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Note

Stepwise synthesis of methyl 4-*O*-[3-*O*-(β-D-xylopyranosyl)-β-D-xylopyranosyl]-β-D-xylopyranoside*

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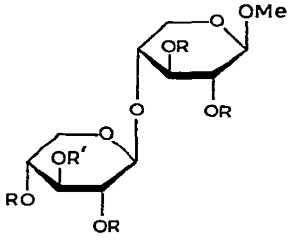
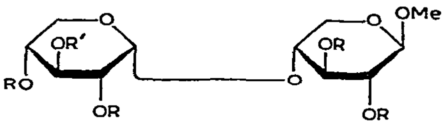
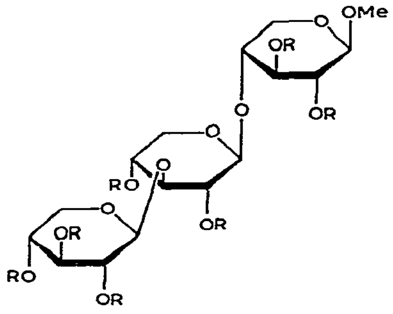
A feature characteristic of wood xylans is a β-D-xylopyranosyl group or a short-chain, (1→4)-β-linked xylo-oligosaccharide attached at O-3 of certain D-xylose



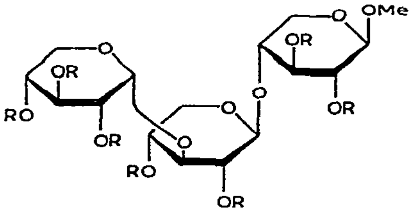
1 R = Ac, R′ = Bzl
4 R = Ac, R′ = H
5 R = R′ = Ac



2 R = Ac ; R′ = Bzl
3 R = R′ = H



6 R = Ac
7 R = H
8 R = Me



9 R = Ac
10 R = H
11 R = Me

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*Part XXIII of the series "Alternative Syntheses of Methylated Sugars". For part XXII, see ref. 4.

residues that form the main β-(1→4)-linked polysaccharide backbone[1]. Because of the lack of specific enzymes and conditions for selective acid hydrolysis, only linear xylo-oligosaccharides have been isolated from the products of partial hydrolysis of these abundant natural polymers. We have been interested in synthesis of model compounds that closely reflect the main structural features of native xylans. Such are, for example, methyl β-glycosides of β-D-xylo-oligosaccharides, where the aglycon imitates the situation in the main chain of the polysaccharide. The object of the present work was the synthesis of methyl 4-*O*-[3-*O*-(β-D-xylopyranosyl)-β-D-xylopyranosyl]-β-D-xylopyranoside (**7**). Preparation of the 3′-*O*-α-D-linked compound **10**, whose intermediate **9** was formed and isolated in the course of this work, is also described. Syntheses of methyl 3,4-di-*O*-(β-D-xylopyranosyl)-β-D-xylopyranoside, a branched isomer of **7**, as well as of other, positionally isomeric, methyl β-D-xylotriosides, were described elsewhere in this Series[2-4].

The condensation of methyl 2,3-di-*O*-acetyl-β-D-xylopyranoside[5] with 2,4-di-*O*-acetyl-3-*O*-benzyl-α-D-xylopyranosyl bromide in acetonitrile, with mercuric cyanide as the acid acceptor and catalyst, yielded two crystalline disaccharide derivatives (**1** and **2**). The elemental analyses of the substances were consistent with the expected structure, and compounds **1** and **2** showed optical rotations of opposite sign. The α-D configuration of the interglycosidic linkage in **2** was confirmed when the compound was converted (by debenzylation and deacetylation) into the known[6], crystalline, methyl 4-*O*-(α-D-xylopyranosyl)-β-D-xylopyranoside (**3**). Crystalline nucleophile **4**, the key intermediate in synthesis of **7**, was obtained from **1** by debenzylation. Acetylation of **4** gave **5**, identical with methyl penta-*O*-acetyl-β-xylobioside[7,8] (**5**), thus proving the β-D configuration of the interglycosidic linkage in **1** and products of its further conversion.

The reaction of **4** with 2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl bromide gave trisaccharide derivatives **6** and **9**, which were isolated by chromatography, and both obtained crystalline. The assignment of configuration of the interglycosidic linkage at the nonreducing end in **6** and **9** was based on the values of the specific optical rotation found for these compounds. Deacetylation of **6** and **9** gave crystalline glycosides **7** and **10**, and the fully methylated derivatives **8** and **11** were also obtained crystalline. The molecular weight (526) of **8** could be calculated[9] from the *m/e* values of the peaks aA_1 and bcA_1 present in its mass spectrum ($M = aA_1 + bcA_1 + 16 = 175 + 335 + 16$). The observed molecular weight is in agreement with the compound's being a methyl hepta-*O*-methylaldopentotriaoside. It follows from the fact that the mass spectra of **8** and **11** were qualitatively identical, taking into account the proven stereochemistry of the interglycosidic linkage in **1–5**, that compounds **6–8** and **9–11** differ merely in the stereochemistry of the interglycosidic linkage at the nonreducing end of the molecules.

EXPERIMENTAL

General methods. — Melting points were determined on a Kofler hot-stage.

Optical rotations (22°; *c* 1, chloroform, unless stated otherwise) were measured with a Perkin–Elmer Model 141 automatic polarimeter. Mass spectra (74 eV) were obtained with a JMS-100D instrument at an emission of 300 μA. The evaporation temperature was 280°, and that of the ionizing chamber, 150°.

T.l.c. was performed on Silica Gel G and column chromatography on dry-packed Silica Gel 60 (Merck, 9385), with *A*, 7:1 carbon tetrachloride–acetone; *B*, 8:1 benzene–acetone; *C*, 9:2 chloroform–methanol; *D*, 2:3 cyclohexane–ethyl acetate; and *E*, 4:1 benzene–acetone. Detection was effected by charring with 5% (v/v) sulfuric acid in ethanol. The solution of hydrogen bromide in dichloromethane[10] used contained 0.1 g of HBr/mL (determined by weighing).

Microanalyses were performed with a Perkin–Elmer Model 240 automatic analyzer. Solutions were dried with anhydrous sodium sulfate and concentrated at 40°/2 kPa.

Methyl 2,3-di-O-acetyl-4-O-(2,4-di-O-acetyl-3-O-benzyl-α- (**2**) *and β-D-xylopyranosyl)-β-D-xylopyranoside* (**1**). — A solution of hydrogen bromide in dichloromethane (45 mL) was added to a solution of 1,2,4-tri-*O*-acetyl-3-*O*-benzyl-α,β-D-xylopyranose[11] (6.75 g, 18.4 mmol) in dichloromethane (15 mL) and the mixture was kept for 30 min at room temperature. After evaporation with intervening addition of toluene, a solution of the residue in the minimum amount of acetonitrile was added to a mixture of Drierite (10 g), methyl 2,3-di-*O*-acetyl-β-D-xylopyranoside (2.2 g, 9.06 mmol), and mercuric cyanide (2.3 g, 9.1 mmol) in acetonitrile (75 mL), and the mixture was stirred for 1 h at room temperature and with the exclusion of moisture. T.l.c. (solvent *A*) then showed the presence of two main products (R_F 0.25 and 0.35) of which the slower-moving one predominated, and the mixture was processed conventionally. The crude product was chromatographed on a column of silica gel to give a fraction containing mainly the product having R_F 0.35, and crystallization from ethanol gave chromatographically pure **2** (1.35 g, 26.8%), m.p. 150–152° and $[\alpha]_D$ +5°, after recrystallization from the same solvent (Found: C, 56.21; H, 6.17. $C_{26}H_{34}O_{13}$ calc.: C, 56.30; H, 6.18%).

Eluted next was a fraction containing mainly the product having R_F 0.25, and crystallization from ethanol gave chromatographically pure **1** (3.2 g, 63.7%), m.p. 140–141°, $[\alpha]_D$ −98.2°, after recrystallization from ethanol (Found: C, 56.31; H, 6.24%).

Methyl 4-O-(α-D-xylopyranosyl)-β-D-xylopyranoside (**3**). — Compound **2** (1.05 g) in ethanol (100 mL) was hydrogenated over 5% palladium-on-charcoal catalyst (0.2 g) at room temperature until the reaction was complete, as shown by t.l.c. (solvent *B*). After conventional isolation, chromatographically pure methyl 2,3-di-*O*-acetyl-4-*O*-(2,4-di-*O*-acetyl-α-D-xylopyranosyl)-β-D-xylopyranoside was obtained in theoretical yield. Crystallization from methanol gave material melting at 172–173° and having $[\alpha]_D$ +29.5° (Found: C, 49.01; H, 6.25. $C_{19}H_{28}O_{13}$ calc.: C, 49.13; H, 6.08%).

The foregoing compound (0.6 g) in methanol (20 mL) was treated with M methanolic sodium methoxide (1 mL) for 2 h. T.l.c. (solvent *C*) then showed that the reaction was complete and that a product indistinguishable from an authentic standard of 3 (R_F 0.1), prepared[6] independently, had been formed. The solution was deionized with Dowex 50-W (H^+ form) resin, and crystallization from ethanol–acetone gave **3**, m.p. 149–150° (lit.[6] m.p. 150–150.5°).

Methyl 2,3-di-O-acetyl-4-O-(2,4-di-O-acetyl-β-D-xylopyranosyl)-β-D-xylopyranoside (**4**), *and methyl penta-O-acetyl-β-xylobioside* (**5**). — Compound **1**, when treated as described for the hydrogenation of **2**, gave the partially acetylated disaccharide derivative **4** in theoretical yield, m.p. 103–104° (from ethanol), $[\alpha]_D$ —97.1° (Found: C, 49.22; H, 6.29. $C_{19}H_{28}O_{13}$ calc.: C, 49.13; H, 6.08%).

Compound **4** (100 mg) was treated with 2:1 acetic anhydride–pyridine (2 mL) for 2 h at room temperature. The mixture was processed conventionally and the product crystallized from ethanol to give **5**, m.p. 145–146° (lit.[7,8] m.p. 145–146.5°).

Methyl 2,3-di-O-acetyl-4-O-[2,4-di-O-acetyl-3-O-(2,3,4-tri-O-acetyl-α- (**9**) *and -β-D-xylopyranosyl)-β-D-xylopyranosyl]-β-D-xylopyranoside* (**6**). — Tri-*O*-acetyl-α-D-xylopyranosyl bromide[12] (5.5 g, 16.2 mmol) was added to a mixture of **4** (2.5 g, 5.38 mmol), Drierite (10 g), and mercuric cyanide (2.04 g, 8.07 mmol) in acetonitrile (60 mL) and the mixture was stirred with exclusion of moisture for 18 h. T.l.c. (solvent *D*) then showed the absence of the bromide (R_F 0.7) and the presence of only traces of **4** (R_F 0.2). The main components of the mixture were the trisaccharide derivatives **6** (R_F 0.25) and **9** (R_F 0.3), and products having the same chromatographic mobility as authentic standards[13] of 2,3,4-tri-*O*-acetyl-α,β-D-xylopyranose and peracetates of trehalose-type xylobioses (R_F > 0.5) were also present. The mixture was processed conventionally and the crude product was chromatographed. Fractions corresponding to pure trisaccharide derivatives were collected, and the intermediate, mixed fraction was rechromatographed to give chromatographically pure, desired products.

Compound **6**; yield 2.5 g (64.3%) had m.p. 147–149° (from methanol, plates), $[\alpha]_D$ —99° (Found: C, 49.63; H, 5.97. $C_{30}H_{42}O_{20}$ calc.: C, 49.86; H, 5.86%).

Compound **9**; yield 0.7 g, (18%), had m.p. 120–127° (from methanol, needles), $[\alpha]_D$ —4° (Found: C, 49.90; H, 5.77%).

Methyl 4-O-[3-O-(α- (**10**) *and β-D-xylopyranosyl)-β-D-xylopyranosyl]-β-D-xylopyranoside* (**7**). — The foregoing acetates **9** and **6** were deacetylated as described for the preparation of **3**, and the deacetylated products **10** and **7** were obtained chromatographically pure in theoretical yield [that they were not cross-contaminated could be checked by t.l.c. (solvent *C*, double development); compared with the acetates **6** and **9**, glycosides **7** and **10** showed reversed chromatographic mobilities]. Compounds **7** and **10** crystallized readily, but did not melt sharply, even after several recrystallisations.

Compound **7** had m.p. 197–204° (from methanol), $[\alpha]_D$ —82° (water); R_F 0.5 (Found: C, 44.96; H, 6.73. $C_{16}H_{28}O_{13}$ calc.: C, 44.86; H, 6.59%).

Compound **10** had R_F 0.45. It was dimorphous; crystallization from aqueous ethanol most frequently gave material having m.p. 218–223° and $[\alpha]_D$ +30.5 to

+31.5° (water). Occasionally, a double m.p. at 223–225 and 231–232° was observed, the latter material having $[\alpha]_D$ +31 to +32° (Found: C, 44.81; H, 6.54%).

Each of **7** and **10** (~200 mg) was dissolved in *N*,*N*-dimethylformamide (10 mL) and powdered sodium hydride (0.3 g) was added, followed after 15 min by methyl iodide (0.5 mL). The mixture was stirred at room temperature with the exclusion of atmospheric moisture and carbon dioxide for 2 h, diluted with water (10 mL), neutralized (pH 7.5) with 10% acetic acid, and partioned between cholroform and water. The chloroform solution was dried and evaporated with the addition of xylene to remove *N*,*N*-dimethylformamide. The crude product was eluted from a column of silica gel, to remove traces of undermethylated material (R_F <0.1, solvent *E*), to give chromatographically pure products (~85% yield).

Compound **8** had 106–107° (from isopropyl ether–hexane), $[\alpha]_D$ —83.6° (Found: C, 52.57; H, 7.92. $C_{23}H_{42}O_{13}$ calc.: C, 52.46; H, 8.06%).

Compound **11** had m.p. 64–65° (from isopropyl ether–hexane), $[\alpha]_D$ +14.2° (Found: C, 52.28; H, 7.81%).

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