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Note

Specific reactivity of the *O*-(β-D-glucopyranosyl-(1→6)-D-glucopyranose) linkage with acetic anhydride in the presence of trimethylsilyl trifluoromethanesulfonate

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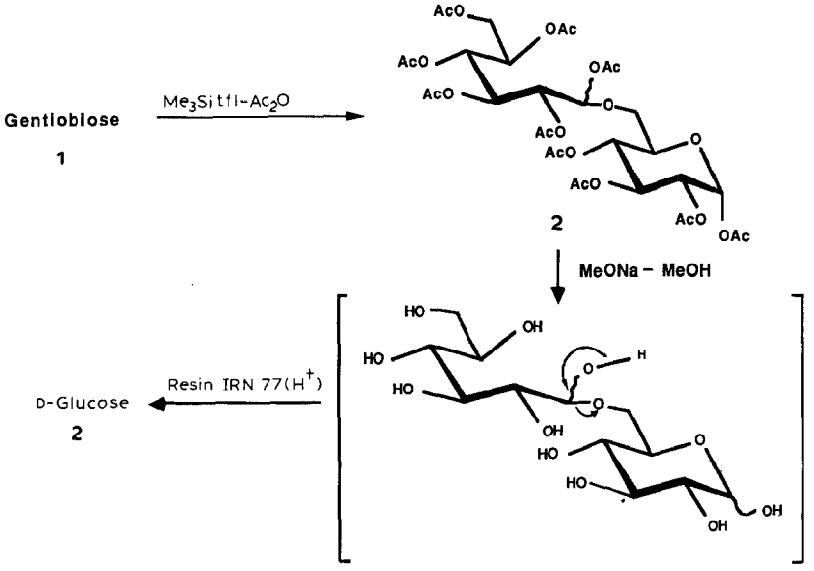
We have recently shown[1] that trimethylsilyl trifluoromethanesulfonate (triflate) is a good promotor for peracetylation of mono- and oligo-saccharides by acetic anhydride, and that high stereospecificity was obtained at C-1 of the reducing unit[2]. An unexpected reaction was observed, however, with gentiobiose (**1**) whether the (1→6)-β-D-linked disaccharide was peracetylated or not .

The α-D-(1→6)-linked isomaltose (3) was acetylated to give the octaacetate derivative **4** having an axial acetyl group at C-1 of the reducing unit. This latter observation was in accord with the results obtained during previous investigations[1] on α- and β-(1→4)-, α- and β-(1→3)-, and β-(1→2)-D-glucobioses where α-octa-



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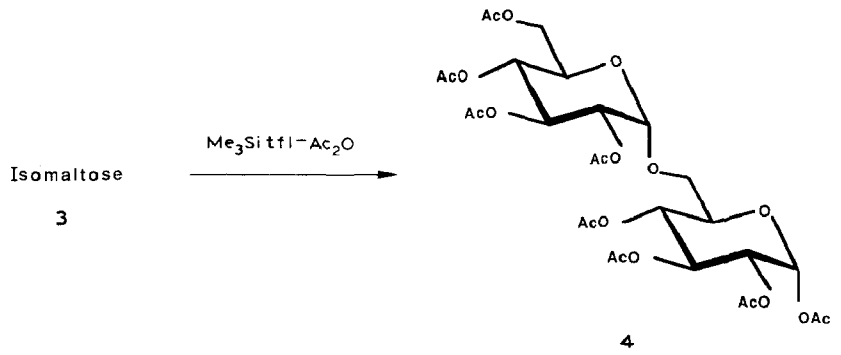
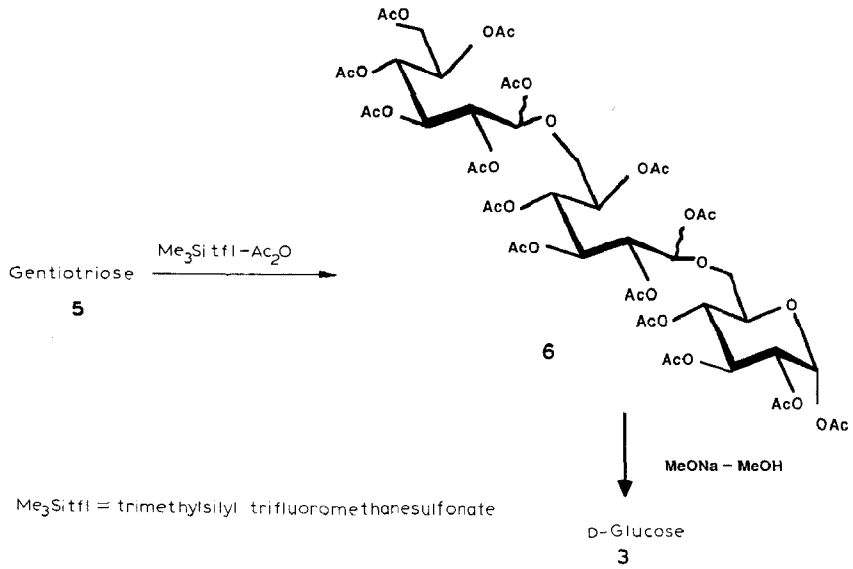


acetates were formed in 85–90% yield (β-octaacetates were present among other minor unidentified products). Acetylation of **1** with acetic anhydride–trimethylsilyl triflate, gave in a 1:1 ratio, two products (**2**) which were separated by h.p.l.c. or "flash" chromatography. N.m.r. and mass spectrometry, showed the two products to be two isomeric decaacetates resulting from ring opening of the nonreducing unit. Furthermore, deacetylation by the Zemplén reaction led to two molecules of D-glucose. In the same manner, treatment of gentiotriose[3] (**5**) gave pentadeca-acetate derivatives (**6**) by double ring opening of the nonreducing units, and Zemplén deacetylation led to three molecules of D-glucose.



To our knowledge, this is the first example of a chemical reaction leading, in two steps with high specificity, to the cleavage of a *O*-(β-D-glucopyranosyl)-(1→6)-D-glucose linkage. The reactions known up to now in this field are the preferential but nonspecific, cleavage of (1→6) bonds during acetolysis[4] of oligo- and polysaccharides, and the greater effectiveness of the Fenton reagent on (1→6)-linked, nonsubstituted disaccharides, as compared to (1→4)-linked ones[5]. Other chemical

methods that have been used to distinguish α from β linkages are the oxidation by chromium trioxide in acetic acid[6–8] or by ozone[9,10], and the more recent ring cleavage of methyl glycopyranosides with dimethylboron bromide[11] leading to ring-opened products.

EXPERIMENTAL

General methods. — Melting points were determined with a Büchi "Tottoli" type instrument and are uncorrected. Optical rotations were measured with a Perkin–Elmer 241 instrument. ^{1}H- and ^{13}C-n.m.r. spectra were recorded at room temperature for solutions in C_6D_6 [internal standard $(CH_3)_4Si$] with a Bruker AM 300 spectrometer. Proton-signal assignments were made from 1D and 2D (COSY) spectra; for ^{1}H–^{1}H COSY, standard pulse-sequence and procedure were used with 512 free-induction decays and 1 K data points, for time-domain data matrices. Mass spectra in the f.a.b. (+) mode were recorded with a quadrupole Nermag R10.10C spectrometer, fitted with a PDP 11-73 (DEC) computer; atoms were accelerated with an M. scan (Wallis) Ar gun under an accelerating potential of 8.5 kV. Reactions were monitored by t.l.c. on silica-precoated aluminium sheets "Alufolien" 60 F_{254} (Merck). Preparative column chromatography was performed on Silica Gel 60 (0.04–0.063 mm, Merck). Trimethylsilyl trifluoromethanesulfonate was purchased from Fluka Chemical AG and used as a 50% solution in dry dichloromethane; acetylations were performed with trimethylsilyl triflate from freshly opened vials.

[*6*-O-*(1*R,S*)-1-Acetoxy-2,3,4,5,6-penta*-O-*acetyl*-D-*glucityl)-1,2,3,4-tetra*-O-*acetyl*-α-D-*glucopyranose* (**2**). — To a suspension of gentiobiose (**1**; 0.25 g) in acetic anhydride (10 mL), stirred magnetically in an ice bath, was added slowly, dropwise, a 50% solution of trimethylsilyl triflate (1.5 mL) in dry dichloromethane. After 2.5 h, the mixture was poured into $NaHCO_3$–ice water solution (50 mL) and extracted with dichloromethane (2 × 50 mL). After being dried (Na_2SO_4), the solution was evaporated to afford an amorphous solid (0.54 g); t.l.c. (9:1 ether–cyclohexane) showed two poorly separated spots (R_F 0.32) in an ~1:1 ratio according to ^{13}C- and ^{1}H-n.m.r. spectral data. The two products were separated by "flash" chromatography on 35 g of Silica Gel 60 and the same elution system, into fractions: pure **2a**, a mixture (280 mg) of **2a**, **2b** and byproducts (<10%), and pure **2b**.

Compound **2a**. Thick oil (120 mg), $[\alpha]_D^{20}$ +60° (*c* 1.5, chloroform); ^{1}H-n.m.r. (C_6D_6): δ 6.59 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 6.14 (d, 1 H, $J_{1',2'}$ 4.7 Hz, H-1'), 5.97 (t, 1 H, $J_{2',3'} = J_{3',4'}$ 5.2 Hz, H-3'), 5.84 (dd, 1 H, $J_{4',5'}$ 5.9 Hz, H-4'), 5.80 (dd, 1 H, $J_{2,3}$ 10.3, $J_{3,4}$ 9.5 Hz, H-3), 5.71 (t, 1 H, H-2'), 5.40 (m, 1 H, H-5'), 5.34 (dd, 1 H, H-2), 5.31 (dd, 1 H, $J_{4,5}$ 10.3 Hz, H-4), 4.48 (dd, 1 H, $J_{5',6'a}$ 4.4, $J_{6'a,6'b}$ 12.1 Hz, H-6'a), 4.21 (dd, 1 H, $J_{5',6'b}$ 5.8 Hz, H-6'b), 4.14 (m, 1 H, H-5), 3.87 (dd, 1 H, $J_{5,6a}$ 2.5, $J_{6a,6b}$ 11.2 Hz, H-6a), 3.64 (dd, 1 H, $J_{5,6b}$ 5.0 Hz, H-6b), 1.962 (s), 1.856(s), 1.811(2s), 1.808(s), 1.804(s), 1.801(s), 1.722(s), 1.647(s), and 1.637(s) (10 OAc); ^{13}C-n.m.r. (C_6D_6): δ 95.03 (C-1'), 89.43 (C-1), 71.21, 70.55, 70.38, 70.18, 69.89, 69.51, 69.12, 68.28 (C-2,3,4,5,2',3',4',5'), 69.38 (C-6), and 61.87 (C-6').

Compound **2b**. Thick oil (30 mg, fraction of pure second product), $[\alpha]_D^{20}$ +61° (*c* 0.75, chloroform); ^{1}H-n.m.r. (C_6D_6): δ 6.64 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 6.16 (d, 1 H, $J_{1',2'}$ 4.7 Hz, H-1'), 5.91 (dd, 1 H, $J_{2',3'}$ 5.8, $J_{3',4'}$ 4.4 Hz, H-3'), 5.77 (t, 1 H, $J_{2,3} = J_{3,4}$ 10.2 Hz, H-3), 5.72 (dd, 1 H, $J_{4',5'}$ 6.7 Hz, H-4'), 5.64 (dd, 1 H, H-2'), 5.49 (dd, 1 H, H-2), 5.47 (dd, 1 H, $J_{4,5}$ 10.3 Hz, H-4), 5.38 (m, H-5'), 4.45 (dd, 1 H, $J_{5'6'a}$ 3.8, $J_{6'a,6'b}$ 12.3 Hz, H-6'a), 4.20 (dd, 1 H, $J_{5'6'b}$ 5.6 Hz, H-6'b), 4.04 (m, 1 H, H-5), 3.91 (dd, 1 H, $J_{5,6a}$ 2.7, $J_{5,6b}$ 5.3, $J_{6a,6b}$ 11.2 Hz, H-6a,H-6b), 1.926(s), 1.869(s), 1.776(2s), 1.769(2s), 1.746(s), 1.743(s), 1.703(s), and 1.619(s) (10 OAc); ^{13}C-n.m.r. (C_6D_6): δ 95.99 (C-1'), 89.64 (C-1), 71.55, 70.74, 70.54, 69.86, 69.69, 69.57, 68.59, 68.27 (C-2,3,4,5,2',3',4',5'), 69.23 (C-6), and 61.75 (C-6').

Compounds **2a** and **2b** gave identical results in mass spectrometry; f.a.b.-m.s. (+) (matrix PEG 200): *m/z* 721 (M − 59, no molecular ion in that case), 679 (721 − CH_2=C=O)$^+$, 661 (721 − CH_3CO_2H)$^+$, 619 (661 − CH_2=C=O)$^+$, and 559 (619 − CH_2=CO=O)$^+$; f.a.b. m.s. (matrix PEG 200 with addition of NaCl): *m/z* 803 (M + Na)$^+$, 761 (803 − CH_2=C=O)$^+$, 743 (803 − CH_3CO_2H)$^+$, and 701 (761 − CH_3CO_2H)$^+$.

Anal. Calc. for $C_{32}H_{44}O_{22}$: C, 49.23; H, 5.64; O, 45.12. Found: (**2a**) C, 49.73; H, 5.88; O, 45.31; (**2b**) C, 49.29; H, 5.53; O, 45.31.

Deacetylation of **2a** *or* **2b**. Compound **2** (0.5 g) was treated with a 0.1M solution of sodium methoxide in methanol (4 mL) overnight at room temperature. IRN 77 (H^+) cation-exchange resin was added to neutrality and the solution was concentrated (after filtration) to dryness. Reacetylation of the residue (0.22 g) with acetic anhydride (6 mL) and pyridine (6 mL), afforded after the usual workup α,β-D-glucose pentaacetate (0.48 g), identified by ^{13}C-n.m.r. spectroscopy.

*1,2,3,4-Tetra-*O*-acetyl-6-*O*-(2,3,4,6-tetra-*O*-acetyl-α-*D*-glucopyranosyl)-α-*D*-glucopyranose* (**4**). — Isomaltose (**3**; 100 mg) was treated with acetic anhydride (6 mL) at 0° (ice bath), and then a 50% solution of trimethylsilyl triflate in dichloromethane (1 mL) was added dropwise and slowly, and the mixture was stirred magnetically for 2.5 h. The mixture was worked up as described for compound **1**, and afforded a thick oily product (200 mg); t.l.c. (1:1, v/v ethyl acetate–hexane) indicated that only one product had been obtained; ^{1}H-n.m.r. (C_6D_6): δ 6.51 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 5.79 (dd, 1 H, $J_{2',3'}$ 10.2, $J_{3',4'}$ 9.3 Hz, H-3'), 5.76 (dd, 1 H, $J_{2,3}$ 10.3, $J_{3,4}$ 9.3 Hz, H-3), 5.29 (dd, 1 H, $J_{3',4'}$ 9.2, $J_{4',5'}$ 10.2 Hz, H-4'), 5.26 (dd, 1 H, $J_{3,4}$ 9.3, $J_{4,5}$ 10.2 Hz, H-4), 5.20 (dd, 1 H, $J_{1,2}$ 3.8, $J_{2,3}$ 10.3 Hz, H-2), 5.15 (d, 1 H, $J_{1',2'}$ 3.7 Hz, H-1'), 5.40 (dd, 1 H, H-2'), 4.31 (dd, 1 H, $J_{5',6'a}$ 4.9, $J_{6'a,6'b}$ 12.2 Hz, H-6'a), 4.18 (dd, 1 H, $J_{5',6'b}$ 2.4 Hz, H-6'b), 4.14 (2 m, 2 H, H-5,5'), 3.98 (dd, 1 H, $J_{5,6a}$ 5.3, $J_{6a,6b}$ 11.3 Hz, H-6a), 3.46 (dd, 1 H, $J_{5,6b}$ 3.2 Hz, H-6b); 1.789, 1.776, 1.774, 1.701, 1.700, 1.698, 1.646, and 1.609 (8 $COCH_3$); ^{13}C-n.m.r. (C_6D_6): δ 95.64 (C-1'), 89.22 (C-1), 71.39, 70.68, 70.54, 70.45, 69.77, 69.51, 69.12, 67.98 (C-2,3,4,5,2',3',4',5'), 66.56 (C-6), 62.17 (C-6'), and 20.26–19.89 (8 $COCH_3$).

O-[*(1*R,S*)-1-Acetoxy-2,3,4,5,6-penta-*O*-acetyl-*D*-glucityl*]-*(1→6)*-O-[*(1*R,S*)-1-acetoxy-2,3,4,5-tetra-*O*-acetyl-*D*-glucityl*]-*(1→6)-1,2,3,4-tetra-*O*-acetyl-α-*D*-gluco-*

pyranose (**6**). — Gentiotriose (**5**; 100 mg) was treated with acetic anhydride and trimethylsilyl triflate as previously described for gentiobiose (3 h). The reaction afforded a thick oily product (200 mg); ^{1}H-n.m.r. (C_6D_6): δ 6.7–6.6, 6.2-5.2, 4.5–3.2 (ring H), and 2.1-1.5 ($COCH_3$); ^{13}C-n.m.r. (C_6D_6): δ 100.90*, 96.01*, 94.99*, 94.89, 94.61, 89.76, 89.72, and 89.51* (*signals with relatively double intensity); f.a.b.-m.s. (+) (matrix PEG 200 with addition of NaCl): *m/z* 1193 [1170 + 23; M + Na)$^+$].

Deacetylation, as described earlier for **1**, afforded after reesterification α,β-D-glucose pentaacetate.

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