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Note

Chemical synthesis of 2-*O*-(4-*O*-methyl-α-D-glucopyranosyluronic acid)-D-xylose*

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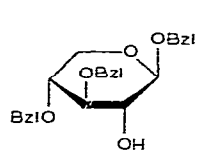
Xylans from gymnosperms are characterised by side-chains of 4-*O*-methyl-α-D-glucuronic acid linked to O-2 of D-xylose; 2-*O*-(4-*O*-methyl-α-D-glucopyranosyluronic acid)-D-xylose (**6**) has been isolated after partial hydrolysis of several xylans. A chemical synthesis of **6** has not been described, but stereoselective synthesis[2] of the methyl β-glycoside methyl ester **8**, using methyl 2,3-di-*O*-benzyl-1-chloro-1-deoxy-4-*O*-methyl-α,β-D-glucopyranuronate[2,3] (**2**) as the glycosylating agent, has been described. Also, the tetra-acetate (**9**) of **8** is identical[2] with the compound formulated[4] as an α-glycoside and obtained[5] by conversion of **6** of natural origin. We now report a chemical synthesis of **6**.



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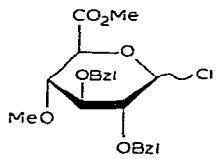

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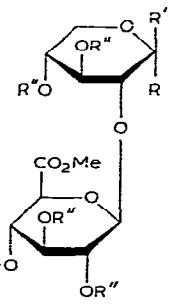
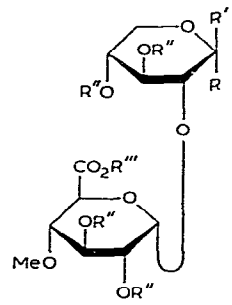
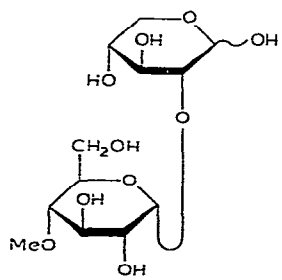


	R	R′	R″
3	H	OBzl	Bzl
7	HOH		H
11	H	OMe	H



	R	R′	R″	R‴
4	H	OBzl	Bzl	Me
5	HOH		H	Me
6	HOH		H	H
8	H	OMe	H	Me
9	H	OMe	Ac	Me



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*Synthesis and Reactions of Uronic Acid Derivatives, Part XXII. For Part XXI, see ref. 1.

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TABLE I

^{13}C-N.M.R. DATA FOR 5–8 AND 11 IN D_2O

Compound	*Ring*[a]	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*MeO-1*	*MeO-4*	*MeO-6*
5	C-α	90.8	77.8	72.1	70.7	61.9				
	C-β[b]	99.2	79.9	75.5	70.7	66.1				
	C′	98.0	72.1	73.2	82.5	70.7	173.2		61.1	54.4
6	C-α	90.9	77.8	72.2	70.8	61.9				
	C-β[b]	99.1	79.9	75.6	70.8	66.2				
	C′	98.0	72.2	73.4	82.9	70.8	174.4		61.3	
7	C-α[b]	93.2	82.3	73.1	70.6	62.0				
	C-β	96.7	83.3	76.9	70.6	66.4				
	C′[c]	105.3	74.3	76.0	82.6	74.2	172.4		61.5	54.7
8	C	105.6	79.1	75.4	70.7	66.1		58.6		
	C′	99.3	72.1	73.2	82.5	70.7	173.3		61.1	54.4
11	C	104.2	82.4	76.2	70.1	65.8		58.0		
	C′	103.8	74.4	75.8	82.4	74.4	172.1		61.2	54.5

[a]C, reducing end-unit; C′, non-reducing end-unit. [b]Preponderating anomer in equilibrated aqueous solution. [c]Splitting of C-1′ signal; the signal for C-1′ of the less-abundant β-form appears at 104.2 p.p.m.; the intensity ratio observed for these two resonances reflects the anomeric ratio present in the equilibrated aqueous solution.

The reaction of **2** with the readily obtainable[6] benzyl 3,4-di-*O*-benzyl-β-D-xylopyranoside (**1**) in the presence of silver perchlorate and triethylamine[3,7,8] yielded two products (**3** and **4**) which were isolated by chromatography. Catalytic hydrogenolysis of the benzyl groups from **3** and **4** gave the crystalline methyl esters **7** and **5**, respectively, in good overall yields. The α-linked compound **5** was saponified with aqueous sodium hydroxide, to give **6** which was indistinguishable (p.c.) from the product isolated[9,10] from wood xylans, and the $[\alpha]_D$ value of which, as expected, was the same as that of the equilibrium value observed for **5**. Treatment of the syrupy acid **6** with diazomethane regenerated crystalline **5**, which is a suitable derivative for the identification of **6**, previously characterised[2,5] as the tetra-acetate **9** or by laborious conversion[11] into **10**.

In addition to the mode of synthesis and $[\alpha]_D$ values for **3**–**7**, the structures of **5**–**7** are also indicated by their ^{13}C-n.m.r. spectra (Table I), the analysis of which was based on data for D-xylose[12], isomeric D-xylo-oligosaccharides[13], methyl (methyl 4-*O*-methyl-α-D-glucopyranosid)uronate[14], and synthetic model-compounds[2] **8** and **11**. The chemical-shift data for **5** and **6** are similar, the small differences being due to the lower pH of the solution of **6**. The difference in the ^{13}C-chemical shifts for the D-xylose residues of **5** and **7**, as compared with those for D-xylose, are consistent with the expected α- and β-effects arising from the 4-*O*-methyl-α- or -β-D-glucosyluronic acid group.

EXPERIMENTAL

General. — Melting points were determined on a Kofler hot-stage. Optical rotations (22°) were measured with a Perkin–Elmer Model 141 automatic polarimeter. ^{13}C-N.m.r. spectra (D_2O, internal MeOH) were recorded at ambient temperature with a WP-60 Bruker instrument in the deuterium-lock mode. Proton-decoupled F.t.-spectra were measured by using a repetition time of 1.1 s, a pulse-width of 3 μs (30°), 3750-Hz sweep-width, and 4k real data-points.

T.l.c. was performed on Silica Gel G and column chromatography on dry-packed Silica Gel 60 (equilibrated prior to packing with 40% of the mobile phase) with *A*, benzene–methyl acetate (12:1); *B*, benzene–acetone (30:1); and *C*, chloroform–methanol (6:1). Detection was effected by charring with sulfuric acid. The purity and identity of **6** was confirmed by t.l.c. on cellulose (Lucefol, Lachema, Brno) and by p.c. on Whatman No. 1 paper with *D*, ethyl acetate–acetic acid–water (18:7:8), and detection with aniline hydrogen phthalate. Dichloromethane was dried with phosphorus pentaoxide and distilled. The reactions involving silver perchlorate were performed with the exclusion of direct light and atmospheric moisture.

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

2-O-(Methyl 4-O-methyl-α- (**5**) *and -β-*D*-glucopyranosyluronate)-*D*-xylopyranose* (**7**). — Silver perchlorate (2.9 g, 14.3 mmol), followed by a solution of **2** in dichloromethane (0.2M, 71.5 ml), was added at −10° to a mixture of **1** (3 g, 7.15 mmol) and triethylamine (2.9 ml, 21.4 mmol) in dichloromethane (72 ml). The mixture was allowed to warm to ~20° and, after 0.5 h, t.l.c. (solvent *A*) showed the absence of starting materials. The mixture was diluted with chloroform, solid sodium hydrogencarbonate (2 g) was added, and, after being stirred for 5 min, the mixture was filtered. The filtrate was washed successively with M hydrochloric acid, saturated aqueous sodium hydrogencarbonate, dried, and concentrated, and the residue, t.l.c. of which revealed two main products (R_F 0.65 and 0.45, solvent *B*, double development), was subjected to column chromatography. The faster-moving product, containing mainly benzyl 3,4-di-*O*-benzyl-2-*O*-(methyl 2,3-di-*O*-benzyl-4-*O*-methyl-α-D-glucopyranosyl-uronate)-β-D-xylopyranoside (**4**), was collected and hydrogenolysed (methanol, 5% Pd/C). When the reaction was complete (t.l.c.), the mixture was filtered and concentrated, and the residue was crystallised from ethanol, to give **5** (1.48 g, 4.17 mmol, 58.8%), m.p. 174–176° (from ethanol), $[\alpha]_D$ +133 (extrapolated)→+127 (3.5 min)→+106° (90 min, equil.; *c* 0.6, water) (Found: C, 44.22; H, 6.14. $C_{13}H_{22}O_{11}$ calc.: C, 44.06; H, 6.26%).

Eluted second was benzyl 3,4-di-*O*-benzyl-2-*O*-(methyl 2,3-di-*O*-benzyl-4-*O*-methyl-β-D-glucopyranosyluronate)-β-D-xylopyranoside (**3**; 1.17 g, 1.46 mmol, 20%), m.p. 84–86°, $[\alpha]_D$ +33° (*c* 1, chloroform) (Found: C, 71.89; H, 6.67. $C_{48}H_{52}O_{11}$ calc.: C, 71.62; H, 6.51%). The total yield of the isolated condensation products was 79.3% (based on **1**), and the αβ-ratio was 2.9:1.

Catalytic debenzylation of **3** (0.59 g), as described above, gave **7** (0.25 g, 96.5%), m.p. 194–195.5° (from ethanol), $[\alpha]_D$ −12 (extrapolated)→−13 (3 min)→−14° (60 min, equil.) (Found: C, 44.20; H, 6.43. $C_{13}H_{22}O_{11}$ calc.: C, 44.06; H, 6.26%).

2-O-(4-O-Methyl-α-D-glucopyranosyluronic acid)-D-xylose (**6**). — M Sodium hydroxide (0.4 ml) was added at 0° to a solution of **5** (68 mg) in water (3 ml). After 30 min at room temperature, t.l.c. showed the absence of **5**. The solution was treated with Dowex 50W (H^+) resin and concentrated, to give amorphous **6** (57 mg, 88%), which was chromatographically homogeneous and indistinguishable from the aldobiouronic acid isolated[9,10] from wood hemicellulose (R_F 0.45, solvent *D*) and had $[\alpha]_D$ +104° (*c* 1.2, water). The literature $[\alpha]_D$ values[15] cover the range +70 to +110°.

A solution of **6** (50 mg) in water and methanol (1:2, 3 ml) was treated dropwise with ethereal diazomethane, with stirring, until a faint yellow colour persisted (1 min). T.l.c. (solvent *C*) then showed the presence of mainly **5**, together with a small proportion of material having the same chromatographic mobility as the β-glycoside **8** (R_F 0.5). The crude product was purified by chromatography, and **5** (40 mg, 77%) crystallised readily from ethanol; m.p. 174–176° (after recrystallisation).

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