OAc, R^2 = OTs$
d; $R^1 = OH, R^2 = I$
e; $R^1 = OH, R^2 = H$
f; $R^1 = OMs, R^2 = H$
g; $R^1 = N_3, R^2 = H$
h; $R^1 = NHAc, R^2 = H$



(3)
a; R = OCOPh
b; R = OH
c; R = OMs



(4)

m.p. 266°, $[\alpha]_D^{24}$ + 132°, in 88% yield.‡ Mild acidic treatment of (**1b**) afforded 78% of benzyl 2-acetamido-3-*O*-

† Formerly classified as *Bacillus subtilis* ATCC 9945.

‡ All compounds reported gave satisfactory elemental analysis. Optical rotation measurements of all compounds were carried out in chloroform solution (*c* 1) except in the case of the final product, compound (**4**), the rotation of which was measured in ethanol–water 1 : 1, at equilibrium.

benzyl-2-deoxy-α-D-glucopyranoside (**2a**), m.p. 176°, $[\alpha]_D^{27}$ + 157°. Selective tosylation of (**2a**) gave 77% of benzyl 2-acetamido-3-*O*-benzyl-2-deoxy-6-*O*-*p*-tolylsulphonyl-α-D-glucopyranoside (**2b**), as a syrup which crystallized after prolonged standing, m.p. 130—131°, $[\alpha]_D^{25}$ + 120°, and which was characterized by its 4-*O*-acetyl derivative (**2c**) m.p. 152—152·5°, $[\alpha]_D^{27}$ + 108°. Treatment of (**2b**) with potassium iodide in *NN*-dimethylformamide gave 80% of benzyl 2-acetamido-3-*O*-benzyl-2,6-dideoxy-6-iodo-α-D-glucopyranoside (**2d**), m.p. 174°, $[\alpha]_D^{25}$ + 97°, which was converted into benzyl 2-acetamido-3-*O*-benzyl-2,6-dideoxy-α-D-glucopyranoside (**2e**), m.p. 161—162°, $[\alpha]_D^{24}$ + 118° by treatment either with Raney nickel or by hydrogen (atmospheric pressure) in the presence of Pd/C catalyst (10%) and triethylamine, in 80% yield. Further evidence for the structure of (**2e**) was obtained by its conversion into 2-acetamido-2,6-dideoxy-D-glucose (*N*-acetyl-D-quinovosamine) and the corresponding D-quinovosamine, which had physical constants identical to those reported.[7,8]

Treatment of (**2e**) with methanesulphonyl chloride in pyridine gave 76% of the crystalline benzyl 2-acetamido-3-*O*-benzyl-2,6-dideoxy-4-*O*-methanesulphonyl-α-D-glucopyranoside (**2f**), m.p. 208—209° (decomp.), $[\alpha]_D^{22}$ + 124°. Compound (**2f**) was treated with an excess of sodium benzoate in *NN*-dimethylformamide to give benzyl 2-acetamido-4-*O*-benzoyl-3-*O*-benzyl-2,6-dideoxy-α-D-galactopyranoside (**3a**), m.p. 147—148°, $[\alpha]_D^{23}$ + 195°, in 56% yield, which could be converted into the known 2-amino-2,6-dideoxy-D-galactose (D-fucosamine).[9] Saponification of (**3a**) afforded 83% of benzyl 2-acetamido-3-*O*-benzyl-2,6-dideoxy-α-D-galactopyranoside (**3b**), m.p. 180—181°, $[\alpha]_D^{25}$ + 172°.

Compound (**3b**) was treated with methanesulphonyl chloride in pyridine to give 72% of benzyl 2-acetamido-3-*O*-benzyl-2,6-dideoxy-4-*O*-methanesulphonyl-α-D-galactopyranoside (**3c**), m.p. 198—199° (decomp.), $[\alpha]_D^{23}$ + 163°. Displacement of the methanesulphonyloxy group in (**3c**) with sodium azide in hexamethylphosphortriamide at 135° gave the expected benzyl 2-acetamido-4-azido-2,4,6-trideoxy-α-D-glucopyranoside (**2g**), m.p. 170—171°, $[\alpha]_D^{27}$ + 128°, in 60% yield. Selective reduction of the azide function in (**2g**) with hydrogen in the presence of Pd/C catalyst (10%) at atmospheric pressure, followed by acetylation, gave 46% of benzyl 2,4-diacetamido-3-*O*-benzyl-2,4,6-trideoxy-α-D-glucopyranoside (**2h**), m.p. 244—245°, $[\alpha]_D^{22}$ + 106°. Pressure hydrogenation (70 lb/in²) of (**2g**) in the presence of the same catalyst, gave the desired 2,4-diacetamido-2,4,6-trideoxy-D-glucose (**4**) in 50% yield. Compound (**4**) was found to be identical with the 2,4-diacetamido-sugar of *B. licheniformis* (on the basis of i.r., m.p., chromatography, and *X*-ray diffraction data).

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