

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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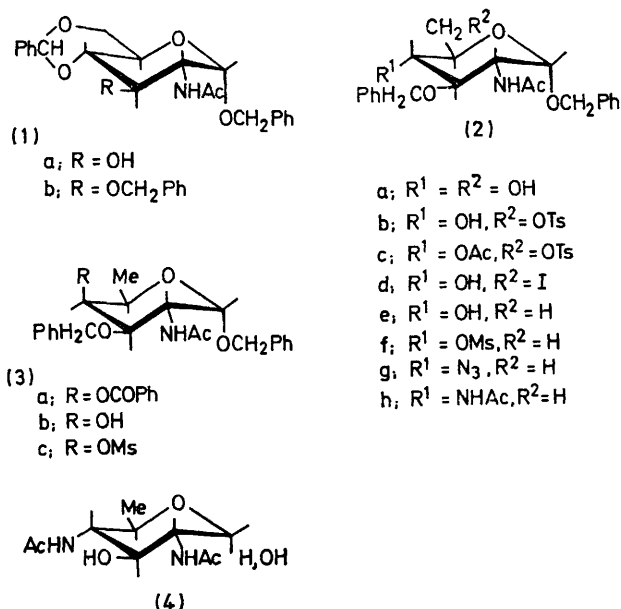
Summary Benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy- α -D-glucopyranoside (**1a**) obtained from 2-acetamido-2-deoxy-D-glucose was converted into benzyl 2-acetamido-3-*O*-benzyl-2,6-dideoxy- α -D-glucopyranoside (**2e**); double inversion of configuration at C-4 in (**2e**) with introduction of an 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 Jeanloz¹ 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*-acetyl bacillosamine) 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 shown⁵ 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**),



m.p. 266°, $[\alpha]_D^{24} + 132^\circ$, 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°, $[\alpha]_D^{27} + 157^\circ$. 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°, $[\alpha]_D^{25} + 120^\circ$, and which was characterized by its 4-O-acetyl derivative (**2c**) m.p. 152—152.5°, $[\alpha]_D^{27} + 108^\circ$. 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°, $[\alpha]_D^{25} + 97^\circ$, which was converted into benzyl 2-acetamido-3-O-benzyl-2,6-dideoxy- α -D-glucopyranoside (**2e**), m.p. 161—162°, $[\alpha]_D^{24} + 118^\circ$ 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.), $[\alpha]_D^{22} + 124^\circ$. 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°, $[\alpha]_D^{23} + 195^\circ$, 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°, $[\alpha]_D^{25} + 172^\circ$.

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.), $[\alpha]_D^{23} + 163^\circ$. 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°, $[\alpha]_D^{27} + 128^\circ$, 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°, $[\alpha]_D^{22} + 106^\circ$. 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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