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Synthesis of Manninotriose Undecaacetate

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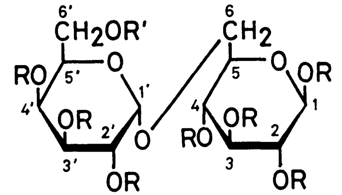
Synopsis. Manninotriose undecaacetate has been prepared from melibiose. Tritylation of melibiose, followed by acetylation gave 6′-*O*-trityl-*β*-melibiose heptaacetate. Detritylation of the compound gave hepta-*O*-acetyl-*β*-melibiose, which was condensed with tetra-*O*-benzyl-D-galactopyranosyl chloride. Deacetylation of the condensation product, followed by hydrogenolysis and acetylation afforded the title compound.

Manninotriose, *O*-*α*-D-galactopyranosyl-(1→6)-*O*-*α*-D-galactopyranosyl-(1→6)-D-glucose, has been found in a free form in an ash manna from *Fraxinus ornus* and *F. rotundifolia*, and it has been well known that this trisaccharide is a component of a tetrasaccharide: stachyose.[1] The enzymic synthesis of manninotriose from melibiose has been reported in a literature,[2] but a chemical synthesis has never been described.

In connection with the preceding papers,[3,4] we have attempted to synthesize manninotriose undecaacetate (**6**) from melibiose (**1**) chemically. When **1** was treated with trityl chloride in pyridine and the product was subsequently acetylated, 6′-*O*-trityl-*β*-melibiose heptaacetate (**2**) was obtained as crystals in 65% yield.

Detritylation of **2** with hydrogen bromide in glacial acetic acid afforded 1,2,2′,3,3′,4,4′-hepta-*O*-acetyl-*β*-melibiose (**3**). Condensation between **3** and 2,3,4,6-tetra-*O*-benzyl-D-galactopyranosyl chloride[5] (**4**) gave 1,2,2′,3,3′,4,4′-hepta-*O*-acetyl-2″,3″,4″,6″-tetra-*O*-benzyl-*β*-manninotriose (**5**) as a chromatographically homogeneous solid. Deacetylation of **5**, followed by catalytic hydrogenolysis and subsequent acetylation afforded **6** as crystals in 30% yield. Compound **6** was identified by direct comparison with an authentic sample prepared by hydrolysis of stachyose.[6]



1: R=R′=H
2: R=Ac, R′=Tr
3: R=Ac, R′=H
5: R=Ac, R′=2,3,4,6-tetra-*O*-benzyl-*α*-D-galactopyranosyl
6: R=Ac, R′=2,3,4,6-tetra-*O*-acetyl-*α*-D-galactopyranosyl

Experimental

General. Melibiose and stachyose were purchased from a commercial source. Melting points were determined in capillary tubes, and are uncorrected. Solutions were evaporated under diminished pressure. IR spectra were determined for potassium bromide discs with a Hitachi 225 spectrophotometer. Optical rotations were recorded on a Japan Spectroscopic DIP-SL polarimeter. ^{1}H NMR spectra were determined at 60 MHz with a Varian A-60D spectrometer in deuteriochloroform with tetramethylsilane as an internal standard, and the peak positions are given in δ-values. TLC was performed on a silica gel (Wakogel B-10) plate, and silica gel (Wakogel C-200) was used for a column chromatography.

*1,2,2′,3,3′,4,4′-Hepta-*O*-acetyl-6′-*O*-trityl-β-melibiose (**2**).* To a solution of melibiose (**1**, 200 mg, 0.58 mmol) in dry pyridine (10 ml), trityl chloride (976 mg, 3.50 mmol) was added, and the mixture was agitated for 97 h at ambient temperature. Then, acetic anhydride (5 ml) was added to the reaction mixture. After 15 h, the mixture was poured into ice cold water (200 ml) and triphenylmethanol was removed by filtration. The filtrate was evaporated, and the residue was purified by a column chromatography using 1 : 5 (v/v) 2-butanone–toluene as eluent to give 424 mg of a chromatographically homogeneous product (R_f 0.43 on TLC in 1 : 4 (v/v) 2-butanone–toluene). Recrystallization from 80% aqueous ethanol gave 332 mg (65%) of **2**, mp 108—112 °C, $[\alpha]_D^{22}+79.1°$ (*c* 1.05, chloroform), ^{1}H NMR: δ 1.88 (s, 3, OAc), 1.98 (s, 6, 2×OAc), 2.02 (s, 12, 4×OAc), 5.74 (d, 1, J=8.0 Hz, H-1), 6.35 (d, 1, J=3.5 Hz, H-1′).

Found: C, 61.22; H, 5.71%. Calcd for $C_{45}H_{50}O_{18}$: C, 61.50; H, 5.73%.

*1,2,2′,3,3′,4,4′-Hepta-*O*-acetyl-β-melibiose (**3**).* To a solution of **2** (318 mg) in glacial acetic acid (2.0 ml), glacial acetic acid (0.2 ml) saturated with hydrogen bromide was added under ice cooling. After stirring for 2 min, the precipitated bromotriphenylmethane was filtered off and the filtrate was quenched into ice cold water (60 ml). The solution was extracted with chloroform repeatedly and the combined chloroform layer was washed with dilute sodium hydrogencarbonate solution and water. After drying over sodium sulfate, the extract was evaporated. The residue was purified by a column chromatography using 1 : 2 (v/v) 2-butanone–toluene as eluent to give 181 mg (79%) of **3** as a chromatographically homogeneous solid (R_f 0.39 on TLC in 20 : 1 (v/v) chloroform–ethanol), $[\alpha]_D^{21}+132.9°$ (*c* 0.82, chloroform). ^{1}H NMR: δ 1.98 (s, 6, 2×OAc), 2.04 (s, 3, OAc), 2.09 (s, 6, 2×OAc), 2.12 (s, 3, OAc), 2.13 (s, 3, OAc), 5.67 (d, 1, J=8.0 Hz, H-1), 6.27 (d, 1, J=4.0 Hz, H-1′).

Found: C, 49.07; H, 5.56%. Calcd for $C_{26}H_{36}O_{18}$: C, 49.06; H, 5.70%.

*2,3,4,6-Tetra-*O*-benzyl-D-galactopyranosyl Chloride (**4**).* The compound was prepared by the method of Austin *et al.*[5]

*1,2,2′,2″,3,3′,3″,4,4′,4″,6″-Undeca-*O*-acetyl-β-manninotriose (**6**).* To a solution of **3** (1.10 g, 1.73 mmol) and **4** (3.14 g, 5.62 mmol) in dry benzene (30 ml), mercury(II) cyanide (1.5 g) and "Drierite" (3.0 g) were added. The mixture was heated under reflux for 17 h, and an insoluble matter was removed by a centrifugal separator. The supernatant solution was washed with sodium hydrogencarbonate solution and water. The benzene solution was dried over sodium sulfate and evaporated. The residue was purified by a column chromatography using 1 : 5 (v/v) 2-butanone–toluene as eluent to give

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1.78 g (89%) of 1,2,2′,3,3′,4,4′-hepta-*O*-acetyl-2″,3″,4″,6″-tetra-*O*-benzyl-*β*-manninotriose (**5**) as a chromatographically homogeneous solid (R_f 0.52 on TLC in 1 : 3 (v/v) 2-butanone–toluene).

Compound **5** (1.70 g) was deacetylated in 0.1 M methanolic sodium methoxide (30 ml) overnight. The solution was neutralized with Amberlite IR-120 (H^+) resin and evaporated. The residue was hydrogenated in methanol (35 ml) in the presence of palladium black under a hydrogen atmosphere (3.4 kg/cm^2) for 20 h in a Parr apparatus. The catalyst was filtered off and the filtrate was evaporated. The residue was acetylated with acetic anhydride (3 ml) and sodium acetate (0.3 g). The product was purified by a column chromatography using 1 : 5 (v/v) acetone–benzene to give 409 mg of a product which showed a single spot at R_f 0.38 on TLC in the same solvent. Recrystallization from ethanol afforded 268 mg (30%) of **6**, mp 106—107.5 °C, $[\alpha]_D^{21}+132.7$ °C (c 0.98, chloroform). ^{1}H NMR: δ 1.96 (s, 6, 2×OAc), 2.00 (s, 6, 2×OAc), 2.01 (s, 3, OAc), 2.05 (s, 9, 3×OAc), 2.09 (s, 6, 2×OAc), 2.11 (s, 3, OAc), 5.70 (d, 1, J=8.0 Hz, H-1). The IR and ^{1}H NMR spectra were superimposable on those of an authentic sample.

Found: C, 49.46; H, 5.51%. Calcd for $C_{40}H_{54}O_{27}$: C, 49.69; H, 5.63%.

*Compound **6** from Stachyose.* Manninotriose was prepared from stachyose by the method of Tanret.6) The product was acetylated to give **6** in 47% yield, mp 106—107.5 °C, $[\alpha]_D^{21}+137°$ (c 1.27, chloroform). (Found: C, 49.48; H, 5.56%).

References

1) D. French, *Adv. Carbohydr. Chem.*, **9**, 170 (1954).

2) D. French, *Adv. Carbohydr. Chem.*, **9**, 157 (1954).

3) T. Suami, T. Otake, T. Nishimura, and T. Ikeda, *Carbohydr. Res.*, **26**, 234 (1973).

4) T. Suami, T. Otake, T. Nishimura, and T. Ikeda, *Bull. Chem. Soc. Jpn.*, **46**, 1014 (1973).

5) P. W. Austin, F. E. Hardy, J. G. Buchanan, and J. Baddiley, *J. Chem. Soc.*, **1965**, 1419.

6) C, Tanret, *C. R. Acad. Sci.*, **134**, 1586 (1902).