Simple Synthesis of Methyl 2-*O*-β-D-Xylopyranosyl-α-L-arabinofuranoside, a Fragment of Natural Arabinoglucuronoxylans

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Methyl 3,5-di-*O*-benzoyl-α-L-arabinofuranoside, prepared by a five-step synthesis from L-arabinose, was condensed with 2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl bromide under modified Koenigs—Knorr conditions using mercuric cyanide as a catalyst and acid scavenger in dichloromethane, giving a high yield (77 %) of the *O*-protected disaccharide *VIII*. Removal of acyl groups afforded the desired model compound – methyl 2-*O*-β-D-xylopyranosyl-α-L-arabinofuranoside. ^{1}H and ^{13}C NMR spectra of the synthesized compounds are also presented.

A basic feature of arabinoglucuronoxylans, representing mainly hemicelluloses of annual plants, is branching of the backbone created from β-(1→4)-linked D-xylopyranosyl residues with an α-L-arabinofuranosyl moiety at O-3 or O-2, respectively and 4-*O*-methyl-α-D-glucopyranosyluronic acid linked to O-2 of certain D-xylopyranosyl units. Furthermore, this type of xylans of some monocotyl plants is also slightly branched with 2-*O*-β-D-xylopyranosyl-α-L-arabinofuranosyl fragments at O-3 [1—4] (Fig. 1).

In study of the structure and the properties of the various branched xylan polysaccharides are especially useful model substances – synthetically prepared lower oligosaccharides and their methyl β-glycosides, where the β-glycosidically linked aglycone imitates the situation of connecting with polysaccharide backbone chain. In order to complete a series of model oligosaccharides of arabino- and glucuronoxylans the synthesis of disaccharide *IX* is described in this paper.

The starting point in the synthesis of nucleophile *V* was methyl α-L-arabinofuranoside, prepared easily in large scale from L-arabinose [5], which was then partially acylated with benzoyl chloride in pyridine [6]. Obtained intermediate *I* was treated with acetone in the presence of dry HCl to give the crystalline 5-*O*-benzoyl-1,2-*O*-isopropylidene-β-L-arabinofuranose (*II*) characterized also as a corresponding 3-acetate *III*. The conversion *II*→*V* was done in two steps – by blocking the OH group at position C-3 with benzoyl group followed by deisopropylidenation and subsequent methyl glycosidation [7]. From the isolated mixture of methyl 3,5-di-*O*-benzoyl-α- and β-L-arabinofuranosides, which was poorly separable, the compound *V* (pure α-anomer) was obtained by a repeated column chromatography in a 25 % yield only. This separation allowed us to isolate also pure β-anomer *VI* (8 %).

The coupling step of the synthesis of the nucleophile *V* with the glycosylating agent *VII,* prepared from per-*O*-acetylated D-xylose using 33 % HBr in acetic acid [8], was done in dichloromethane with mercuric cyanide as a promoter. These were the best conditions to attain the highest stereoselectivity of this condensation reaction in favour of creating the β-(1→2)-glycosidic bond from bromide *VII* and nucleophile *V*. After 2 h at room temperature the reaction mixture contained, according to TLC, disaccharide *VIII* as the main product, no bromide *VII*, only traces of *V* and a small amount of the hydrolysis product of *VII*. The column chromatography of the worked-up reaction mixture revealed that it contains, with the exception of the main disaccharide *VIII*, obtained in 76.8 % yield, also a small amount of its α-anomer (*ca.* 8 %, further not investigated). Finally, the deacylation of disaccharide *VIII* by sodium methoxide in methanol afforded the title model compound – methyl 2-*O*-β-D-xylopyranosyl-α-L-arabinofuranoside (*IX*) (Fig. 2).

Compounds *I*, *III*, *V*, *VI*, *VIII*, and *IX* that were hitherto unknown were fully characterized by usual physical constants, and the structures of all synthesized saccharides were confirmed by inspection of their ^{1}H and ^{13}C NMR spectral data.

EXPERIMENTAL

Melting points were determined on a Kofler hot stage. Optical rotations (D, 20 ℃, ρ = 10.0 g dm^{-3}) were measured with a Perkin—Elmer Model 141 automatic polarimeter. Elemental analyses were done with a Fisons EA 1108 analyzer. All reactions were mon-

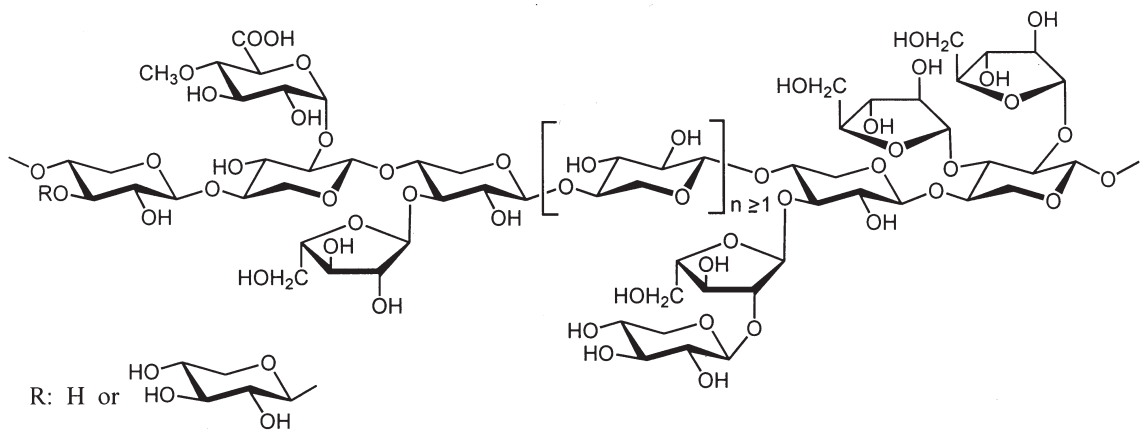
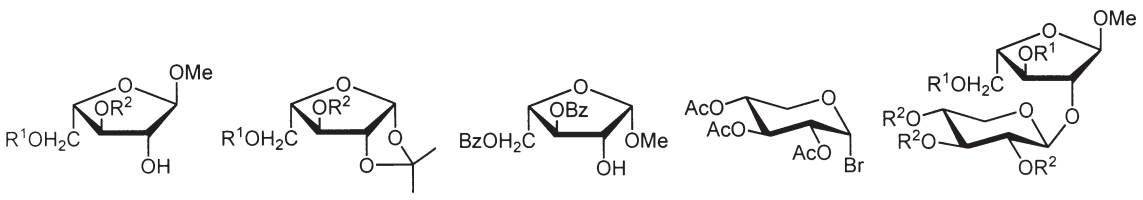


Fig. 1. A basic structural feature of arabinoglucuronoxylans.



I R^1 = Bz; R^2 = H
V R^1 = R^2 = Bz
II R^1 = Bz; R^2 = H
III R^1 = Bz; R^2 = Ac
IV R^1 = R^2 = Bz
VI
VII
VIII R^1 = Bz; R^2 = Ac
IX R^1 = R^2 = H

Ac = acetyl, Bz = benzoyl

Fig. 2. Structures of the prepared compounds.

itored by TLC on glass plates precoated with silica gel (Kieselgel G, Merck) spraying the chromatograms with a 10 % sulfuric acid in ethanol and charring them on a hot plate effected detection. Preparative chromatography was performed on dry-packed silica gel (Kieselgel 60, 0.063—0.200 mm, Merck) that, prior to packing, was first equilibrated with 40 % of the mobile phase. ^{1}H and ^{13}C NMR spectra (in $CDCl_3$ unless specified otherwise, internal standard Me_4Si) were recorded on a Bruker AVANCE DPX 300 instrument operating at 300.13 and 75.46 MHz frequencies, respectively. For the assignment of signals, 1D NOESY, DEPT and HSQC experiments were used. When reporting assignments of signals, the data for the xylopyranosyl residue are identified by a prime and those for the phenyl moiety by a double prime.

Methyl 5-*O*-Benzoyl-α-L-arabinofuranoside (*I*)

Methyl α-L-arabinofuranoside, prepared from L-arabinose [5], (8.2 g; 50 mmol) was dissolved in dry pyridine (40 cm^3) and to this stirred solution kept between −5 to −10 °C benzoyl chloride (6.4 cm^3; 55 mmol) was slowly and dropwise added. The mixture was stirred at that temperature for 4 h and then it was poured into ice water (250 cm^3). The suspension was extracted with chloroform (4 × 50 cm^3), the extract was washed with ice water, dried with sodium sulfate and concentrated finally with toluene (twice). The residue was purified by column chromatography using chloroform—acetone (φ_r = 10 : 1) as an eluent and pure compound *I* was obtained (colourless sirup). Yield = 8.6 g (64.2 %), [α] (chloroform) = −75°. For $C_{13}H_{16}O_6$ (M_r = 268.26) w_i(calc.): 58.20 % C, 6.01 % H; w_i(found): 57.96 % C, 6.06 % H. ^{1}H NMR data were identical with those given in Ref. [6] for D-isomer. ^{13}C NMR spectrum, δ: 166.75 (*C*OPh), 133.26 (C-4″), 129.68 (C-2″ and C-6″), 129.52 (C-1″), 128.42 (C-3″ and C-5″), 108.65 (C-1), 82.65 (C-4), 80.77 (C-2), 77.97 (C-3), 64.47 (C-5), 55.13 (OCH_3).

5-*O*-Benzoyl-1,2-*O*-isopropylidene-β-L-arabinofuranose (*II*)

Compound *I* (5 g; 18.6 mmol) was dissolved in acetone (150 cm^3) containing 1.75 g of HCl (gas) and the mixture was stirred at r.t. for 48 h. Sodium hydrogen carbonate was then added and the neutral reaction mixture was concentrated and extracted with chloroform (3 × 40 cm^3). The extract was washed with wa-

ter, dried with Na_2SO_4, concentrated and product *II* was crystallized from ethanol. Yield = 4.1 g (74.7 %), m.p. = 146—148 °C, [α] (chloroform) = −23°; Ref. [7] gives m.p. = 146—148 °C, [α] (DMSO) = −25°. ^{1}H NMR spectrum, δ: 7.41—8.07 (m, 5H, H_{arom}), 5.96 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1), 4.59 (d, 1H, H-2), 4.53 (d, 2H, $J_{4,5a} = J_{4,5b}$ = 6.1 Hz, H-5a, H-5b), 4.37 (d, 1H, $J_{2,3}$ = 0 Hz, $J_{3,4}$ = 2.5 Hz, H-3), 4.30 (dt, 1H, H-4), 2.45 (bs, 1H, OH), 1.56 and 1.33 (2s, each 3H, Me_2C). ^{13}C NMR spectrum, δ: 166.44 (*C*OPh), 133.21 (C-4″), 129.75 (C-2″ and C-6″), 128.38 (C-1″, C-3″, C-5″), 112.98 (*C*Me_2), 105.73 (C-1), 86.80 (C-2), 84.98 (C-4), 76.28 (C-3), 64.42 (C-5), 26.94 and 26.11 ((*C*H_3)$_2$C).

3-*O*-Acetyl-5-*O*-benzoyl-1,2-*O*-isopropylidene-β-L-arabinofuranose (*III*)

Acetylation of *II* under usual conditions (Ac_2O, dry pyridine, 3 h, r.t.) afforded a crude product that was crystallized from ethanol to give pure compound *III*. Yield = 89 %, m.p. = 115—116 °C, [α] (chloroform) = −4°. For $C_{17}H_{20}O_7$ (M_r = 336.33) w_i(calc.): 60.71 % C, 5.99 % H; w_i(found): 60.48 % C, 6.05 % H. ^{1}H NMR spectrum, δ: 7.41—8.10 (m, 5H, H_{arom}), 5.97 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1), 5.24 (d, 1H, $J_{2,3}$ = 0 Hz, $J_{3,4}$ = 1.6 Hz, H-3), 4.64 (d, 1H, H-2), 4.55 (d, 2H, $J_{4,5a} = J_{4,5b}$ = 7.1 Hz, H-5a, H-5b), 4.41 (dt, 1H, H-4), 2.10 (s, 3H, CH_3CO), 1.60 and 1.34 (2s, each 3H, Me_2C). ^{13}C NMR spectrum, δ: 169.73 (*C*OMe), 166.44 (*C*OPh), 133.09 (C-4″), 129.79 (C-2″ and C-6″), 128.34 (C-3″ and C-5″), 113.14 (*C*Me_2), 105.97 (C-1), 84.37 (C-2), 83.16 (C-4), 76.58 (C-3), 64.11 (C-5), 26.77 and 25.90 ((*C*H_3)$_2$C), 20.79 (*C*H_3CO).

3,5-Di-*O*-benzoyl-1,2-*O*-isopropylidene-β-L-arabinofuranose (*IV*)

To a stirred solution of *II* (4 g; 13.6 mmol) in dry pyridine (28 cm^3) kept at 0 °C benzoyl chloride (4.7 cm^3; 40.5 mmol) was dropwise added. After stirring for 1 h at 0 °C, the reaction mixture was warmed to 55 °C and stirred for another 30 min. The mixture was then cooled to r.t., diluted with dichloromethane (50 cm^3) and the CH_2Cl_2 solution was washed successively with water, 1 M-H_2SO_4, saturated aqueous $NaHCO_3$ and water, and then it was dried with sodium sulfate and concentrated. Crystallization from ethanol gave compound *IV*. Yield = 4.3 g (79.4 %), m.p. = 82—84 °C, [α] (chloroform) = −17°; Ref. [7] gives m.p. = 80—81 °C, [α] (DMSO) = −15°. ^{1}H NMR data were identical with those given in Ref. [7]. ^{13}C NMR spectrum, δ: 166.12 and 165.36 (2 × *C*OPh), 133.55 and 133.06 (2 × C-4″), 129.77 (2 × (C-2″ and C-6″)), 129.06 (2 × C-1″), 128.47 and 128.30 (2 × (C-3″ and C-5″)), 113.24 (*C*Me_2), 106.00 (C-1), 84.53 (C-2), 83.02 (C-4), 77.89 (C-3), 64.21 (C-5), 26.81 and 25.96 ((*C*H_3)$_2$C).

Methyl 3,5-Di-*O*-benzoyl-α-L-arabinofuranoside (*V*) and Methyl 3,5-Di-*O*-benzoyl-β-L-arabinofuranoside (*VI*)

A mixture of compound *IV* (4 g; 10 mmol), dry methanol (150 cm^3), and Dowex 50W (6 g) was stirred at 50 °C for 20 h. After filtration the solution was concentrated. The residue containing a mixture of *V* and *VI* ($n(\alpha)/n(\beta) \approx 5:3$, according to the TLC, hexane—acetone (φ_r = 2 : 1)), was chromatographed and rechromatographed on a column of silica gel. The fractions of R_f = 0.49 were collected and evaporated to give α-anomer *V* as a colourless sirup. Yield = 0.95 g (25.4 %), [α] (chloroform) = −46°. For $C_{20}H_{20}O_7$ (M_r = 372.36) w_i(calc.): 64.51 % C, 5.41 % H; w_i(found): 64.59 % C, 5.51 % H. ^{1}H NMR spectrum, δ: 7.32—8.08 (m, 10H, H_{arom}), 5.18 (d, 1H, $J_{2,3}$ = 0 Hz, $J_{3,4}$ = 3.6 Hz, H-3), 5.08 (s, 1H, $J_{1,2}$ = 0 Hz, H-1), 4.73 (dd, 1H, $J_{4,5a}$ = 3.4 Hz, $J_{5a,5b}$ = 11.2 Hz, H-5a), 4.68 (dd, 1H, $J_{4,5b}$ = 5.1 Hz, H-5b), 4.60 (m, 1H, H-4), 4.43 (s, 1H, H-2), 3.42 (s, 3H, OCH_3). ^{13}C NMR spectrum, δ: 166.67 and 166.21 (2 × *C*OPh), 133.29 and 132.89 (2 × C-4″), 129.85 and 129.60 (2 × (C-2″ and C-6″)), 129.24 and 128.82 (2 × C-1″), 128.20 and 128.14 (2 × (C-3″ and C-5″)), 108.86 (C-1), 81.42 (C-3), 80.59 (C-2), 79.42 (C-4), 64.04 (C-5), 54.76 (OCH_3).

The fractions with R_f = 0.47 were collected and evaporated to give β-anomer *VI* as a colourless sirup. Yield = 0.30 g (8 %), [α] (chloroform) = −11°. For $C_{20}H_{20}O_7$ (M_r = 372.36) w_i(calc.): 64.51 % C, 5.41 % H; w_i(found): 64.61 % C, 5.44 % H. ^{1}H NMR spectrum, δ: 7.37—8.09 (m, 10H, H_{arom}), 5.48 (t, 1H, $J_{2,3} = J_{3,4}$ = 6.0 Hz, H-3), 5.00 (d, 1H, $J_{1,2}$ = 4.6 Hz, H-1), 4.68 (dd, 1H, $J_{4,5a}$ = 4.3 Hz, $J_{5a,5b}$ = 11.6 Hz, H-5a), 4.55 (dd, 1H, $J_{4,5b}$ = 6.2 Hz, H-5b), 4.51 (m, 1H, H-4), 4.43 (dd, 1H, H-2), 3.47 (s, 3H, OCH_3). ^{13}C NMR spectrum, δ: 166.51 and 166.14 (2 × *C*OPh), 133.45 and 132.99 (2 × C-4″), 129.76 and 129.64 (2 × (C-2″ and C-6″)), 129.01 (2 × C-1″), 128.39 and 128.26 (2 × (C-3″ and C-5″)), 102.40 (C-1), 79.89 (C-3), 79.20 (C-2), 76.62 (C-4), 65.51 (C-5), 55.47 (OCH_3).

Methyl 2-*O*-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)-3,5-di-*O*-benzoyl-α-L-arabino-furanoside (*VIII*)

Freshly prepared, crystalline 2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl bromide (*VII*) [8] (0.9 g; 2.66 mmol) was added to a mixture of *V* (0.5 g; 1.34 mmol) and mercuric cyanide (0.4 g; 1.58 mmol) in dry dichloromethane (10 cm^3) and the resulting mixture was stirred with the exclusion of atmospheric moisture at r.t. for 2 h. TLC, toluene—acetone (φ_r = 5 : 1) then showed only traces of nucleophile *V*, the presence of a mixture of *VIII* and its α-anomer (R_f = 0.5) and the product of hydrolysis of *VII* (comparison with a standard). The mixture was worked-up [9] and the residue

was subjected to column chromatography, using linear gradient elution (hexane—acetone, $\varphi_r = 5 : 1 \rightarrow 3 : 1$) to give *VIII* as a colourless sirup. Yield = 0.65 g (76.8 %), $[\alpha]$ (chloroform) = −58°. For $C_{31}H_{34}O_{14}$ (M_r = 630.58) w_i(calc.): 59.04 % C, 5.44 % H; w_i(found): 59.13 % C, 5.47 % H. ^{1}H NMR spectrum, δ: 7.37—8.03 (m, 10H, H_{arom}), 5.22 (t, 1H, $J_{2',3'} = J_{3',4'} = 8.6$ Hz, H-3′), 5.20 (d, 1H, $J_{2,3} = 0$ Hz, $J_{3,4} = 3.8$ Hz, H-3), 5.10 (s, 1H, $J_{1,2} = 0$ Hz, H-1), 4.96 (ddd, 1H, $J_{4',5'a} = 5.1$ Hz, $J_{4',5'b} = 9.1$ Hz, H-4′), 4.95 (dd, 1H, $J_{1',2'} = 7.0$ Hz, H-2′), 4.87 (d, 1H, H-1′), 4.56 (d, 2H, $J_{4,5a} = J_{4,5b} = 4.7$ Hz, H-5a, H-5b), 4.55 (dt, 1H, H-4), 4.32 (s, 1H, H-2), 4.11 (dd, 1H, $J_{5'a,5'b} = 11.8$ Hz, H-5′a), 3.42 (s, 3H, OCH_3), 3.41 (dd, 1H, H-5′b), 2.07, 2.03, and 2.02 (3s, each 3H, 3 × CH_3CO). ^{13}C NMR spectrum, δ: 170.05, 169.86, and 169.53 (3 × *C*OMe), 166.20 and 165.89 (2 × *C*OPh), 133.55 and 133.17 (2 × C-4″), 129.83 (2 × (C-2″ and C-6″)), 129.78 and 129.24 (2 × C-1″), 128.52 and 128.43 (2 × (C-3″ and C-5″)), 107.91 (C-1), 100.20 (C-1′), 86.49 (C-2), 79.52 (C-4), 78.82 (C-3), 71.57 (C-3′), 70.83 (C-2′), 68.91 (C-4′), 64.26 (C-5), 62.35 (C-5′), 55.01 (OCH_3), 20.71 (3 × *C*H_3CO).

Methyl 2-*O*-*β*-D-Xylopyranosyl-*α*-L-arabinofuranoside (*IX*)

1 M-Methanolic solution of sodium methoxide (0.25 cm^3) was added to a solution of *VIII* (0.5 g; 0.79 mmol) in methanol (25 cm^3) and the reaction mixture was kept at r.t. for 90 min. TLC showed complete deacylation and the presence of final product *IX* (R_f = 0.2; chloroform—methanol ($\varphi_r = 5 : 1$)). The solution was neutralized with Dowex 50W (H^+) resin, filtered and concentrated. The residue was freed from methyl benzoate by column chromatography to give *IX* as colourless sirup. Yield = 0.21 g (89.4 %), $[\alpha]$ (methanol) = −85°. For $C_{11}H_{20}O_9$ (M_r = 296.27) w_i(calc.): 44.59 % C, 6.80 % H; w_i(found): 44.36 % C, 7.00 % H. ^{1}H NMR spectrum (in CD_3OD), δ: 4.91 (s, 1H, $J_{1,2} = 0$ Hz, H-1), 4.38 (d, 1H, $J_{1',2'} = 7.6$ Hz, H-1′), 4.04 (s, 1H, $J_{2,3} = 0$ Hz, H-2), 4.02 (dd, 1H, $J_{2',3'} = 3.6$ Hz, $J_{3',4'} = 10.1$ Hz, H-3′), 3.89 (dt, 1H, $J_{3,4} = J_{4,5b} = 5.3$ Hz, $J_{4,5a} = 3.1$ Hz, H-4), 3.86 (dd, 1H, $J_{4',5'a} = 5.3$ Hz, $J_{5'a,5'b} = 11.5$ Hz, H-5′a), 3.78 (dd, 1H, $J_{5a,5b} = 12.0$ Hz, H-5a), 3.65 (dd, 1H, H-5b), 3.49 (ddd, 1H, $J_{4',5'b} = 9.1$ Hz, H-4′), 3.35 (s, 3H, OCH_3), 3.33 (d, 1H, H-3), 3.20 (dd, 1H, H-5′b), 3.17 (dd, 1H, H-2′). ^{13}C NMR spectrum (in CD_3OD), δ: 109.11 (C-1), 104.63 (C-1′), 91.10 (C-2), 84.52 (C-4), 77.82 (C-3), 77.24 (C-3′), 74.93 (C-2′), 71.10 (C-4′), 67.11 (C-5′), 62.74 (C-5), 55.33 (OCH_3).

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REFERENCES

1. Wilkie, K. C. B., *Adv. Carbohydr. Chem. Biochem. 36*, 215 (1979).
2. Kusakabe, I., Ohgushi, S., Yasui, T., and Kobayashi, T., *Agric. Biol. Chem. 47*, 2713 (1983).
3. Ebringerová, A., Hromádková, Z., Alföldi, J., and Berth, G., *Carbohydr. Polym. 19*, 99 (1992).
4. Ebringerová, A., Hromádková, Z., Alföldi, J., and Hříbalová, V., *Carbohydr. Polym. 37*, 231 (1998).
5. Fletcher, H. G., Jr., *Methods Carbohydr. Chem. 2*, 228 (1963).
6. Ning, J. and Kong, F., *Bioorg. Med. Chem. Lett. 7*, 2941 (1997).
7. Génu-Dellac, C., Gosselin, G., and Imbach, J. L., *Carbohydr. Res. 216*, 249 (1991).
8. Schroeder, L. R., Counts, K. M., and Haigh, F. C., *Carbohydr. Res. 37*, 368 (1974).
9. Helferich, B. and Ost, W., *Chem. Ber. 95*, 2612 (1962).