Carbohydrate Research, 106 (1982) 203–216
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

AN APPROACH TO THE SYSTEMATIC SYNTHESIS OF (1→4)-β-D-XYLO-OLIGOSACCHARIDES*

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(Received October 19th, 1981; accepted for publication December 21st, 1981)

ABSTRACT

The first approach to a general synthesis of (1→4)-β-D-xylo-oligosaccharides is described. Thus, 1,2,3-tri-*O*-acetyl-4-*O*-benzyl-β-D-xylopyranose was treated with hydrogen bromide in dichloromethane to give the corresponding glycosyl bromide **3**, which was condensed with 1,2,3-tri-*O*-acetyl-β-D-xylopyranose. The β-linked disaccharide formed, bearing at O-4 of its non-reducing end the selectively removable benzyl group, was submitted to hydrogenolysis to afford a disaccharide nucleophile **21**, having HO-4′ free, which was again treated with **3**. This sequence of reactions was repeated two more times and the isolated products **17**–**20** were deprotected to give a homologous series of lower xylo-oligosaccharides (from the disaccharide to the pentasaccharide), demonstrating thus the feasibility of stepwise construction of xylo-oligosaccharide molecules. The corresponding α-linked oligosaccharides **5**–**8**, present in the mixtures from the condensation reactions, were also isolated and characterized. ^{13}C-N.m.r. spectral characteristics for six homologous series of variously substituted (1→4)-D-xylo-oligosaccharides are presented.

INTRODUCTION

(1→4)-β-D-Xylo-oligosaccharides are found among products of partial hydrolysis of xylans from hardwoods[2]. Their isolation by chromatography is tedious and affords the desired products, particularly xylotriose and higher oligosaccharides, in only low yields. Several syntheses of the lowest member of the series of xylo-oligosaccharides, xylobiose, have been described in the literature[3–6] and very recently[7] we have reported the first chemical synthesis of xylotriose. None of the procedures cited can be extended to the synthesis of higher (1→4)-β-D-xylo-oligosaccharides.

One possibility for a general synthesis of xylo-oligosaccharides constitutes a stepwise construction (sequential synthesis) of the desired oligosaccharide molecule by Koenigs–Knorr reaction. It requires a D-xylosyl halide substituted at positions 2 and 3 with "permanent" blocking groups R and having at position 4 a protecting

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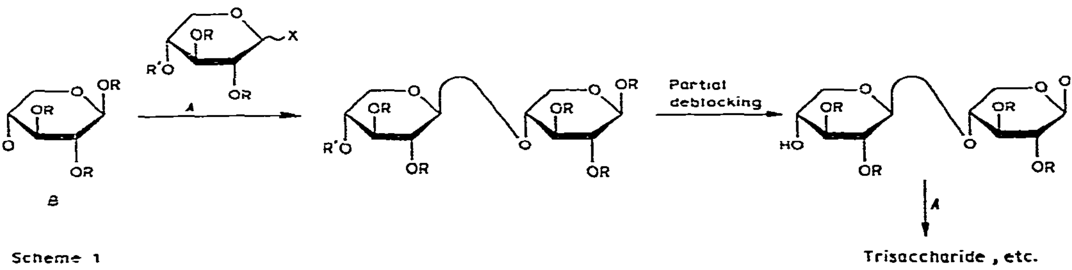
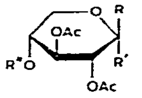
group R′ that may be removed selectively (*A*-type halide). Condensation of *A* with a D-xylose derivative having only HO-4 unsubstituted, for example a nucleophile of type *B*, followed by selective removal of the 4-substituent, would yield a product suitable for another condensation with the same halide (Scheme 1). Theoretically, this approach has no limitations, and its practical limitation lies in the yields of the desired products and the availability of methods for their isolation. In the present work, we describe sequential synthesis of lower xylo-oligosaccharides (from the disaccharide to the pentasaccharide) and thus report for the first time an approach to a general synthesis of (1→4)-β-D-xylo-oligosaccharides. Also presented are ^{13}C-n.m.r. spectral characteristics of six homologous series of variously substituted (1→4)-D-xylo-oligosaccharides prepared through this work.



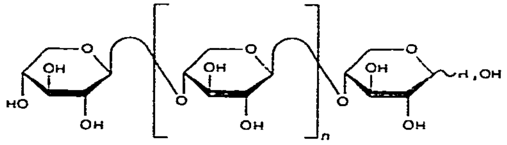
Scheme 1

RESULTS AND DISCUSSION

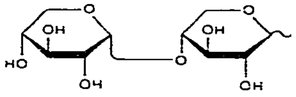
Synthesis. — An important factor in the strategy of chemical synthesis of higher oligosaccharides having the desired anomeric configurations and positions of the inter-sugar linkages is the selection of blocking groups in the molecules reacting. Properly chosen blocking groups in the glycosyl halide and the nucleophile should assure formation of the glycosidic linkage only at the desired position and they should allow for several cycles of selective partial deblocking, leading to nucleophiles suitable for further condensations. Also, the blocking groups should be easily removable when the construction of the desired oligosaccharide chain-length has been achieved. In the D-xylose series, these requirements are satisfied by 2,3-di-*O*-acetyl-4-*O*-chloroacetyl-α-D-xylopyranosyl bromide[8] (**1**) (as a suitable *A*-type D-xylosyl halide) and 1,2,3-tri-*O*-acetyl-β-D-xylopyranose (**2**) (as a *B*-type nucleophile, Scheme 1). However, bromide **1** cannot be prepared without recourse to chromatography during the isolation of several of its precursors and, therefore, its large-scale preparation as required for the sequential synthesis of homo-oligosaccharides, is impractical. In the syntheses of xylo-oligosaccharides described here, 2,3-di-*O*-acetyl-4-*O*-benzyl-α,β-D-xylopyranosyl bromide (**3**) is used as a glycosylating agent and the acetate **2** as the basic nucleophile. Compounds **2** and **3** can both be prepared from one starting material, namely, 1,2,3-tri-*O*-acetyl-4-*O*-benzyl-β-D-xylopyranose[9] (**4**), on the centigram scale in excellent yields, without chromatographic isolation of any intermediates. The condensation reactions were performed in acetonitrile with mercuric



	R	R′	R″
1	H	Br	ClCH$_2$CO
2	OAc	H	H
3		H,Br	Bzl
4	OAc	H	Bzl

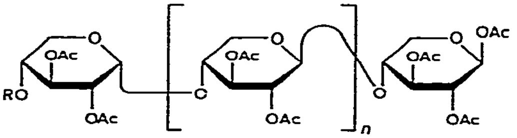


	n	Series
29	0	VII
30	1	VII
31	2	VII
32	3	VII

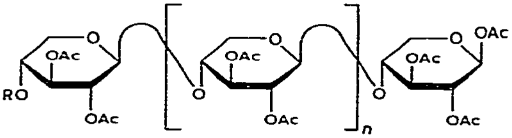


33

cyanide as the catalyst and hydrogen bromide as scavenger, and the α- and β-linked oligosaccharide derivatives formed were isolated by gradient elution from columns of silica gel. When 2–3 molar proportions of **3** were used, the nucleophiles reacted almost completely. The β-linked oligosaccharide was invariably the main product, and the stereoselectivity of formation of the oligosaccharide ($\alpha:\beta \approx 1:1.5$) did not appear to be affected by the chain-length of the nucleophile, as judged by t.l.c. and the isolated yields of pairs of α and β anomers. The configuration at the newly formed interglycosidic linkage in the pairs of compounds **5** and **17**, **6** and **18**, **7** and **19**, and **8** and **20**, tentatively assigned on the basis of specific optical rotation, was confirmed by ^{13}C-n.m.r. spectroscopy (see later). On thin-layer chromatograms, the α-linked oligosaccharide derivatives **5–8** migrated invariably somewhat faster than their β-linked counterparts **17–20**. With the elongation of the oligosaccharide chain, the resolution of the α,β-pairs of products became worse and, in order to distinguish satisfactorily between the pairs of tetrasaccharides **7** and **19** and pentasaccharides **8** and **20**, multiple development of chromatograms was necessary. Therefore, the yields of pure products isolated depended largely upon the efficiency of preparative separation by column chromatography (in some runs, repeated chromatography was necessary).



	n	R	Series
5	0	Bzl	IV
6	1	Bzl	IV
7	2	Bzl	IV
8	3	Bzl	IV
9	0	H	V
10	1	H	V
11	2	H	V
12	3	H	V
13	0	Ac	VI
14	1	Ac	VI
15	2	Ac	VI
16	3	Ac	VI



	n	R	Series
17	0	Bzl	I
18	1	Bzl	I
19	2	Bzl	I
20	3	Bzl	I
21	0	H	II
22	1	H	II
23	2	H	II
24	3	H	II
25	0	Ac	III
26	1	Ac	III
27	2	Ac	III
28	3	Ac	III

The β-linked oligosaccharides **17–20** isolated were submitted to hydrogenolysis, to remove benzyl groups from their terminal nonreducing D-xylosyl groups, and the nucleophiles **21–24** so obtained were treated again with **3**. Oligosaccharides **5–8** were debenzylated similarly and, eventually, by acetylation of **21–24**, and **9–12**, and complete deprotection of the β-linked products, seven homologous series of (1→4)-D-xylo-oligosaccharides were prepared:

Series I: were peracetates of the title β-oligosaccharides having a benzyl group at O-4 of the terminal, nonreducing end-unit (**17–20**);

Series II: were oligosaccharides analogous to those in Series I, but having at C-4 of the terminal non-reducing end-group a hydroxyl group (**21–24**);

Series III: were the peracetates of the title β-oligosaccharides (**25–28**);

Series IV: where oligosaccharides analogous to those in Series I, but containing as the terminal non-reducing group an α-D-xylosyl end-group (**5–8**);

Series V: were oligosaccharides analogous to those in Series II, but containing as the terminal non-reducing group an α-D-xylosyl end-group (**9–12**);

Series VI: were oligosaccharides analogous to these in Series III, but containing as the terminal nonreducing group an α-D-xylosyl group (**13–16**); and

Series VII: were the title xylo-oligosaccharides (**29–32**).

Compounds of Series III and VII showed physical properties very close to those of compounds isolated from products of partial hydrolysis of plant xylans and their acetates[10–14]. Their reported melting points varied somewhat, which is probably associated, in the case of free oligosaccharides, with different anomeric composition, and in the case of the acetates, with polymorphism. The largest discrepancy between the values found and those reported was observed for the melting point of the peracetate of β-xylotriose **26**. A sharp-melting product could not be obtained, even after several recrystallizations from various solvents, although the specific optical rotation found for **26** was in excellent agreement with that reported previously. It is worth mentioning that β-xylotriose peracetate synthesized *via* an independent route[7] did not show a sharp melting point either.

^{13}C-N.m.r. spectroscopy. — Compounds of Series VII produced ^{13}C-n.m.r. spectra practically identical with those of (1→4)-β-D-xylo-oligosaccharides of natural origin[15]. Small, insignificant differences between the recorded and reported chemical shifts for certain carbon atoms are associated with effects resulting from different conditions of measurement. ^{13}C-N.m.r. characteristics for the compounds synthesized are recorded in Table I. The analysis of spectra of compounds within one homologous series of oligosaccharides was based on the variation of peak intensities with chain-length. It has been demonstrated[15] that the similarity of chemical shifts for equivalent carbon atoms of the internal residues may be used to distinguish peaks associated with them from those assigned to terminal groups. The variation of relative intensity of lines arising from internal residues of oligosaccharides with increasing number of residues is depicted in Fig. 1, showing line spectra of peracetates of β-xylo-oligosaccharides, compounds of Series III. Signals of C-1 of the reducing and non-reducing end of these compounds appear in the spectra consistently at 92.2 ±0.1 and ~99.6

TABLE I

^{13}C-N.M.R. SPECTRAL DATA FOR COMPOUNDS **5**–**33**

Compound	*Ring*	*Chemical shifts (p.p.m.)*				
		C-1	*C-2*	*C-3*	*C-4*	*C-5*
5	C	91.9	70.2	72.5	73.4	64.3
	C′	96.4	70.7	71.0	75.2	60.0
6	C	92.1	69.7	72.0	74.9	63.8
	C′	100.4	70.7	72.4	73.5	63.4
	C″	96.4	71.0	71.3	75.3	60.0
7	C	92.1	69.7	71.9	74.9	63.8
	C′	100.3	70.7	71.9	74.6	62.6
	C″	100.3	70.7	72.4	73.4	63.4
	C‴	96.3	71.0	71.3	75.3	60.0
8	C	92.1	69.7	71.9	74.8	63.7
	C′	100.3	70.8	71.9	74.7	62.5
	C″	100.3	70.8	71.9	74.7	62.5
	C‴	100.3	70.8	72.4	73.5	63.4
	C⁗	96.4	71.1	71.4	75.3	60.1
9	C	92.1	70.3	72.8	73.6	64.6
	C′	96.9	70.8	72.8	68.8	62.0
10	C	92.1	69.7	71.9	74.9	64.0
	C′	100.4	70.6	72.5	73.8	63.4
	C″	96.4	71.5	72.9	68.8	61.9
11	C	92.3	70.0	72.2	75.2	64.0
	C′	100.7	71.0	72.2	75.0	63.5
	C″	100.7	71.0	72.8	73.9	62.9
	C‴	96.7	71.7	72.9	68.9	62.1
12	C	92.3	69.9	72.1	75.1	64.0
	C′	100.5	71.0	72.1	75.1	63.5
	C″	100.5	71.0	72.1	75.1	62.5
	C‴	100.5	70.7	72.9	73.9	62.7
	C⁗	96.6	71.7	73.2	69.1	62.2
13	C	91.9	70.1	72.9	73.2	64.3
	C′	96.4	70.8	69.0	69.0	58.8
14	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
15	C	92.1	69.7	71.9	74.6	63.4
	C′	100.1	70.7	71.9	74.6	62.5
	C″	100.1	70.7	72.7	73.1	63.4
	C‴	96.2	71.2	69.0	69.0	58.7
16	C	92.1	69.7	71.9	74.6	63.4
	C′	100.1	70.8	71.9	74.6	62.5
	C″	100.1	70.8	71.9	74.6	62.5
	C‴	100.1	70.8	72.7	73.2	63.4
	C⁗	96.3	71.2	69.0	69.0	58.8
17	C	92.2	69.7	72.1	74.3	63.4
	C′	100.5	71.1	72.9	74.9	63.4
18	C	92.1	69.7	71.9	74.6	63.3
	C′	100.5	70.8	71.9	74.2	62.7
	C″	100.8	71.2	72.8	74.6	63.3
19	C	92.2	69.8	71.9	74.7	63.3
	C′	100.3	70.8	71.9	74.7	62.5
	C″	100.3	70.8	71.9	74.3	62.5
	C‴	100.5	71.2	72.8	74.7	63.3

TABLE I *(continued)*

Compound	*Ring*	*Chemical shifts (p.p.m.)*				
		C-1	*C-2*	*C-3*	*C-4*	*C-5*
20	C	92.3	69.9	72.0	74.8	63.4
	C′	100.3	70.9	72.0	74.8	62.6
	C″	100.3	70.9	72.0	74.8	62.6
	C‴	100.3	70.9	72.0	74.3	62.6
	C⁗	100.3	71.3	73.0	74.8	63.4
21	C	92.3	69.8	72.1	74.5	63.4
	C′	100.1	70.6	74.5	67.9	64.8
22	C	92.2	69.8	72.0	74.8	63.3
	C′	100.4	71.0	72.0	74.3	62.8
	C″	100.2	70.6	74.8	67.8	64.8
23	C	92.1	69.7	71.9	74.7	63.3
	C′	100.2	70.8	71.9	74.7	62.5
	C″	100.2	70.8	71.9	74.2	62.5
	C‴	99.9	70.3	74.7	67.7	64.5
24	C	92.2	69.7	71.9	74.8	63.3
	C′	100.3	70.8	71.9	74.8	62.5
	C″	100.3	70.8	71.9	74.8	62.5
	C‴	100.3	70.8	71.9	74.1	62.5
	C⁗	99.6	70.0	74.8	67.8	64.5
25	C	92.3	70.0	72.1	74.4	63.4
	C′	99.7	70.4	70.7	68.4	61.2
26	C	92.2	69.8	72.0	74.9	63.4
	C′	100.5	70.9	72.0	74.5	62.7
	C″	99.6	70.3	70.3	68.3	61.5
27	C	92.1	69.7	71.8	74.8	63.3
	C′	100.3	70.8	71.8	74.8	62.5
	C″	100.3	70.8	71.8	74.2	62.5
	C‴	99.4	70.3	70.3	68.2	61.4
28	C	92.2	69.8	71.9	74.7	63.4
	C′	100.3	70.8	71.9	74.7	62.5
	C″	100.3	70.8	71.9	74.7	62.5
	C‴	100.3	70.8	71.9	74.2	62.5
	C⁗	99.5	70.3	70.3	68.3	61.5
29	C-α	93.2	72.1[a]	72.6[a]	77.7	60.0
	C-β	97.7	75.1	75.1	77.6	64.1
	C′	103.0	74.0	76.8	70.4	66.4
30	C-α	93.2	72.2[a]	72.6[a]	77.6	60.2
	C-β	97.8	75.0	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
31	C-α	93.2	72.1[a]	72.6[a]	77.6	60.1
	C-β	97.8	75.0	75.0	77.6	64.2
	C′	103.0	73.9	75.0	77.6	64.2
	C″	103.0	73.9	75.0	77.6	64.2
	C‴	103.0	73.9	76.8	70.3	66.4
32	C-α	93.2	72.1[a]	72.6[a]	77.6	60.1
	C-β	97.7	75.0	75.0	77.6	64.2
	C′	102.9	73.9	75.0	77.6	64.2
	C″	102.9	73.9	75.0	77.6	64.2
	C‴	102.9	73.9	75.0	77.6	64.2
	C⁗	102.9	73.9	76.8	70.3	66.4
33	C-α	93.2	72.4[a]	72.9[a]	79.3	61.3
	C-β	97.7	75.1	76.1	79.3	65.5
	C′	101.4	72.9	74.2	70.6	62.8

[a] The assignments may be reversed.

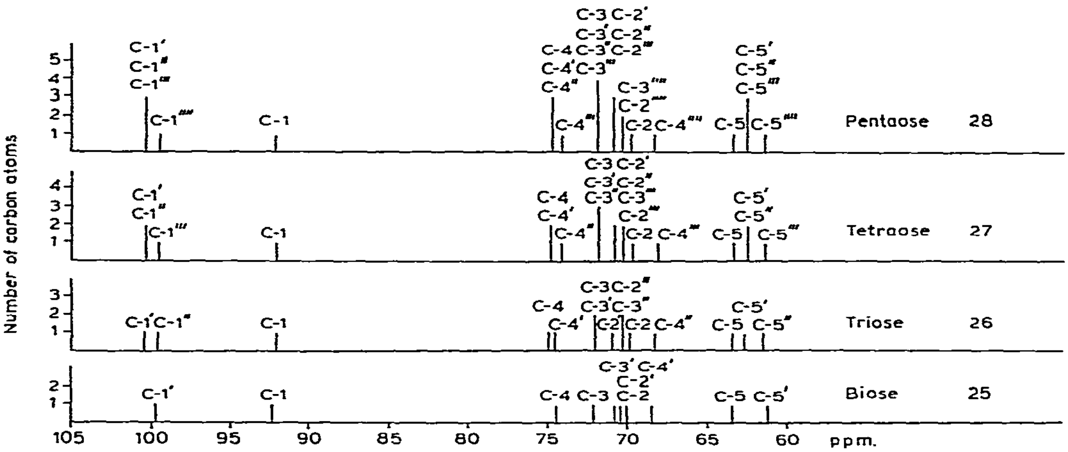


Fig. 1. Comparison of line spectra of peracetates of (1→4)-β-D-xylo-oligosaccharides 25–28.

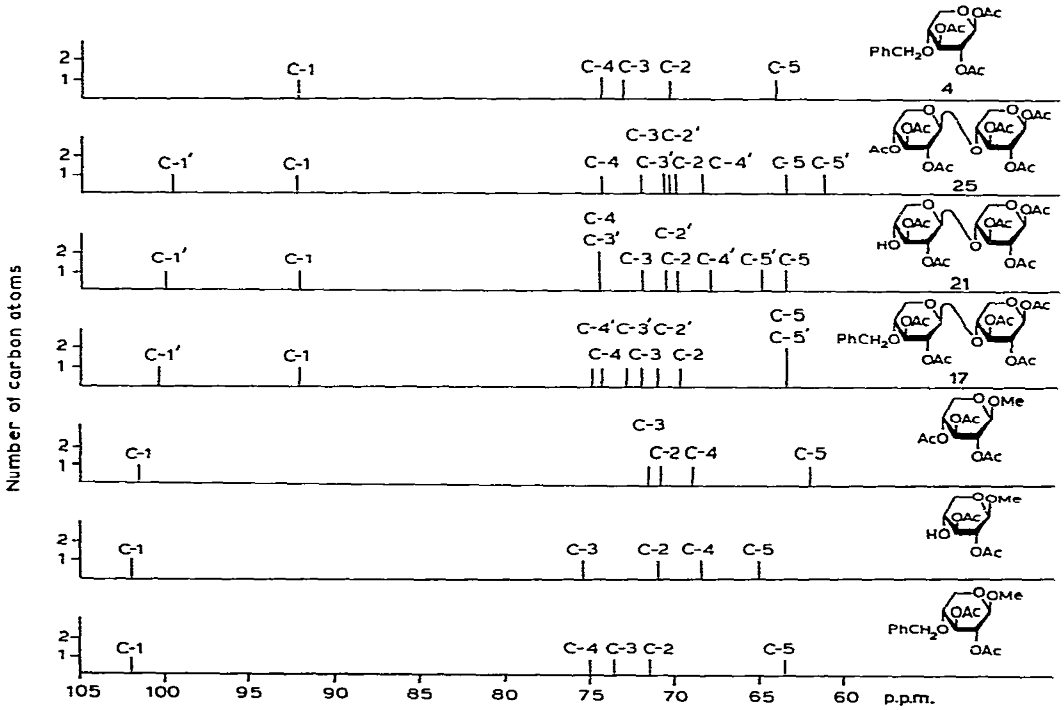


Fig. 2. Comparison of diagnostically significant shifts of lines in the ^{13}C-n.m.r. spectra of disaccharides of Series I–III with similar shifts of lines in the spectra of model monosaccharide derivatives.

p.p.m., respectively. The signal at ~100.4 p.p.m. was readily assigned to C-1 of the internal residues of the oligosaccharides, because it increases in intensity, relative to the former two peaks, as the number of pyranose residues increases. The lines associated with C-4 and C-5 were assigned similarly; the assignment of signals in the spectrum of the disaccharide at 63.4 and 61.2 p.p.m. to C-5 and C-5′ was based on the comparison of chemical shifts of C-5 resonances in the spectra of disaccharides of other series (Table I, Fig. 2).

The assignment of lines associated with carbon atoms of the terminal, non-reducing D-xylosyl groups was confirmed by rationalizing, in the spectra of oligosaccharides of related series, the shifts of certain resonances from the results of chemical reactions performed. As an example of such an assignment, Fig. 2 shows partial line-spectra of **4** (ref. 9), methyl 2,3-di-*O*-acetyl-4-*O*-benzyl-β-D-xylopyranoside[16], methyl 2,3-di-*O*-acetyl-β-D-xylopyranoside[16], and methyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranoside. Compound **4** imitates the reducing group and the other monosaccharides imitate the non-reducing end-group of the disaccharides (and also of higher oligosaccharides in the respective series), and shifts of resonances in their spectra, as a result of the change of chemical environment (caused by hydrogenolysis of the O-4 benzyl group or acetylation of HO-4), may be reasonably expected to occur also in the spectra of related disaccharides. Thus, removal of the benzyl group from methyl 2,3-di-*O*-acetyl-4-*O*-benzyl-β-D-xylopyranoside eliminates the strong positive α-effect[17] and also the negative β-effect of alkylation[17,18]. As a result, the C-4 signal, present in the spectrum of methyl 2,3-di-*O*-acetyl-4-*O*-benzyl-β-D-xylopyranoside at 75 p.p.m., appears in the spectrum of methyl 2,3-di-*O*-acetyl-β-D-xylopyranoside at 68.4 p.p.m. Simultaneously, the signals of C-3 and C-5 are shifted downfield, from 73.6 to 75.4 and from 63.5 to 65.1 p.p.m., respectively. Following acetylation (conversion of methyl 2,3-di-*O*-acetyl-β-D-xylopyranoside into methyl 2,3,4-tri-*O*-acetyl-β-D-xylopyranoside), C-3, 4, and 5 are exposed to effects[19] resulting in a slight downfield shift of the C-4 signal (68.4→69 p.p.m.) and an upfield shift of the C-3 (75.4→71.6 p.p.m.) and C-5 (65.1→62 p.p.m.) signals. Similar, diagnostically important shifts may be observed also in the spectra of the respective disaccharides (Fig. 2) and higher oligosaccharides in all series studied (Table I). Analysis of oligosaccharide derivatives having the α-linked, terminal, non-reducing D-xylosyl group (compounds of Series IV–VI) was performed similarly by using, as an aid, interpreted[20,21] spectra of methyl 2,3-di-*O*-acetyl-4-*O*-benzyl-, 2,3-di-*O*-acetyl-, and 2,3,4-tri-*O*-acetyl-α-D-xylopyranoside, and of analogous methyl β-glycosides of (1→4)-β-D-xylo-oligosaccharides.

^{13}C-N.m.r. spectra of the compounds prepared showed regularities permitting conformation of the configuration of newly-formed interglycosidic linkages in the pairs of compounds of Series I and VI, tentatively assigned on the basis of specific optical rotation. From this point of view, the diagnostically most significant signals were anomeric and C-5 resonances. It may be seen from the data in Table I that spectra of compounds containing only β-glycosidic linkages show two kinds of anomeric resonances. The one at 92.1–92.3 p.p.m. remains a one-carbon signal within one homologous series, whereas the intensity of the line at δ ~100.0 increases with the increasing number of D-xylopyranose residues. Thus, the high-field signal could be unambiguously assigned to C-1 of the acetylated, reducing β-D-xylopyranose residue of the molecules, and the low-field signal was assigned to the other anomeric resonances. In the spectrum of **17**, one double-intensity line at 63.4 p.p.m. is present for C-5 and C-5′. In addition to a signal at δ ~63.3, the spectra of higher oligosaccharides of Series I show in this region a signal at ~62.6 p.p.m. whose relative intensity increases with the increasing chain-length of the oligosaccharides. Therefore, the high-field signal was assigned to the internal D-xylose residues.

The presence of a terminal, non-reducing 2,3-di-*O*-acetyl-4-*O*-benzyl-α-D-xylopyranosyl group in oligosaccharides of Series IV was manifested by a new signal in the region of anomeric resonances. In addition to lines at ~100.4 and 92.2 p.p.m., present also in the spectra of oligosaccharides of Series I, compounds of Series IV show (Table I) a one-carbon signal at δ ~96.4. A signal at a similar δ value, present also in compounds of Series V and VI, is diagnostic of the presence of an α-D-xylosyl residue in these compounds. In the region of C-5 resonances, a characteristic feature of oligosaccharides of Series IV is a line at ~60.0 p.p.m., which may be readily assigned to the terminal, non-reducing α-D-xylosyl group.

The following other regularities may be noted in the spectra of compounds of Series I–VI. A characteristic feature of oligosaccharides of all series is a separate signal for C-4 of the penultimate D-xylose residue (commencing the numbering of these groups from the reducing end). It appears in the spectra at δ 73.1–74.5 and it is, without exception, separated from C-4 lines of any other D-xylose residue. Also, its chemical shift reflects the difference between the shift-effect of α- and β-D-xylosylation and, as such, may serve as another criterion for determining the stereochemistry of interglycosidic linkages in related compounds. In the spectra of compounds of Series I–III having a β-D-xylosyl group attached to O-4 of the penultimate D-xylosyl residue, the signal of this nucleus appears at δ 74.1–74.5, whereas in the spectra of compounds of Series IV–VI, containing an α-D-xylosyl group attached at this position, the corresponding signal appears at δ 73.1–73.9. The chemical shift of C-4 signals of the non-reducing D-xylosyl group depends, of course, upon the substitution at this site (compare Fig. 2).

The chemical shift of C-3 nuclei in all series is exceptionally sensitive towards substitution at the neighbouring position 4. Accordingly, C-3 of the penultimate D-xylose residue of compounds in Series I–III and IV–VI is exposed to different effects. Consequently, signals of C-3 perceiving a negative β-effect of β-D-xylosylation appear in the spectra at δ 71.8–72.1, and C-3 nuclei subjected to effects of α-D-xylosylation produce a line at 72.4–72.9 p.p.m.

Signals of C-2 appear within the range δ 69.7–71.7. Of these, the one appearing at the highest field is that of the reducing end-group, because of the negative β-effect of the acetoxyl group at C-1. The other C-2 signals constitute a relatively complicated system, suggesting the sensitivity of these nuclei towards the effects of substitution several bonds distant, or effects associated with differences in linkage conformation or solvation at the neighboring inter-sugar linkages.

EXPERIMENTAL

General procedures. — Melting points were determined on a Kofler hot-stage. Optical rotations (*c* 1, 22°) were measured with a Perkin–Elmer automatic polarimeter Model 141. Thin-layer chromatography (t.l.c.) was performed with Silica Gel G, and column chromatography with dry-packed Silica Gel 60 (Merck, A. G., Darmstadt, Germany) by the gradient-elution technique, with *A*, 5:1 carbon tetrachloride–acetone; *B*, 12:1 carbon tetrachloride–acetone; *C*, 8:1 carbon tetrachloride–acetone; *D*, 3:2 carbon tetrachloride–ethyl acetate; *E*, 7:1 chloroform–acetone; and *F*, 3:1 carbon tetrachloride–acetone. Prior to packing, the silica gel was equilibrated with 40% of the mobile phase. Detection was effected by charring with 5% (v/v) sulfuric acid in ethanol. The purity of the (1→4)-β-D-xylo-oligosaccharides synthesized was checked by paper chromatography on Whatman No. 1 paper with 18:7:8 ethyl acetate–acetic acid–water as eluant and detection with aniline hydrogenphthalate. ^{13}C-N.m.r. spectra for solutions in $CDCl_3$ (compounds **5**–**28**, internal standard tetramethylsilane) and D_2O (compounds **29**–**33**, internal standard methanol, δ_{Me_4Si} 50.15 p.p.m.) were measured at room temperature with Jeol JMN FX-60 and FX-100 spectrometers.

The solution of hydrogen bromide in dichloromethane contained 0.1 g HBr/mL (determined by weighing). Toluene was refluxed over sodium hydride and freshly distilled. Acetonitrile was dried with calcium hydride and distilled. Dichloromethane was dried with phosphorus pentaoxide and distilled. Solutions in organic solvents were dried with anhydrous sodium sulfate and evaporated at 40°/2 kPa.

Microanalyses were performed with a Perkin–Elmer Model 240 automatic analyzer. The melting points given are values that did not change on further recrystallization. Analytical values within ±0.4% of theory are indicated by the symbol of the element analyzed.

Oligosaccharides of Series I and IV. — A solution of hydrogen bromide in dichloromethane (73 mL) was added to a solution of **4** (13.25 g, 0.0362 mol) in toluene (25 mL) and kept for 15 min at room temperature. After evaporation and subsequent evaporation of fresh portion of toluene (~10 mL) from the residue a solution of the crude bromide **3** in the minimum amount of acetonitrile was added to a stirred mixture of **2** (4 g, 145 mmol) and mercuric cyanide (4.6 g, 18.2 mmol) in acetonitrile (50 mL), and the mixture was stirred for 1 h at room temperature. T.l.c. (solvent *A*) then showed the absence of **3** (R_F 0.65) and the presence of condensation products **5** (R_F 0.45) and **17** (R_F 0.4). A small amount of the unchanged nucleophile **2** (R_F 0.25) was also present. The mixture was evaporated and the residue was partitioned between chloroform and aqueous M potassium bromide solution. The chloroform solution was successively washed with water, dried, evaporated, and the residue was chromatographed (solvents *B*→*C*) to give first *O*-(2,3-di-*O*-acetyl-4-*O*-benzyl-α-D-xylopyranosyl)-(1→4)-1,2,3-tri-*O*-acetyl-β-D-xylopyranose (**5**), 3.9 g (23.1%), m.p. 143–144° (from ethanol), $[\alpha]_D$ +35.1°. *Anal.* ($C_{27}H_{34}O_{14}$) C, H.

Eluted next was *O*-(2,3-di-*O*-acetyl-4-*O*-benzyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-*O*-acetyl-β-D-xylopyranose (**17**), 5.85 g (34.7%), m.p. 132.5–133.5° (from ethanol), $[\alpha]_D$ −64.2°. *Anal.* ($C_{27}H_{34}O_{14}$) C, H.

Similar condensation of **3** with nucleophiles **21–23** afforded:

O-(2,3-Di-O-acetyl-4-O-benzyl-α-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose (**6**), 36%, colorless foam, $[\alpha]_D$ −4.4°, R_F 0.6 (solvent *D*, double development). *Anal.* ($C_{36}H_{46}O_{20}$) C, H.

O-(2,3-Di-O-acetyl-4-O-benzyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose (**18**), 52%, m.p. 104–109° (from methanol), $[\alpha]_D$ −81.9°, R_F 0.5 (solvent *D*, double development). *Anal.* ($C_{36}H_{46}O_{20}$) C, H.

O-(2,3-Di-O-acetyl-4-O-benzyl-α-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose (**7**), 32.5%, colorless foam, $[\alpha]_D$ −31.1°, R_F 0.4 (solvent *D*, double development). *Anal.* ($C_{45}H_{58}O_{26}$) C, H.

O-(2,3-Di-O-acetyl-4-O-benzyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose (**19**), 51%, m.p. 188.5–191° (from ethyl acetate), $[\alpha]_D$ −91.5°, R_F 0.35 (solvent *D*, double development). *Anal.* ($C_{45}H_{58}O_{26}$) C, H.

O-(2,3-Di-O-acetyl-4-O-benzyl-α-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose (**8**), 28%, colorless foam, $[\alpha]_D$ −46.5°, R_F 0.25 (solvent *D*, double development). *Anal.* ($C_{54}H_{70}O_{32}$) C, H.

O-(2,3-Di-O-acetyl-4-O-benzyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose (**20**), 59%, m.p. 225–227° (from 1:3 chloroform–methanol, $[\alpha]_D$ −98.7°, R_F 0.15 (solvent *D*, double development). *Anal.* ($C_{54}H_{70}O_{32}$) C, H.

Oligosaccharides of Series II and V. — A mixture of **17** (5 g) and 5% palladium-on-charcoal catalyst (0.5 g) in 1:1 acetone–methanol (250 mL) was stirred at room temperature under hydrogen until t.l.c. (solvent *A*) showed complete conversion of the starting material (R_F 0.4) into a product (R_F 0.15). After filtration and evaporation, the product (4.1 g, 97%) was crystallized from ethyl acetate–hexane to give *O*-(2,3-di-*O*-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-*O*-acetyl-β-D-xylopyranose (**21**), m.p. 180–181°, $[\alpha]_D$ −73.7°. *Anal.* ($C_{20}H_{28}O_{14}$) C, H.

Similar hydrogenolysis of **18–20** and **5–8** gave in almost theoretical yield:

O-(2,3-Di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose (**22**), m.p. 216–218° (from ethanol), $[\alpha]_D$ −92.3°, R_F 0.3 (solvent *E*), *Anal.* ($C_{29}H_{40}O_{20}$) C, H.

O-(2,3-Di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose (**23**), m.p. 221–222° (from acetone), $[\alpha]_D$ −102.1°, R_F 0.25 (solvent *E*). *Anal.* ($C_{38}H_{52}O_{26}$) C, H.

O-(2,3-Di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose (**24**), m.p. 246–248° (from acetonitrile–methanol), $[\alpha]_D$ −103.7°, R_F 0.2 (solvent *E*). *Anal.* ($C_{47}O_{64}O_{32}$) C, H.

O-(2,3-Di-O-acetyl-α-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose (**9**), m.p. 159–159.5° and 168–169° (dimorphous, from ethyl acetate–hexane). When heating was terminated at 160° and the sample was allowed to come to room temperature, it solidified completely and melted sharply at 168–169°), $[\alpha]_D$ +47.6°, R_F 0.4 (solvent *E*). *Anal.* ($C_{20}H_{28}O_{14}$) C, H.

O-(2,3-Di-O-acetyl-α-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose (**10**), colorless foam, $[\alpha]_D$ −1.7°, R_F 0.35 (solvent *E*). *Anal.* ($C_{29}H_{40}O_{20}$) C, H.

O-(2,3-Di-O-acetyl-α-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose (**11**), m.p. 204–206° (from methanol), $[\alpha]_D$ −32.5°, R_F 0.3 (solvent *E*). *Anal.* ($C_{38}H_{52}O_{26}$) C, H.

O-(2,3-Di-O-acetyl-α-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose (**12**), m.p. 248–250° (from 1:5 chloroform–methanol), $[\alpha]_D$ −50.9°, R_F 0.25 (solvent *E*). *Anal.* ($C_{47}H_{64}O_{32}$) C, H.

Oligosaccharides of Series III and VI. — Acetic anhydride (0.5 mL) was added to a solution of **21** (1 g, 18.7 mmol) in the minimum amount of pyridine and the mixture was kept for 18 h at room temperature. T.l.c. (solvent *A*) then showed complete conversion of the starting material (R_F 0.15) into a product (R_F 0.3). Methanol was added, to decompose the excess of acetic anhydride, and the solution was evaporated. The residue was crystallized from ethanol to afford *O*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-*O*-acetyl-β-D-xylopyranose (hexa-*O*-acetyl-β-xylobiose) (**25**), 1 g (92%), m.p. 154–156°, $[\alpha]_D$ −76°, (lit.[10] m.p. 155.5–156°, $[\alpha]_D$ −74.5°; lit.[11] m.p. 155.5–156°, $[\alpha]_D$ −74.3°; lit.[12] m.p. 155.5–156.5°, $[\alpha]_D$ −75.1°).

Similar acetylation of **22**–**24** and **9**–**12** gave in almost theoretical yield:

O-(2,3,4-Tri-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose (octa-*O*-acetyl-β-xylotriose) (**26**), m.p. 109–115° (from methanol), $[\alpha]_D$ −84.8°, R_F 0.3 (solvent *F*), (lit.[10] m.p. 109–110°, $[\alpha]_D$ −84.3°; lit.[11] m.p. 109–110°, $[\alpha]_D$ −85°; lit.[12] m.p. 108–109.5°, $[\alpha]_D$ −83.5°).

O-(2,3,4-Tri-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylo-

pyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose (deca-*O*-acetyl-β-xylotetraose) (**27**), m.p. 200–201° and 210–211° (dimorphous, from 1:5 chloroform–methanol), $[\alpha]_D$ −95.9°, R_F 0.25 (solvent *F*), (lit.[10] m.p. 201–202°, $[\alpha]_D$ −93.7°; lit.[11] m.p. 199–201°, $[\alpha]_D$ −93.6°; lit.[12] m.p. 200–201°, $[\alpha]_D$ −92.4°).

O-*(2,3,4-Tri-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose* (dodeca-*O*-acetyl-β-xylopentaose) (**28**), m.p. 251–254° (from 1:3 chloroform–methanol), $[\alpha]_D$ −100.4°, R_F 0.15 (solvent *F*), (lit.[10] m.p. 248–249°, $[\alpha]_D$ −97.5°; lit.[11] m.p. 248–249°, $[\alpha]_D$ −97.5°; lit.[12] m.p. 249–250°, $[\alpha]_D$ −98°).

O-*(2,3,4-Tri-O-acetyl-α-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose* (**13**), m.p. 135.5–136.5° (from methanol), $[\alpha]_D$ +45.7°, R_F 0.5 (solvent *F*). *Anal.* ($C_{22}H_{30}O_{15}$) C, H.

O-*(2,3,4-Tri-O-acetyl-α-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose* (**14**), m.p. 113–119° (from ethanol), $[\alpha]_D$ −0.58°, R_F 0.4 (solvent *F*). *Anal.* ($C_{31}H_{42}O_{21}$) C, H.

O-*(2,3,4-Tri-O-acetyl-α-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose* (**15**), m.p. 137–138° (from methanol), $[\alpha]_D$ −29.3°, R_F 0.3 (solvent *F*). *Anal.* ($C_{40}H_{54}O_{27}$) C, H.

O-*(2,3,4-Tri-O-acetyl-α-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-O-(2,3-di-O-acetyl-β-D-xylopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-xylopyranose* (**16**), colorless foam. $[\alpha]_D$ −42.5°, R_F 0.2 (solvent *F*). *Anal.* ($C_{49}H_{66}O_{33}$) C, H.

Oligosaccharides of Series VII. — Methanolic M sodium methoxide (2 mL) was added to a solution of **21** (1 g) or **25** (1.1 g) in methanol (50 mL) and the solution was kept for 2 h at room temperature. T.l.c. (solvent *E*) showed then that the reaction was complete and, after successive neutralization with Dowex 50W (H^+) resin, filtration, and evaporation, chromatographically pure (p.c.) *O*-β-D-xylopyranosyl-(1→4)-D-xylopyranose (xylobiose) (**29**) was obtained as a solid foam (0.55 g, 96%). Crystallization from methanol yielded material melting at 184.5–186°, $[\alpha]_D$ −23° (equil.), (lit.[11] m.p. 188–190°, $[\alpha]_D$ −24.8°; lit.[12] m.p. 184.5–185°, $[\alpha]_D$ −25.6°; lit.[13] m.p. 185–186°, $[\alpha]_D$ −25.5°; lit.[14] m.p. 189°, $[\alpha]_D$ −26°).

Similar deacetylation of **22–24** or **26–28** gave in almost theoretical yield:

O-*β-D-Xylopyranosyl-(1→4)-O-β-D-xylopyranosyl-(1→4)-D-xylopyranose* (xylotriose) (**30**), m.p. 217–219° (from methanol), $[\alpha]_D$ −47.7° (equil.), (lit.[11] m.p. 204–205°, $[\alpha]_D$ −44.4°; lit.[12] m.p. 215–216°, $[\alpha]_D$ −48.1°; lit.[13] m.p. 205–206°, $[\alpha]_D$ −47°; lit.[14] m.p. 214°, $[\alpha]_D$ −48°).

O-*β-D-Xylopyranosyl-(1→4)-O-β-D-xylopyranosyl-(1→4)-O-β-D-xylopyranosyl-(1→4)-D-xylopyranose* (xylotetraose) (**31**), m.p. 223.5–225.5° (from methanol), $[\alpha]_D$ −58° (equil.), (lit.[12] m.p. 224–226°, $[\alpha]_D$ −61.9°; lit.[11,13] $[\alpha]_D$ −57.8° and −60°, respectively, for amorphous **31**).

O-β-D-Xylopyranosyl-(1→4)-O-β-D-xylopyranosyl-(1→4)-O-β-D-xylopyranosyl-(1→4)-O-β-D-xylopyranosyl-(1→4)-D-xylopyranose (xylopentaose) (**32**), m.p. 231–233° (from 90% methanol), $[\alpha]_D$ −70.1° (equil.), (lit.[12] m.p. 240–242°, $[\alpha]_D$ −71.4°; lit.[11,13] $[\alpha]_D$ −62.4° and −66°, respectively, for amorphous **32**).

O-α-D-Xylopyranosyl-(1→4)-D-xylopyranose (**33**). — Compounds **9** and **13** was treated as described for the preparation of oligosaccharides of Series VII, and **33**, when crystallized from methanol, melted at 170–178° and had $[\alpha]_D$ +109.5° (equil.). It was chromatographically pure (p.c., R_{Xyl} 0.45) and clearly separated from its β anomer **29** (R_{Xyl} 0.3). *Anal.* ($C_{10}H_{18}O_9$) C, H.

ACKNOWLEDGMENTS

The authors thank M. Matulová for ^{13}C-n.m.r. measurements, G. Košický for the measurements of optical rotation, and K. Paule for microanalyses.

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