Chemical synthesis of xylotriose (4-*O*-(4-*O*-β-D-xylo-pyranosyl-β-D-xylopyranosyl)-D-xylopyranose)

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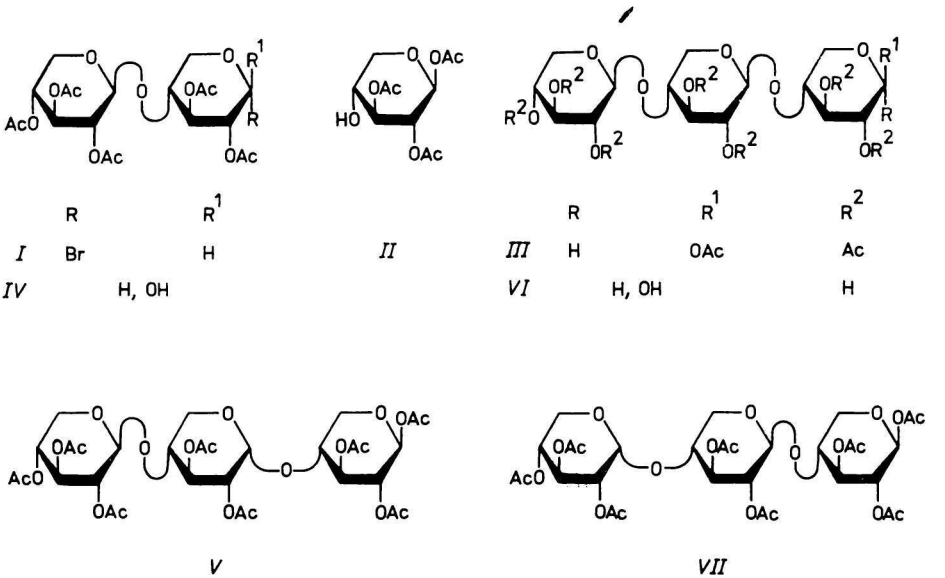
Condensation of penta-*O*-acetylxylobiosyl bromide with 1,2,3-tri-*O*-acetyl-β-D-xylopyranose gave octa-*O*-acetyl-β-xylotriose, and its deacetylation yielded xylotriose. ^{13}C-N.m.r. spectrum of octa-*O*-acetyl-β-xylotriose is compared with spectra of acetates of two other, isomeric, (1→4)-linked D-xylotrioses.

Конденсацией пента-*O*-ацетилксилобиозилбромида с 1,2,3-три-*O*-ацетил-β-D-ксилопиранозой была получена окта-*O*-ацетил-β-ксилотриоза и ее деацетилированием ксилотриоза. Спектры ^{13}C-ЯМР окта-*O*-ацетил-β-ксилотриозы сравниваются со спектрами ацетатов двух изомерных (1→4)-D-ксилотриоз.

β-(1→4)-D-Xylooligosaccharides (xylodextrins) are important model compounds in studies of various properties of natural xylan type polysaccharides. Their preparation by partial hydrolysis of xylans and separation of hydrolyzate components by chromatography is tedious and affords the desired products, especially higher oligosaccharides in low yields only. Until recently, of the xylodextrin series only xylobiose [1—4] has been chemically synthesized. Within a systematic synthesis of xylooligosaccharides we have carried out a sequential synthesis of lower xylodextrins including xylotriose [5], using 2,3-di-*O*-acetyl-4-*O*-benzyl-D-xylopyranosyl bromide as the glycosylating agent. Now we report on an alternative approach to the preparation of xylotriose, namely, using as a glycosylating agent the halide derived from the easily available [4] xylobiose per-*O*-acetate. The same glycosyl halide was successfully used [6] in the synthesis of methyl β-xylotrioside.

Condensation of penta-*O*-acetylxylobiosyl bromide (*I*) with 1,2,3-tri-*O*-acetyl-β-D-xylopyranose (*II*) [7] was performed using mercuric cyanide as a catalyst and hydrogen bromide scavenger. Owing to side reactions of the highly reactive *I* [6] its threefold molar excess had to be used to make the nucleophile *II* react completely. From the complicated reaction mixture the desired β-xylotriose per-*O*-acetate *III* was isolated in ~51% yield, together with a large amount of

crystalline hydroxy derivative *IV*, the hydrolysis product of *I*. Compound *IV* is an intermediate in the synthesis of xylobiose [4] but has not been isolated and characterized thus far. In addition to *III* and *IV* a small amount of a substance, moving on t.l.c. slightly faster than *III*, was also isolated. In analogy with products of similar reactions [5] we have assumed that the substance could be the α isomer of *III*, namely, the trisaccharide *V*, having the acetate of xylobiose linked α-glycosidically to 1,2,3-tri-*O*-acetyl-β-D-xylopyranose (see formula *V* in Table 1). Compared with *III*, compound *V* showed a more positive specific optical rotation ($-13.5°$ *vs.* $-84.8°$) and, in agreement with the assumed structure *V*, its ^{13}C-n.m.r. spectrum showed, *inter alia*, intense lines in the region of anomeric resonances at 99.3, 96.4, and 91.9 p.p.m. (C-1″, C-1′, and C-1). The signals for C-5 were at 64.2, 61.3, and 59.4 p.p.m. (C-5, C-5″, and C-5′). The chemical shifts of anomeric and C-5 carbon nuclei, taking into account the shift effects of substituents at the neighbouring carbon atoms, are diagnostic for the assignment of anomeric configurations [8], that is of the stereochemistry of the interglycosidic linkages in oligosaccharides (Scheme 1). The ^{13}C-n.m.r. spectral data for the synthesized substances and model compounds [5, 7] used as an aid in the assignments are in Table 1. A comparison of the spectra of *III* and *V* with that of an isomeric D-xylotriose per-*O*-acetate *VII* shows that the diagnostically important regions in the spectra of these substances differ sufficiently to permit the use of the given data in sequential linkage analysis of related structures.



Scheme 1

As shown by its ^{13}C-n.m.r. spectrum, 2,3-di-*O*-acetyl-4-*O*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-D-xylopyranose (*IV*) was isolated as a mixture of α and β forms of which the former was the preponderating one (approximate α:β ratio, 2:1). The carbon-signal assignments in the spectrum of this substance were done taking into account the line intensities, and chemical shifts in the spectra of 2,3-di-*O*-acetyl-4-*O*-benzyl-α,β-D-xylopyranose [7] and acetates of homologous series of xylodextrins [5].

The desired xylotriose hexa-*O*-acetate *III* crystallized readily from methanol and less readily from the recommended [11] mixture of ethyl acetate—hexane, but a sharply melting material [9—11] could not be obtained from either solvent. The purity and identity of the substance with the described compound is proved by the excellent agreement of the specific optical rotation found for *III* with the literature values. The same follows from the ^{13}C-n.m.r. spectrum of the substance which was fully interpretable with the aid of analyzed spectra of similar oligosaccharides [5]. We are unable to explain the discrepancy between the found melting point and the one given in the literature. It should be noted, however, that β-xylotriose hexa-*O*-acetate [5] prepared in an independent manner had the same specific optical rotation as the substance described herein and it did not show a sharp melting point either.

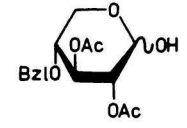
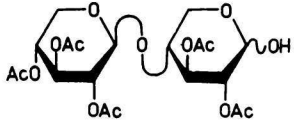
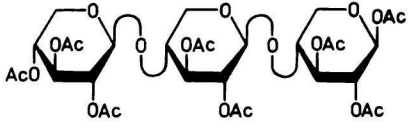
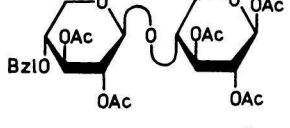
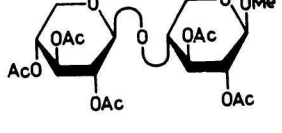
Deacetylation of *III* yielded xylotriose (*VI*). Crystallization from 90% ethanol (recommended solvent [12]) gave material showing higher melting point than that given in the literature [9, 11—13]. Since the specific optical rotation found for an equilibrated solution of *VI* was in excellent agreement with the data in the literature, the difference between the found and the reported melting points may be caused by different anomeric composition of the two products, or by polymorphism of the substance. The ^{13}C-n.m.r. spectrum of *VI* (Table 1) was virtually identical to the recently published spectrum of xylotriose of natural origin [14]. The small differences in the chemical shifts found for the individual carbon atoms are associated with different conditions of measurements.

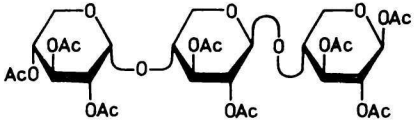
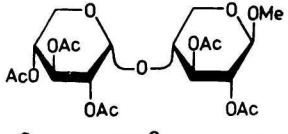
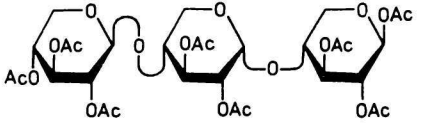
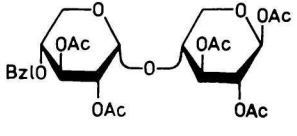
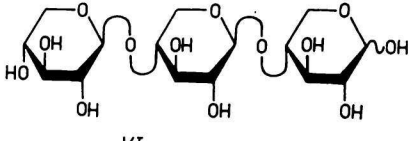
Experimental

Melting points were determined on a Kofler hot-stage. Optical rotations were measured with a Perkin—Elmer automatic polarimeter, Model 141. Thin-layer chromatography (t.l.c.) on Silica Gel G (Merck, A.G., Darmstadt) and preparative chromatography by gradient elution from columns of dry-packed Silica Gel 60 (Merck, A.G., Darmstadt), were performed with chloroform—ethyl acetate; *A*. 10:1, *B*. 8:1. Detection was effected with 5% (v/v) sulfuric acid in ethanol and heating until permanent char spots were visible.

Table 1

^{13}C-NMR chemical shifts of the studied substances and model compounds

Compound	Solvent	Ring[a]	Chemical shift (δ, p.p.m.)				
			C-1	C-2	C-3	C-4	C-5
	$CDCl_3$	C-α[b]	90.1	71.2	71.6	75.4	59.4
		C-β	95.5	73.2	73.7	75.1	63.8
	$CDCl_3$	C-α[b]	90.1	70.3	71.5	75.2	58.7
		C-β	95.6	72.7	73.0	75.2	63.2
		C′	99.5	70.3	70.3	68.4	61.3
IV							
	$CDCl_3$	C	92.2	69.8	72.0	74.9	63.4
		C′	100.4	71.0	72.0	74.5	62.7
		C″	99.6	70.3	70.3	68.3	61.5
III							
	$CDCl_3$	C	92.2	69.7	72.1	74.3	63.4
		C′	100.5	71.1	72.9	74.9	63.4
	$CDCl_3$	C	102.0	71.3	72.6	75.1	62.9
		C′	99.7	70.4	70.4	68.4	61.6

	$CDCl_3$	C	92.1	69.7	71.9	74.7	63.4
		C′	100.2	70.8	72.8	73.2	63.4
		C″	96.3	71.2	69.0	69.0	58.8
VII							
	$CDCl_3$	C	101.7	71.5	73.1	73.9	63.8
		C′	96.2	70.8	69.1	69.1	58.7
	$CDCl_3$	C	91.9	69.5	72.8	73.0	64.2
		C′	96.4	69.9	70.9	74.9	59.4
		C″	99.3	70.2	70.2	68.2	61.3
V							
	$CDCl_3$	C	91.9	70.2	72.5	73.4	64.3
		C′	96.4	70.7	71.0	75.2	60.0
	D_2O	C-α	93.2	72.2	72.6	77.6	60.2
		C-β[b]	97.8	75.1	75.0	77.6	64.3
		C′	103.0	73.9	75.0	77.6	64.3
		C″	103.0	73.9	76.9	70.4	66.5
VI							

a) C — reducing residue; C′ — nonreducing residue in disaccharides, or internal residue in trisaccharides; C″ — nonreducing residue in trisaccharides.

b) Preponderating anomer.

Noise-decoupled ^{13}C-n.m.r. spectra we measured for solutions in $CDCl_3$ (internal standard TMS) and D_2O (internal standard methanol, δ_{TMS} 50.15 p.p.m.), with a Jeol JNM FX-60 spectrometer. Solutions in organic solvents were dried with anhydrous sodium sulfate, and concentrated at 40°C/2 kPa.

1,2,3-Tri-O-acetyl-4-O-[2,3-di-O-acetyl-4-O-(2,3,4-tri-O--acetyl-β-D-xylopyranosyl)-β-D-xylopyranosyl]-β-D-xylopyranose (III)

A solution of bromide *I* in acetonitrile (freshly prepared [6] from hexa-*O*-acetyl-β--xylobiose (7.25 g; 13.56 mmol)) was added into a mixture of 1,2,3-tri-*O*-acetyl-β-D-xylopyranose (*II*) (1.25 g; 4.52 mmol) and mercuric cyanide (1.7 g; 6.73 mmol) in acetonitrile (25 ml), and the mixture was stirred at room temperature and with the exclusion of atmospheric moisture for 30 min. A complicated reaction mixture had been formed, and the following compounds were identified by t.l.c.: the starting material *II* (R_f 0.2), the desired product *III* (R_f 0.45), its α analogue *V* (R_f 0.5), and the product *IV* (R_f 0.4) of hydrolysis of *I*. Conventional processing and chromatography (solvent $A \rightarrow B$) yielded in a chromatographically pure state:

Compound *V* (0.32 g, 9.42%), which could not be crystallized, $[\alpha]_D^{21} = -13.5°$ (*c* 1, chloroform).

For $C_{31}H_{42}O_{21}$ (750.65) calculated: 49.60% C, 5.64% H; found: 49.38% C, 5.57% H.

Compound *III* (1.75 g, 51.52%), m.p. 109—115°C (from methanol), $[\alpha]_D^{21} = -84.8°$ (*c* 1, chloroform). Ref. [9] gives m.p. 109—110°C, $[\alpha]_D = -85°$, Ref. [10] m.p. 109—110°C, $[\alpha]_D = -85°$, Ref. [11] m.p. 108—109.5°C, $[\alpha]_D = -83.5°$.

Compound *IV*, m.p. 173—176°C (from ethanol), $[\alpha]_D^{21} = -47°$ (*c* 1, chloroform).

For $C_{20}H_{28}O_{14}$ (492.42) calculated: 48.78% C, 5.73% H; found: 48.72% C, 5.87% H.

4-O-(4-O-β-D-Xylopyranosyl-β-D-xylopyranosyl)-D-xylopyranose (VI)

Deacetylation (Zemplén) of *III* (1.5 g) and conventional processing gave *VI* (0.67 g, 81%, from 90% ethanol), m.p. 222—224°C. Recrystallization from methanol gave material melting at 217—219°C, and the original optical rotation, $[\alpha]_D^{21} = -47.7°$ (*c* 1, water, equil.), remained practically unchanged. Ref. [9] gives m.p. 204—205°C, $[\alpha]_D^{25} = -44.4°$, Ref. [11] m.p. 215—216°C, $[\alpha]_D = -48.1°$, Ref. [12] m.p. 205—206°C, $[\alpha]_D = -47°$, Ref. [13] m.p. 214°C, $[\alpha]_D^{22} = -48°$.

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