SYNTHESIS OF METHYL 3,4-DI-O-(β-D-XYLOPYRANOSYL)-β-D-XYLOPYRANOSIDE, A METHYL β-XYLOTRIOSIDE RELATED TO BRANCHED XYLANS*

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The condensation of 2,3,4-tri-O-acetyl-α-D-xylopyranosyl bromide (*I*) with methyl 2-O-benzyl-β-D-xylopyranoside (*II*) afforded methyl 2-O-benzyl-3,4-di-O-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-β-D-xylopyranoside (*III*). Hydrogenolytic cleavage of the benzyl group from *III* and subsequent deacetylation led to the crystalline title methyl β-xylotrioside (*V*) related to branched xylans. Compound *V* was characterized by its crystalline per-O-acetate *VI* and per-O-methyl derivative *VII*.

Xylans are known to be the main type of noncellulose polysaccharides of hardwoods. Their main chain consists of 1→4-β-glycosidically linked D-xylopyranose units branched by a 1→2-α-glycosidically linked 4-O-methyl-D-glucuronic acid[1]. It follows from the methylation analysis that the main chain of xylans isolated from some species of plants[2] is branched by 1→3-β-glycosidically linked xylodextrins (1→4-β-glycosidically linked xylooligosaccharides). The partial hydrolysis of xylans affords, *inter alia*, a homologous series of xylodextrins; xylooligosaccharides, representing the branching site at $C_{(3)}$ of the fundamental backbone by xylose or xylodextrins, have so far not been isolated owing to the lack of chemical conditions of specific depolymerization or the lack of specific enzymes. This paper describes a simple synthesis (Scheme 1) of the branched methyl β-xylotrioside *V* representing the branching site at $C_{(3)}$ of xylans.

The starting material for the synthesis of glycoside *V* was the easily accesible 2,3,4-tri-O-acetyl-α-D-xylopyranosyl bromide[3] (*I*) and methyl 2-O-benzyl-β-D-xylopyranoside (*II*). The latter was obtained by deacetylation of the corresponding per-O-acetate[4] in a better overall yield from 2-O-benzyl-D-xylose, than originally reported[5].

Compounds *I* and *II* were condensed under conditions of Helferich modification[6,7] of the Königs–Knorr synthesis of glycosides using a 50% excess of the amount of bromide *I*, calculated for the total substitution of the hydroxyl groups in *II*.

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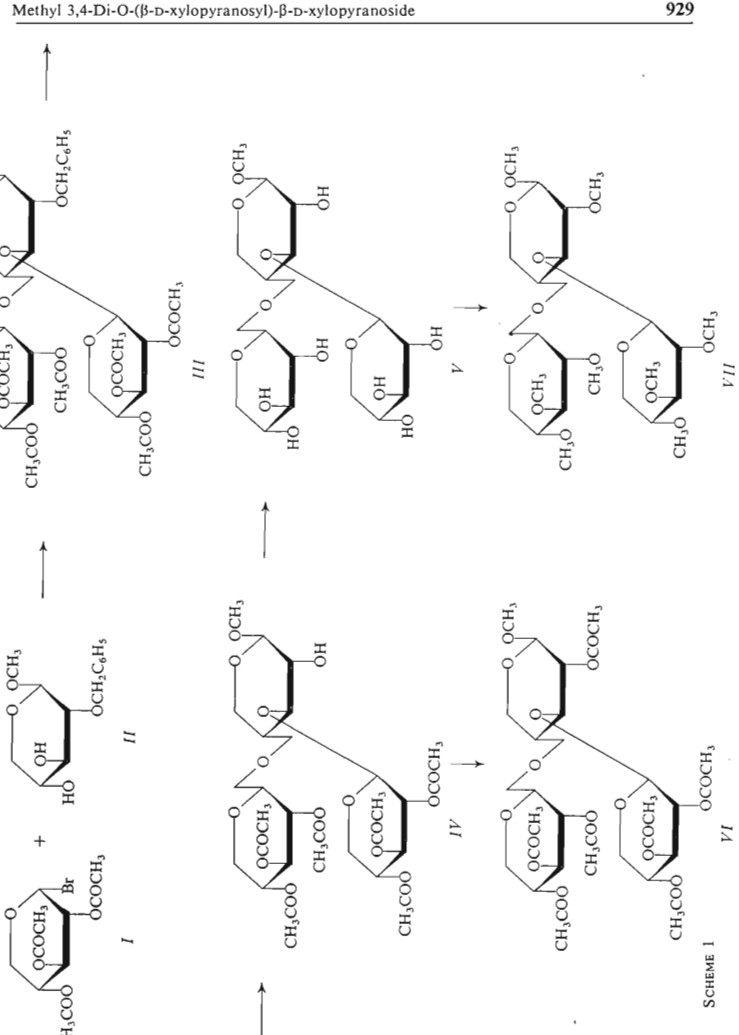

SCHEME 1

As shown by thin layer chromatography, the reaction was complete within 15 min and the trisaccharide derivative *III* could be isolated from the reaction mixture in approximately 60% yield by direct crystallization. In accordance with the presumed structure, the mass spectrum of *III* showed a little peak of molecular ions at *m/e* 770. The successive eliminations of acetic acid, benzyl alcohol and a methoxy radical from the molecular ions was reflected by the presence of intense peaks of ions $[M-CH_3COOH]^+$, $[M-{\cdot}OCH_3-2\,CH_3COOH]^+$ and $[M-{\cdot}OCH_3-2\,CH_3.\,.COOH-C_6H_5CH_2OH]^+$ at *m/e* 710, 619, and 511, respectively. The benzyl group in the molecule was proved by the appearance of intense peaks of tropylium ions at *m/e* 91, whereas the fully acetylated xylose units were revealed by peaks of ions of series *aA* and *cA* (for nomenclature see ref.[8]) at *m/e* 259, 217, 199, 157, 139 and 97. The configuration of the interglycosidic linkage (β-D-*xylo*) was deduced on the basis of the high negative value of specific rotation of product *III* and also basing on the fact that the same substance was isolated, although in a smaller yield, from condensation of *I* with *II* by the König–Knorr reaction in the presence of silver carbonate. As known[9,10], 1,2-*cis*-acylglycosyl halides react with alcohols under these reaction conditions with inversion of configuration at the anomeric centre of the glycosyl halide to form 1,2-*trans*-glycosides.

The hydrogenolytic splitting of the benzyl group from *III* furnished 2-hydroxy derivative *IV*, the acetylation of which afforded per-O-acetyl derivative *VI* of the title glycoside *V*. Its mass spectrum displayed, in agreement with the anticipated structure peaks at *m/e* 765 ($[M+CH_3CO]^+$, *cf.*[11]), 722 (M^+), 691 ($bacA_1$), 662 ($[M-CH_3COOH]^+$), 602 $[(M-2\,CH_3COOH]^+]$, 542 ($[M-3\,CH_3{-}COOH]^+$). The very abundant ions at *m/e* 259 were due to the presence of fully acetylated D-xylose unit in the molecule.

Deacetylation (according to Zemplén) of *IV* led to the desired crystalline methyl 3,4-di-O-(β-D-xylopyranosyl)-β-D-xylopyranoside (*V*), which upon methylation afforded the crystalline per-O-methyl derivative *VII*. The molecular weight of *VII* (526) was proved by calculation, using the *m/e* values of peaks associated with ions of series abA_1 and cA_1 present in the spectrum, according to equation[8]: $abA_1 + cA_1 + 16 = 335 + 175 + 16$. The presence of peaks at *m/e* 115, those of series $abcJ_1$ at *m/e* 395 and the presumed low intensity of bJ_1 series (the very weak peak at *m/e* 75), as well as the absence of peaks of ions bcJ_1 at *m/e* 235 were diagnostic of the 1→3 linkage between *b* and *c* units.

EXPERIMENTAL

Melting points were determined on a Kofler micro hot-stage. Optical rotations were measured with an automatic Perkin–Elmer, model 141, polarimeter, mass spectra (70 eV) with a Jeol JMS 100 D apparatus. For thin layer chromatography on Silica gel G (Merck) and preparative chromatography on Silica gel (Merck) following solvent systems were employed: benzene–acetone 3 : 1 (A), 6 : 1 (B) and chloroform–methanol 3 : 1 (C). Prior to dry packing into columns the

silica gel was conditioned with 40% of the mobile phase instead of the recommended 10% (ref.[12]). Solutions in organic solvents were dried with anhydrous sodium sulphate and, unless stated otherwise, concentrated at 40°C/2 kPa.

Methyl 2-O-Benzyl-β-D-xylopyranoside (*II*)

Methanolic 1M sodium methoxide (3 ml) was added to a solution of methyl 3,4-di-O-acetyl-2-O--benzyl-β-D-xylopyranoside (12·95 g, synthesized[4] from 2-O-benzyl-D-xylose, 15·2 g) in methanol (70 ml) and the mixture was allowed to stand at room temperature for 1 h; at this time a complete conversion of the starting material into the product was shown by TLC (R_F 0·9 and 0·3, respectively). The solution was then deionized with Dowex 50 W (H^+-form), filtered, concentrated and crystallized. Yield 8·65 g (53·8% based on 2-O-benzyl-D-xylose), m.p. 90—91·5°C (ether--heptane). Reported[5] m.p. 90—90·5°C for the substance obtained in a 32·8% yield by treatment of 2-O-benzyl-D-xylose with methanolic HCl.

Methyl 2-O-Benzyl-3,4-di-O-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-β-D-xylopyranoside (*III*)

a) 2,3,4-Tri-O-acetyl-α-D-xylopyranosyl bromide (*I*, 8·8 g, 26 mmol) was added to a mixture of glycoside *II* (2·2 g, 8·65 mmol), mercuric cyanide (3·28 g, 13 mmol) and drierite (5 g) in acetonitrile. After 15 min of stirring at room temperature with the exclusion of moisture, when TLC showed (solvent system B) the absence of both starting materials, sodium hydrogen carbonate (2 g) was added and the mixture stirred for another 15 min. The mixture was then filtered, the solid washed with benzene and the filtrate concentrated. The residue was partitioned between benzene and aqueous 1M solution of potassium bromide, the benzene layer was washed with water and concentrated to give the product *III* (4·15 g, 62%), m.p. 164—166°C (ethanol) in a chromatographically pure state. Recrystallization afforded the analytical sample, m.p. 164·5 to 165·5°C, $[\alpha]_D^{20}$ −73·8 (*c* 1, chloroform). For $C_{35}H_{46}O_{19}$ (770·7) calculated: 54·53% C, 6·01% H; found: 54·50% C, 6·02% H.

b) Substance *I* (4 g, 11·8 mmol) was added to a stirred mixture of glycoside *II* (1 g, 3·39 mmol), silver carbonate (1·63 g, 5·9 mmol), drierite (2·5 g) and iodine (0·1 g) in ethanol-free chloroform (10 ml). After 24 h of stirring with the exclusion of moisture, TLC (solvent system B) showed the presence of *III*, both starting materials and a considerable amount of the product of hydrolysis of bromide *I*. The mixture was worked up in a usual manner and the product chromatographed on a column of silica gel; yield 1·18 g (39%) of substance identical with *III* prepared by method *a*).

Methyl 3,4-Di-O-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-β-D-xylopyranoside (*IV*)

A mixture of *III* (3·0 g) and 5% palladium on charcoal (0·3 g) in acetone–methanol 1 : 1, (~100 ml) was stirred in a hydrogen atmosphere at room temperature until TLC (solvent system B) showed a total conversion of the starting material (R_F 0·6) to the product *IV* (R_F 0·4). After filtration and concentration, *IV* was crystallized from acetone–ethanol to yield 2·35 g (88·4%) of a chromatographically pure substance; m.p. 180—181°C (after recrystallization), $[\alpha]_D^{20}$ −108·7 (*c* 1·2, chloroform). For $C_{28}H_{40}O_{19}$ (680·6) calculated: 49·40% C, 5·92% H; found: 49·31% C, 5·94% H.

Acetylation with acetic anhydride in pyridine afforded per-O-acetate *VI*, m.p. 149·5—151·5°C, $[\alpha]_D^{20}$ −106 (*c* 1, chloroform). For $C_{30}H_{42}O_{20}$ (722·6) calculated: 49·86% C, 5·86% H; found: 49·68% C, 5·79% H.

Methyl 3,4-Di-O-(β-D-xylopyranosyl)-β-D-xylopyranoside (*V*)

0·1M Methanolic sodium methoxide (3 ml) was added to a suspension of *IV* (2 g) in methanol (40 ml) and the mixture was stirred at 40°C until the starting material dissolved (~10 min). The reaction was left at room temperature for 2 h at which time TLC (solvent system C) revealed the presence of product *V* (R_F 0·3) only. The solution was then concentrated to 10 ml, percolated through a layer (2 × 2 cm) of silica gel to remove the alkalinity and the sorbent was washed with a small volume of methanol. The methanolic solution was concentrated to afford the crystalline, chromatographically pure *V* (1·15 g, 90%), m.p. 216·5–217·5°C, $[\alpha]_D^{20}$ −78·2 (*c* 1, water). For $C_{16}H_{28}O_{13}$ (428·4) calculated: 44·85% C, 6·58% H; found 44·83% C, 6·60% H.

Methyl 2-O-Methyl-3,4-di-O-(2,3,4-tri-O-methyl-β-D-xylopyranosyl)-β-D-xylopyranoside (*VII*)

Sodium hydride (0·3 g) was added to a solution of *V* (0·25 g) in dimethylformamide (10 ml) and the mixture was stirred at room temperature for 10 min. Methyl iodide (0·5 ml) was added and the mixture stirred at about 15°C with the exclusion of moisture and CO_2 for 1 h. The mixture was diluted with water (10 ml), neutralized to pH 7 with dilute acetic acid, the product was extracted with chloroform and the organic solvents were removed at an elevated temperature with several additions of xylene. The syrupy product obtained in this way contained, according to TLC (solvent system C), mainly *VII* (R_F 0·5) and traces of the undermethylated material (R_F 0·1–0·2). Purification on silica gel column furnished the pure *VII* (0·22 g, 80·6%). M.p. 105–106°C (ether), $[\alpha]_D^{20}$ −104·8 (*c* 1·05, chloroform). For $C_{23}H_{42}O_{13}$ (526·6) calculated: 52·46% C, 8·04% H; found: 52·38% C, 8·00% H.

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