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Note

Synthesis of 3,4-diacetamido-3,4,6-trideoxy-L-glucose*

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We have recently shown[1] that treatment of benzyl 2,3-anhydro-6-deoxy-4-*O*-methylsulfonyl-β-L-gulopyranoside (**1**) with sodium azide in *N*,*N*-dimethylformamide afforded two isomeric products: the syrupy benzyl 2,4-diazido-2,4,6-trideoxy-β-L-altropyranoside and the crystalline benzyl 2,4-diazido-2,4,6-trideoxy-β-L-idopyranoside. The 2,4-diazido-β-L-*altro* derivative was a product of the *trans*-diaxial opening[2] of the 2,3-anhydro ring by the azide ion accompanied by the nucleophilic displacement of the 4-methylsulfonyloxy group by the same ion. The formation of the L-*ido* isomer was assumed to proceed *via* an epoxide ring migration[1]. Opening of the 2,3-epoxide by attack of the azide ion at C-3 accompanied by reaction of the same ion at C-4, was expected to yield another product, namely, benzyl 3,4-diazido-3,4,6-trideoxy-β-L-glucopyranoside (**2**). We now report the isolation and characterization of this diazido derivative and its conversion into 3,4-diacetamido-3,4,6-trideoxy-L-glucose (**6**), an amino sugar which hitherto had not been described.

In an attempt to purify the just described, crude benzyl β-L-*altro* derivative, the syrup was treated with 3,5-dinitrobenzoyl chloride to give a mixture from which the pure, crystalline benzyl 3,4-diazido-3,4,6-trideoxy-2-*O*-(3,5-dinitrobenzoyl)-β-L-glucopyranoside (**3**) was obtained. Analysis of the n.m.r. spectrum of **3** (Fig. 1) showed all the coupling constants to be high (8–10 Hz), in agreement with a β-L-*gluco* configuration in the $^1C_4$ conformation. The positions of the two azide residues was also established by n.m.r. spectroscopy as described for the other diazido derivatives[1]. The mother liquor contained a syrupy product which gave the known 3-*O*-acetyl-2,4-diacetamido-2,4,6-trideoxy-β-L-altropyranoside by deacylation followed by reduction and acetylation. Treatment of **3** with sodium methoxide gave the crystalline benzyl 3,4-diazido-3,4,6-trideoxy-β-L-glucopyranoside (**2**). Reduction of **2** with lithium aluminium hydride followed by *N*-acetylation gave the crystalline benzyl 3,4-diacetamido-3,4,6-trideoxy-β-L-glucopyranoside (**4**), which was further characterized by its 2-*O*-acetyl derivative (**5**). In contrast to the other β-L compounds synthesized in this series[1], compounds **2**, **3**, and **4** had negative optical rotation values.

*Dedicated to the memory of Professor W. Z. Hassid.

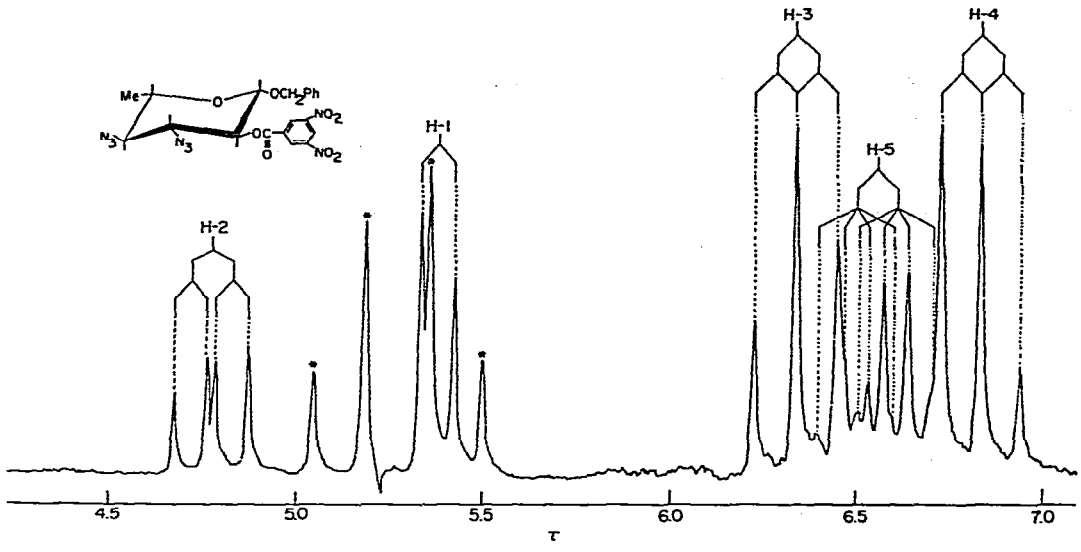
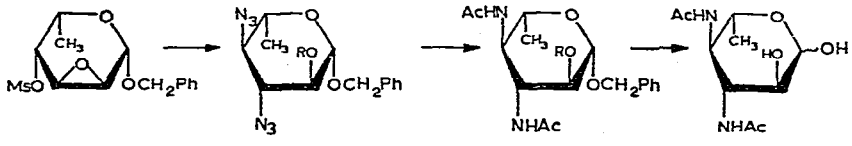


Fig. 1. Partial n.m.r. spectrum of benzyl 3,4-diazido-3,4,6-trideoxy-2-*O*-(3,5-dinitrobenzoyl)-*β*-L-glucopyranoside (3) at 90 MHz in chloroform-*d*; (*) indicates the AB pair of doublets of the benzylic CH_2.

Reversal of Hudson's rotation rules has been observed by Guberman and Horton[3] in the case of the anomeric 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-(2,4-dinitroanilino)-D-glucopyranoses. The rotatory anomaly was attributed to the nitro group at the *ortho* position of the aryl moiety. It may be assumed that the nitro groups in **3** affect the rotation of this compound in a similar manner, but we have no explanation for the anomalous rotatory behavior of compounds **2** and **4***.



1 **2** R = H; **3** R = 3,5 — $(NO_2)_2$ — C_6H_3CO **4** R = H; **5** R = Ac **6**

Hydrogenolysis of **4** gave 3,4-diacetamido-3,4,6-trideoxy-L-glucose (**6**), which was purified by paper chromatography to give a crystalline product. Compound **6** was reduced by sodium borohydride to give the corresponding diacetamidotrideoxyhexitol which consumed one molar proportion of periodate.

*After his work was submitted for publication, an article describing the synthesis of methyl 3,4-diamino-3,4,6-trideoxy-2-*O*-methyl-α-L-glucopyranoside dihydrochloride and methyl 3,4-diacetamido-3,4,6-trideoxy-2-*O*-methyl-α-L-glucopyranoside has reached us[4]. The two derivatives were reported to have strong levorotations.

EXPERIMENTAL

Melting points were measured in capillary tubes on a Büchi apparatus and are not corrected. Evaporations were conducted *in vacuo*. Optical rotations were determined with a Perkin–Elmer 141 polarimeter. N.m.r. spectra were recorded with a Bruker 90-MHz spectrometer. The i.r. spectra were recorded with a Perkin–Elmer Infracord spectrometer. Columns were prepared with silica gel (E. Merck, No. 7734). Paper chromatography was performed with Whatman No. 1 paper and the spots were detected with silver nitrate[5]. Periodate oxidation studies were carried out by the spectrophotometric method[6] and the u.v. absorption was measured with a Zeiss spectrophotometer at 224 nm.

*Benzyl 3,4-diazido-3,4,6-trideoxy-2-*O*-(3,5-dinitrobenzoyl)-β-*L*-glucopyranoside* (**3**). — Benzyl 2,3-anhydro-6-deoxy-4-*O*-methylsulfonyl-β-L-gulopyranoside[1] (**1**, 1.74 g) was treated with sodium azide (2.9 g) in *N,N*-dimethylformamide (100 ml) as previously described[1] to give a mixture of a crude syrup (0.64 g, 40%) and a crystalline product (0.34 g, 21%). The crude syrup was dissolved in pyridine (5 ml), and 3,5-dinitrobenzoyl chloride (0.8 g) was added. This mixture was stirred overnight at room temperature, extracted with chloroform, and the extract washed with water. Evaporation of the chloroform gave a solid that was dissolved in benzene (5 ml), and fractionated on a silica gel column (25 g). Elution with benzene gave a crystalline residue that was recrystallized from methanol (yield 0.34 g, 13%, based on **1**), m.p. 119–120°; $[\alpha]_D^{22}$ −54° (*c* 1.0, chloroform); n.m.r. data (chloroform-*d*): see Fig. 1; in addition, τ 0.62–0.93 (3 H, multiplet, dinitrobenzoyl), 2.82 (5 H, singlet, benzylic phenyl) and 8.51 (3 H, doublet, CH_3–C-5).

Anal. Calc. for $C_{20}H_{18}N_8O_8$: C, 48.2; H, 3.6; N, 22.5. Found: C, 48.1; H, 3.5; N, 22.7.

*Benzyl 3,4-diazido-3,4,6-trideoxy-β-*L*-glucopyranoside* (**2**). — To a suspension of **3** (0.32 g) in methanol (3 ml) was added M sodium methoxide solution (a few drops). The mixture was kept overnight at room temperature, and then neutralized with acetic acid (10%) and evaporated. The residue was extracted with chloroform and the extract was washed successively with a 0.5M sodium hydroxide solution, 0.5M hydrochloric acid, and water. Evaporation of the solvent gave a syrup that was crystallized from petroleum ether (yield 0.12 g, 70%), m.p. 60–61°; $[\alpha]_D^{22}$ −57° (*c* 1.0, chloroform).

Anal. Calc. for $C_{13}H_{16}N_6O_3$: C, 51.3; H, 5.3; N, 27.6. Found: C, 51.2; H, 5.2; N, 27.5.

*Benzyl 3,4-diacetamido-3,4,6-trideoxy-β-*L*-glucopyranoside* (**4**). — A solution of **2** (0.2 g) in ether (10 ml) was added dropwise to a suspension of lithium aluminium hydride (0.3 g) in ether (5 ml), and the mixture was boiled for 1 h under reflux. Excess of the hydride was destroyed by successive additions of ethanol and water, and the mixture was filtered. The filtrate was evaporated and the residue treated with acetic anhydride (0.1 ml) in methanol (5 ml) in the presence of silver acetate (0.1 g). The mixture was kept overnight at room temperature, the salts were filtered off, and the

filtrate evaporated to give a solid that was crystallized from acetone (yield 110 mg, 50%), m.p. 292–295° (dec.); recrystallization from acetone–methanol gave an analytical sample, m.p. 300–302°; $[\alpha]_D^{22}$ −12° (*c* 0.75, methanol).

Anal. Calc. for $C_{17}H_{24}N_2O_5$: C, 60.7; H, 7.1; N, 8.3. Found: C, 60.7; H, 7.0; N, 8.2.

*Benzyl 3,4-diacetamido-3-*O*-acetyl-3,4,6-trideoxy-β-*L*-glucopyranoside* (**5**). — Compound **4** (110 mg) was acetylated with acetic anhydride (0.1 ml) in pyridine (3 ml) to give a crystalline product that was recrystallized from acetone–methanol (yield 90 mg, 71%), m.p. 258–260°; $[\alpha]_D^{22}$ +60° (*c* 0.6, *N,N*-dimethylformamide).

Anal. Calc. for $C_{19}H_{26}N_2O_6$: C, 60.3; H, 6.9; N, 7.4. Found: C, 60.0; H, 6.9; N, 7.3.

*3,4-Diacetamido-3,4,6-trideoxy-*L*-glucose* (**6**). — Compound **4** (60 mg) was dissolved in methanol (20 ml) and hydrogenolyzed in the presence of palladium-on-charcoal catalyst (10%) at 4 atm for 20 h. The catalyst was removed by filtration and the filtrate was evaporated. The residue was purified by preparative paper chromatography on Whatman No. 3 paper (prewashed with ethanol and water) in 25:6:25 (upper phase) 1-butanol–acetic acid–water as the solvent system. The material eluted from the paper chromatogram was crystallized from ethanol–acetone to give 21 mg (48%) of pure compound, m.p. 213–216° (dec.); $[\alpha]_D^{22}$ −155 (20 min) → −153° (2 h) (*c* 0.6, water); R_{Glc} 2.38 in 4:1:1 1-butanol–ethanol–water and 2.07 in 25:6:25 (upper phase) 1-butanol–acetic acid–water.

Anal. Calc. for $C_{10}H_{18}N_2O_5$: C, 48.8; H, 7.4; N, 11.4. Found: C, 48.9; H, 7.3; N, 11.1.

To a solution of **6** (14 mg) in water (1 ml) was added sodium borohydride (8 mg). The solution was kept for 2 h at room temperature, then neutralized with acetic acid (10%), and passed through a column (1 × 6 cm) of Amberlite MB-3 resin. The expected diacetamidodideoxyhexitol was eluted with water (20 ml), and the eluate was evaporated to give a glassy residue (10.6 mg). The consumption of periodate (mole) per mole of diacetamidodideoxyhexitol was: 0.8 (1 h) and 0.96 (4 h).

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REFERENCES

1 A. Liav (Levy) and N. Sharon, *Carbohyd. Res.*, 30 (1973) 109.
2 F. H. Newth, *Quart. Rev.* (London), 13 (1959) 30.
3 S. Guberman and D. Horton, *J. Org. Chem.*, 32 (1967) 294.
4 H. H. Baer and C.-W. Chiu, *Carbohyd. Res.*, 31 (1973) 347.
5 N. Sharon and R. W. Jeanloz, *J. Biol. Chem.*, 235 (1960) 1.
6 R. D. Guthrie, *Methods Carbohyd. Chem.*, 1 (1962) 435.