Syntheses of 3,4-Dideoxy-3-enosides and the Corresponding 3,4-Dideoxy Sugars

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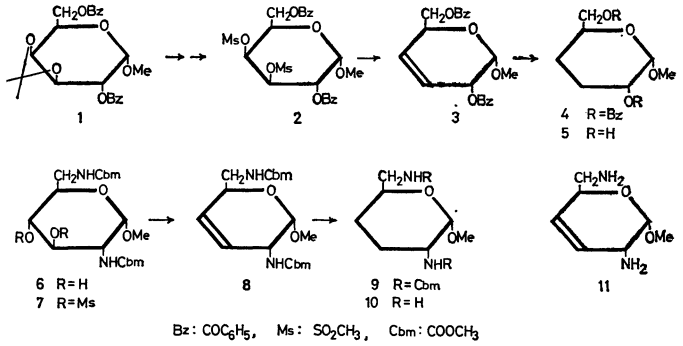
From a biological point of view studies on unsaturated sugars have been drawing attention in recent years, but the introduction of 3,4-unsaturated linkages into sugars is rarely reported. Recently, we described the synthesis of 3′,4′-dideoxykanamycin B,[1] which is active against drug-resistant bacteria, by utilizing a 3,4-unsaturated intermediate. The present work was undertaken to see if a practical method could be worked out for converting aminoglycosidic antibiotics into their unsaturated and dehydroxylated derivatives.



Here we described the syntheses of methyl 3,4-dideoxy-α-D-*erythro*-hexopyranoside (**5**) and methyl 2,6-diamino-2,3,4,6-tetradeoxy-α-D-*erythro*-hexopyranoside (**10**). The syntheses were achieved by way of the corresponding 3,4-unsaturated intermediates. Methyl 3,4-*O*-isopropylidene-α-D-galactopyranoside prepared from methyl α-D-galactopyranoside was benzoylated to give **1**. Removal of the isopropylidene group followed by mesylation gave the corresponding di-*O*-mesyl derivative (**2**). When **2** was treated with sodium iodide and zinc dust in DMF at 130°C for 1.5 hr according to the procedure of Tipson and Cohen[2] and Horton *et al.*,[3] a 3,4-unsaturated derivative, namely, methyl 2,6-di-*O*-benzoyl-3,4-dideoxy-α-D-*erythro*-hex-3-enopyranoside (**3**) was obtained in a yield of 93%, syrup, $[\alpha]_D^{22}$ −17.3° (*c* 1, $CHCl_3$); NMR (in $CDCl_3$): τ 4.05 (2-proton slightly broadened singlet, H-3,4), $J_{1,2}$ 4 Hz, $J_{2,(3,4)} = J_{(3,4),5}$ ~0 Hz. Catalytic hydrogenation of **3** gave methyl 2,6-di-*O*-benzoyl-3,4-dideoxy-α-D-*erythro*-hexopyranoside (**4**), mp 70—71°C, $[\alpha]_D^{22}$ +56.7° (*c* 1, $CHCl_3$). Removal of the protecting groups of **4** gave methyl 3,4-dideoxy-α-D-*erythro*-hexopyranoside (**5**), syrup, $[\alpha]_D^{22}$ +126° (*c* 1.1, water); NMR (in D_2O): τ 5.28 (1-proton doublet, $J_{1,2}$ 3.5 Hz, H-1), τ 7.9—8.6 (4-proton multiplet, H-3,3,4,4).

Methyl 2,6-dideoxy-2,6-dimethoxycarbonylamido-α-D-glucopyranoside (**6**), mp 175—177°C, $[\alpha]_D^{21}$ +108° (*c* 0.7, water) prepared from neamine was mesylated to give the corresponding di-*O*-mesyl derivative (**7**), mp 193—195°C, $[\alpha]_D^{23}$ +94° (*c* 1.5, $CHCl_3$); NMR (in $CDCl_3$): τ 6.77 and 6.90 (each 3-proton singlet, SO_2-CH_3). 3,4-Unsaturation was performed likewise in a yield of 90% to give a 3-eno derivative (**8**), mp 157—158°C, $[\alpha]_D^{20}$ −35° (*c* 0.7, methanol); NMR (in $CDCl_3$): τ 4.29 (2-proton slightly broadened singlet, H-3,4), $J_{1,2}$ 4.2 Hz, $J_{2,(3,4)} = J_{(3,4),5}$ ~0 Hz, $J_{2,5}$ ~4 Hz. Catalytic hydrogenation of **8** gave the corresponding tetradeoxy derivative (**9**), syrup, $[\alpha]_D^{19}$ +126° (*c* 0.7, methanol). Removal of the protecting groups of **9** gave methyl 2,6-diamino-2,3,4,6-tetradeoxy-α-D-*erythro*-hexopyranoside (**10**) as needles of monosulfate, mp>180°C, $[\alpha]_D^{22}$ +128° (*c* 1, water). Removal of the protecting groups of **8** gave methyl 2,6-diamino-2,3,4,6-tetradeoxy-α-D-*erythro*-hex-3-enopyranoside (**11**) as needles of monosulfate hemihydrate, mp>180°C, $[\alpha]_D^{22}$ +26° (*c* 1, water); NMR (in D_2O): τ 3.95 (2-proton slightly broadened singlet, H-3,4).

1) H. Umezawa, S. Umezawa, T. Tsuchiya, and Y. Okazaki, *J. Antibiotics*, **24**, 485 (1971).
2) R. Tipson and A. Cohen, *Carbohyd. Res.*, **1**, 338 (1965).
3) E. Albano, D. Horton, and T. Tsuchiya, *ibid.*, **2**, 349 (1966)