Synthesis of 2,4-di-O-β-D-xylopyranosyl-D-xylopyranose

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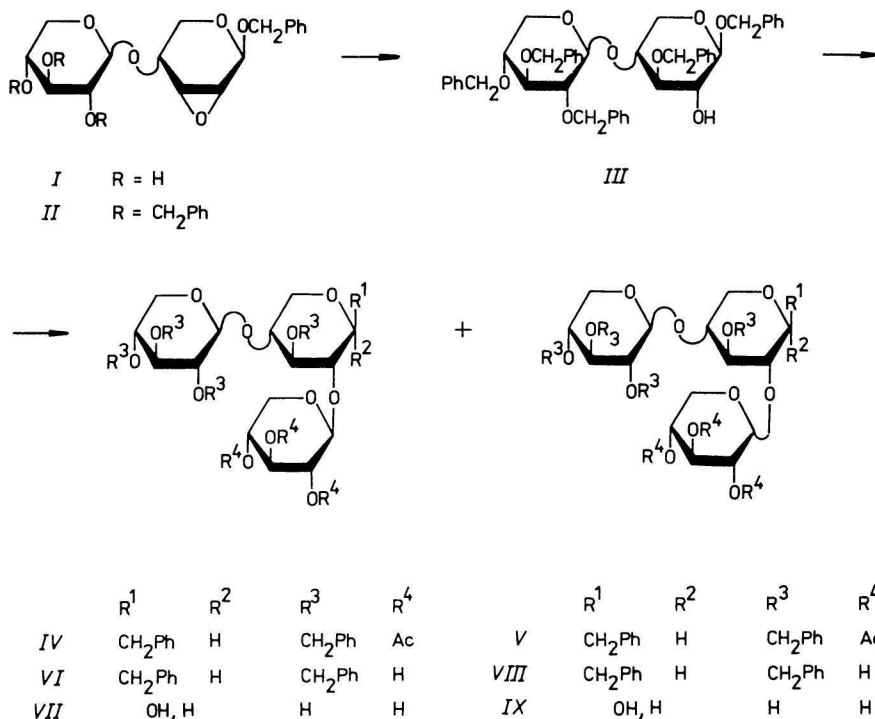*809 33 Bratislava*

Benzylation of benzyl 2,3-anhydro-4-O-β-D-xylopyranosyl-β-D-ribopyranoside followed by nucleophilic opening of the anhydro ring in the fully substituted product with benzyl alcoholate anion in benzyl alcohol gave benzyl 3,2',3',4'-tetra-O-benzyl-β-xylobioside. Treatment of the foregoing compound in acetonitrile with 2,3,4-tri-O-acetyl-α-D-xylopyranosyl bromide in the presence of mercuric cyanide afforded the β-linked trisaccharide as the main product ($\alpha:\beta = 2:7$). Removal of blocking groups by catalytic hydrogenolysis yielded then the title oligosaccharide. ^{13}C-N.m.r. spectral characteristics of the title trisaccharide and its 2-O-α-D-xylopyranosyl isomer are presented.

Бензилированием бензил-2,3-ангидро-4-O-β-D-ксилопиранозил-β-D--рибопиранозида и последующим открытием ангидро кольца в полностью замещенном продукте анионом бензилалкоголята в бензиловом спирте был получен бензил 3,2',3',4'-тетра-O-бензил-β-ксилобиозид. Конденсацией последнего в среде ацетонитрила с 2,3,4-три-O-ацетил-α-D-ксилопиранозилбромидом в присутствии цианистой ртути получили β-вязанный трисахарид в качестве главного продукта ($\alpha:\beta = 2:7$). Титулярный трисахарид был получен удалением блокирующих групп каталитическим гидрогенолизом. В работе приведены ^{13}C-ЯМР характеристики 2,4-ди-O-β-D-ксилопиранозил-D-ксилопиранозы и ее 2-O-α-D-ксилопиранозил изомера.

Xylan type polysaccharides containing a D-xylopyranosyl group at C-2 of certain D-xylose residues that form the main polysaccharide chain have been isolated from cell walls of some plants [1, 2]. The synthesis of 2-O-β-D-xylopyranosyl xylose, a disaccharide that represents the branching point of such a polysaccharide has been previously described [3]. We now report a synthesis (Scheme 1) of a related trisaccharide *VII*.

The starting point in the synthesis of *VII*, undertaken within systematic syntheses of D-xylooligosaccharides, was the readily obtainable [4], crystalline benzyl 2,3-anhydro-4-O-β-D-xylopyranosyl-β-D-ribopyranoside (*I*). Benzylation

	R¹	R²	R³	R⁴		R¹	R²	R³	R⁴
IV	CH₂Ph	H	CH₂Ph	Ac	V	CH₂Ph	H	CH₂Ph	Ac
VI	CH₂Ph	H	CH₂Ph	H	VIII	CH₂Ph	H	CH₂Ph	H
VII	OH, H		H	H	IX	OH, H		H	H

Scheme 1

of the foregoing substance with benzyl bromide and silver oxide in *N,N*-dimethyl-formamide under the conditions of benzylation of the corresponding methyl glycoside [5] afforded crystalline, fully substituted product *II*. Nucleophilic opening of the anhydro ring in *II* with benzyl alcoholate anion in benzyl alcohol gave crystalline derivative *III*, a nucleophile for the next glycosylation reaction. It is known [6] that in the reactions of alkyl 2,3-anhydro-β-D-ribopyranosides the attack of nucleophiles occurs regioselectively at C-3, and D-xylose derivatives are formed in high yields.

When compound *III* was allowed to react in acetonitrile with 2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl bromide [7] and mercuric cyanide the α- and β-linked trisaccharide derivatives *V* and *IV* were formed, the latter of which could be isolated without chromatography. Since the nucleophile *III* and the trisaccharide *V* show the same chromatographic mobilities, compound *V* could be obtained only from reactions carried out with a large excess of the glycosyl halide (3 equivalents). This assured complete reaction of *III*, verified by conventional processing and deacetylation (Zemplén) of a portion of the thus obtained reaction mixture and thin-layer chromatography (t.l.c.) on Silica gel G: no saccharide derivatives could

be detected in the region of chromatographic mobility of *III*. Since in these mixtures the only carbohydrate component not containing acetyl groups and, thus, not expected to react under the conditions of deacetylation was the nucleophile *III*, its conversion could be monitored by t.l.c. of the deacetylated reaction mixture. Chromatography of the material that remained in the mother liquor, after the main portion of *IV* had crystallized gave a further crop of *IV*, and also the α-linked trisaccharide derivative *V*. The title product *VII* was obtained by removal of blocking groups from *IV* by hydrogenolysis. Similar treatment of *V* afforded 2-*O*-α-ᴅ-xylopyranosyl-4-*O*-β-ᴅ-xylopyranosyl-ᴅ-xylopyranose (*IX*). The sequence of monosaccharides in *VII* and *IX* follows from the mode of the synthesis, and the stereochemistry of the newly-formed glycosidic linkages in *IV* and *V*, and thus also in the products of their further conversions, was tentatively assigned on the basis of specific optical rotations found for *IV* and *V* (see Experimental). The correctness of assignments done in this way was confirmed by ^{13}C-n.m.r. spectra of *VII* and *IX* (Table 1) the analysis of which was carried out with the aid of

Table 1

^{13}C-N.m.r. chemical shifts for model compounds and trisaccharides *VII* and *IX*

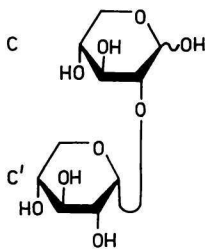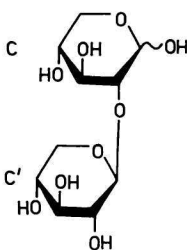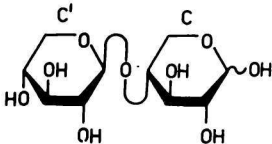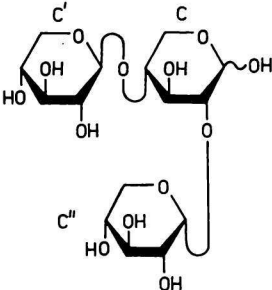| Compound	Ring	Chemical shift, p.p.m.[a]				
		C-1	C-2	C-3	C-4	C-5
	C-α	90.9	77.1	72.5	70.7	62.1
	C-β[b]	98.2	79.4	75.6	70.7	66.2
	C'-α	97.8	72.7	74.2	70.7	62.7
	C'-β	99.0				
	C-α[b]	93.1	81.9	73.0	70.4	61.7
	C-β	96.5	82.9	74.5	70.4	66.2
	C'-α	105.9	74.3	76.7	70.4	66.2
	C'-β	104.9				

Table 1 (Continued)

Compound	Ring	Chemical shift, p.p.m.[a]				
		C-1	C-2	C-3	C-4	C-5
	C-α	93.2	72.1[c]	72.6[c]	77.7	60.0
	C-β[b]	97.7	75.1	75.1	77.6	64.1
	C'	103.0	73.9	76.8	70.4	66.4
	C-α	90.8	77.3	70.7	78.0	60.2
	C-β[b]	98.1	79.5	73.8	78.0	64.1
	C'	103.2	74.1	76.9	70.5	66.5
	C''-α	98.1	72.8	74.1	70.7	62.8
	C''-β	99.2				
	C-α[b]	92.8	81.6	71.1	77.5	59.7
	C-β	96.4	82.9	73.9	77.5	63.9
	C'	103.0	73.9	76.8	70.4	66.3
	C''-α	105.8	74.3	76.8	70.4	66.3
	C''-β	105.0				

a) Internal standard methanol, δ_{TMS} 50.15 p.p.m.; b) more abundant form in equilibrated aqueous solution; c) the assignments may be reversed.

interpreted spectra of 2-O-α- and 2-O-β-D-xylopyranosyl-D-xylose [8] and 4-O-β-D-xylopyranosyl-D-xylose [8, 9], taking into account the ratio of anomers present in equilibrated aqueous solution, manifested by characteristic line intensities corresponding to carbon atoms of the reducing end-unit of the trisaccharides.

Experimental

Melting points were determined on a Kofler hot-stage. Optical rotations were measured with a Perkin—Elmer Model 141 automatic polarimeter. T.l.c. on Silica Gel G (Merck, A.G., Darmstadt) and column chromatography by continuous gradient elution from dry-packed columns of Silica Gel 60 (Merck, A.G., Darmstadt), conditioned prior to packing with 40% of the mobile phase, was performed with: *A*. carbon tetrachloride—acetone 30:1, *B*. carbon tetrachloride—acetone 15:1, *C*. benzene—acetone 30:1, *D*. benzene—acetone 15:1, *E*. carbon tetrachloride—ethyl acetate 6:1, *F*. carbon tetrachloride—ethyl acetate 8:1, and *G*. chloroform—methanol 15:1. Detection was effected by spraying with 5% (v/v) sulfuric acid in ethanol and heating until permanent char spots were visible. The purity of the final product *VII* was checked also by paper chromatography on Whatman No. 1 filter paper with *H*. ethyl acetate—pyridine—water 8:2:1, and detection with anilinium hydrogen phthalate.

^{13}C-N.m.r. spectra were measured in D_2O (25°C, internal standard methanol, δ_{TMS} 50.15 p.p.m.) using Jeol FX-60 spectrometer. The accumulations were done at a repetition time of 2 s, pulse width of 4 μs (45°), sweep width 4000 Hz and 8 K real data points. Solutions were dried with anhydrous sodium sulfate and concentrated at 40°C/2 kPa, unless stated otherwise.

Benzyl 2,3-anhydro-4-O-(2,3,4-tri-O-benzyl-β-D-xylopyranosyl)- *-β-D-ribopyranoside (II)*

Silver oxide (55 g) and benzyl bromide (55 ml) was added to a solution of *I* (10 g) in *N,N*-dimethylformamide (100 ml) and the mixture was stirred with the exclusion of direct light for 8 h. Fresh portion of reagents (20 g of Ag_2O and 20 ml of benzyl bromide) was added and the stirring was continued for 16 h. The mixture was diluted with chloroform (10 ml), filtered and the volatile components were distilled off, finally at 110°C/133 Pa. The residue was extracted with benzene, the extract was concentrated and crystallization from chloroform—ethanol (~1:2) gave chromatographically pure *II* (11 g), m.p. 105—106°C. The material in the mother liquor was chromatographed (solvents $A \rightarrow B$) to give a further amount of *II* (3.2 g, total yield 88.7%). Recrystallization of a portion from the same solvent afforded the analytical sample, m.p. 107—108°C, $[\alpha]_D^{22} = 0°$ (*c* 2, chloroform), $[\alpha]_D^{22} = -14.6°$ (*c* 1.5, pyridine).

For $C_{38}H_{40}O_8$ (624.70) calculated: 73.05% C, 6.45% H; found: 72.80% C, 6.32% H.

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

Sodium hydride (3.5 g) was added slowly, with the exclusion of atmospheric moisture and carbon dioxide, to stirred benzyl alcohol (100 ml), and the mixture was stirred under these conditions until clear solution was formed. After addition of *II* (10 g), the mixture was

heated at 90—100°C for 5 h, diluted with ethanol (200 ml) and deionized with Dowex 50 W (H^+) resin. The filtrate was concentrated to yield a sirup containing mainly *III*, as shown by t.l.c. (R_f 0.6, *cf.* 0.55 for the starting material, solvent *D*). Chromatography of the crude product on a column of silica gel (solvents $C \rightarrow D$) gave *III* (9.1 g, 77%). Crystallization from ether—hexane (twice) afforded the analytical sample melting at 90—92°C and showing $[\alpha]_D^{22} = -40.6°$ (*c* 1, chloroform).

For $C_{45}H_{48}O_9$ (732.83) calculated: 73.74% C, 6.60% H; found: 73.80% C, 6.30% H.

Benzyl 3-O-benzyl-2-O-(2,3,4-tri-O-acetyl-α- (V) and -β-D-xylopyranosyl)-4-O-(2,3,4-tri-O-benzyl--β-D-xylopyranosyl)-β-D-xylopyranoside (IV)

To a mixture of *III* (1.5 g; 2.04 mmol) and mercuric cyanide (0.76 g; 3.06 mmol) in acetonitrile (20 ml) was added 2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl bromide (2.1 g; 6.12 mmol) and the mixture was stirred with the exclusion of atmospheric moisture for 1/2 h. The mixture was processed in the usual manner [10] and crystallization from methanol gave benzyl 3-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-4-*O*-(2,3,4-tri-*O*-benzyl-β-D-xylopyranosyl)-β-D-xylopyranoside (*IV*, 0.9 g), m.p. 126—127°C and $[\alpha]_D^{22} = -51.2°$ (*c* 1, chloroform), after recrystallization from the same solvent (R_f 0.3, solvent *E*).

For $C_{56}H_{62}O_{16}$ (991.05) calculated: 67.86% C, 6.30% H; found: 68.07% C, 6.22% H.

A further crop of *IV* (0.5 g, total yield of *IV* 70%, based on the amount of *III*) and also benzyl 3-*O*-benzyl-2-*O*-(2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl)-4-*O*-(2,3,4-tri-*O*-benzyl--β-D-xylopyranosyl)-β-D-xylopyranoside (*V*, 0.4 g, 20%, R_f 0.4, *cf.* 0.4 for the starting material *III*, solvent *E*) was obtained by chromatography on silica gel (solvents $F \rightarrow E$) of the material that remained in the mother liquor, after the bulk of *IV* had been crystallized. Crystallization from methanol—ether (twice) gave the analytical sample of *V*, m.p. 83—85°C, $[\alpha]_D^{22} = +3.2°$ (*c* 0.95, chloroform).

Found: 67.86% C, 6.46% H.

Benzyl 3-O-benzyl-4-O-(2,3,4-tri-O-benzyl--β-D-xylopyranosyl)-2-O-β-D-xylopyranosyl--β-D-xylopyranoside (VI)

Methanolic 1 mol l^{-1} sodium methoxide in methanol was added to a mixture of *IV* (1 g) in methanol (50 ml) to strong alkalinity. After 1/2 h at room temperature, at which time the product started to crystalize, the mixture was diluted with benzene and t.l.c. of the homogeneous solution showed that the reaction was complete, and that only *VI* was present (R_f 0.6, solvent *G*). The mixture was deionized with Dowex 50 W (H^+) resin, filtered, concentrated, and the residue was crystallized from ethanol to give pure *VI* (0.8 g, 91.9%), m.p. 169.5—171°C, $[\alpha]_D^{22} = -40.2°$ (*c* 1, chloroform).

For $C_{50}H_{56}O_{13}$ (864.95) calculated: 69.42% C, 6.52% H; found: 69.74% C, 6.57% H.

2,4-Di-O-β-D-xylopyranosyl-D-xylopyranose (VII)

A mixture of *VI* (3.6 g) and 5% palladium-on-charcoal catalyst (0.7 g) in acetone—ethanol (1 : 2, 150 ml) was stirred at room temperature in a hydrogen atmosphere. When the reaction was complete (~ 1 h), as shown by t.l.c. (solvent *G*), the mixture was processed conventionally and the chromatographically pure product (R_{xyl} 0.3, solvent *H*) was lyophilized to give pure *VII* (1.7 g, 98.8%) as a white amorphous powder, $[\alpha]_D^{22} = +26°$ (*c* 1, water). Its ^{13}C-n.m.r. spectrum did not contain signals indicating the presence of impurities.

Benzyl 3-O-benzyl-4-O-(2,3,4-tri-O-benzyl--β-D-xylopyranosyl)-2-O-α-D-xylopyranosyl--β-D-xylopyranoside (VIII)

Compound *V* (0.4 g) was deacetylated as described in the preparation of *VI*. After conventional processing and crystallization from ether—methanol compound *VIII* (0.3 g, 86%) melted at 161—163°C and had $[\alpha]_D^{22} = +3.2°$ (*c* 0.96, chloroform, after recrystallization from the same solvent).

For $C_{50}H_{56}O_{13}$ (864.95) calculated: 69.42% C, 6.52% H; found: 69.25% C, 6.51% H.

2-O-α-D-xylopyranosyl-4-O-β-D-xylopyranosyl--D-xylopyranose (IX)

Compound *VIII* (0.2 g) was hydrogenated as described in the preparation of *VII* and the product (0.09 g, 94%) was lyophilized to give *IX*, $[\alpha]_D^{22} = +69.4°$ (*c* 0.96, water). The substance was chromatographically pure (R_{xyl} 0.3, solvent *H*) and its ^{13}C-n.m.r. spectrum did not contain signals indicating impurities.

References

1. Banerji, N., Murty, V. L. N., and Mukherjee, A. K., *Indian J. Chem. 3,* 457 (1965).
2. Tomoda, M. and Tanaka, M., *Chem. Pharm. Bull. 21,* 989 (1973).
3. Kováč, P. and Petráková, E., *Chem. Zvesti 34,* 537 (1980).
4. Kováč, P., *Chem. Zvesti 33,* 365 (1979).
5. Kováč, P., *J. Carbohyd. Nucleosides, Nucleotides 4,* 165 (1977).
6. Guthrie, R. D., in *The Carbohydrates: Chemistry and Biochemistry,* Vol. IA. (Pigman, W. and Horton, D., Editors.) Pp. 423—478. Academic Press, New York, 1972.
7. Schroeder, L. R., Counts, K. M., and Haigh, F. C., *Carbohyd. Res. 37,* 368 (1974).
8. Petráková, E. and Kováč, P., *Chem. Zvesti,* in press.
9. Gast, J. C., Atalla, R. H., and McKelvey, R. D., *Carbohyd. Res. 84,* 137 (1980).
10. Helferich, B. and Ost, W., *Chem. Ber. 95,* 2616 (1962).

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