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Note

Synthesis of trisaccharides related to an arabinoglucan*

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We have previously reported an investigation of the structure of the water-soluble polysaccharide, designated as GIa, which was isolated from the bark of *Melia azadirachta* (Meliaceae)[1,2]. GIa is a (1→4)-α-D-glucan having one (1→6)-α-L-arabinofuranosyl group for every five D-glucose residues. GIa showed a strong antitumor effect against Sarcoma-180. We report herein the synthesis, as model compounds, of trisaccharides that contain the basic structural features of the arabinoglucan.

The synthesis of trisaccharide **8**, which corresponds to the partial structure unit of GIa (**1**), was started by condensation of methyl 2,3-di-*O*-acetyl-4-*O*-(2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl)-β-D-glucopyranoside (**3**) [which had been prepared from methyl 2,3,2′,3′,4′-penta-*O*-acetyl-6,6′-di-*O*-trityl-β-D-maltoside (**2**)] with 2,3,5-tri-*O*-benzoyl-α-L-arabinofuranosyl bromide[3,4] (**6**); the latter compound had been prepared from methyl 2,3,5-tri-*O*-benzoyl-α-L-arabinofuranoside and **2** from methyl β-D-maltoside by direct tritylation and subsequent acetylation according to the method of Koizumi and Utamura[5]. The α-L-linked trisaccharide, methyl 2,3-di-*O*-acetyl-4-*O*-(2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl)-6-*O*-(2,3,5-tri-*O*-benzoyl-α-L-arabinofuranosyl)-β-D-glucopyranoside (**7**) was obtained in 62% yield from **3**. Its ^{1}H-n.m.r. spectrum showed signals characteristic for three benzoyl, one methoxyl, and five acetyl groups. Compound **7** was *O*-deacylated with triethylamine to give methyl *O*-α-D-glucopyranosyl-(1→4)-*O*-[(α-L-arabinofuranosyl)-(1→6)]-β-D-glucopyranoside (**8**), the ^{1}H-n.m.r. spectrum of which indicated three anomeric protons and the ^{13}C-n.m.r. spectrum (Table I) three anomeric carbon atoms. Introduction of the α-L-arabinofuranosyl group at O-6 deshielded C-6 by 5.8 p.p.m. as compared with methyl β-D-glucopyranoside[6] (δ 61.9).

Similarly, methyl 2,3,6-tri-*O*-acetyl-4-*O*-(2,3-di-*O*-acetyl-α-D-glucopyranosyl)-β-D-glucopyranoside (**5**), which was prepared from **4** according to the method of Koizumi and Utamura[5], and bromide **6** in nitromethane containing mercuric cyanide gave, after column chromatography, in 62% yield (based on **5**), a trisaccharide containing a (1→6)-linked α-L-arabinofuranosyl residue, methyl *O*-

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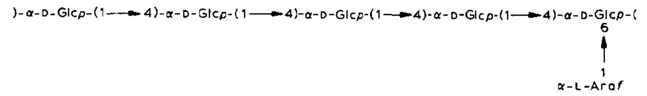
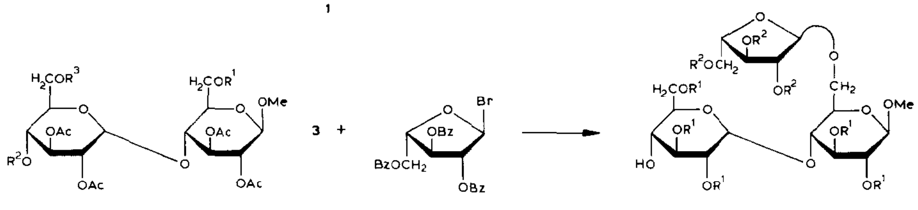


$$\text{)-}\alpha\text{-D-Glc}p\text{-}(1\rightarrow4)\text{-}\alpha\text{-D-Glc}p\text{-}(1\rightarrow4)\text{-}\alpha\text{-D-Glc}p\text{-}(1\rightarrow4)\text{-}\alpha\text{-D-Glc}p\text{-}(1\rightarrow \underset{\underset{\underset{\alpha\text{-L-Ara}f}{1}}{\uparrow}}{4)\text{-}\alpha\text{-D-Glc}p\text{-}(\,6})$$

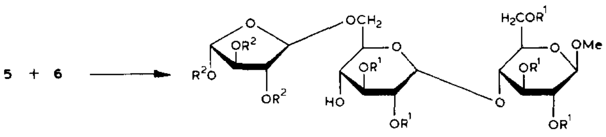
1



6

2 $R^1 = Tr, R^2 = Ac, R^3 = Tr$
3 $R^1 = R^2 = H, R^3 = Ac$
4 $R^1 = Ac, R^2, R^3 = PhCH$
5 $R^1 = Ac, R^2 = R^3 = H$

7 $R^1 = Ac, R^2 = Bz$
8 $R^1 = R^2 = H$



9 $R^1 = Ac, R^2 = Bz$
10 $R^1 = R^2 = H$

TABLE I

^{13}C-N.M.R. DATA (δ) FOR COMPOUNDS **3** AND **5–10**[a]

Carbon atom	*Compound*						
	3	**5**	**6**	**7**	**8**	**9**	**10**
C-1	101.1	101.5		101.1	104.4	101.5	104.3
2	72.2	72.3		72.1	74.1	70.9	74.0
3	72.7	72.3		72.6	77.2	70.9	77.4
4	75.5	75.6		75.2	78.9	74.6	78.7
5	72.3	72.8		73.7	74.6	72.3	74.6
6	62.9	61.2		65.1	67.7	63.5	62.2
C-1′	95.8	95.3		95.6	101.3	98.1	101.0
2′	71.1	69.5		70.9	73.1	69.8	72.9
3′	71.7	70.2		71.7	74.1	70.3	74.0
4′	68.7	68.9		68.7	70.4	69.1	70.7
5′	70.2	70.6		70.6	73.9	69.5	75.7
6′	62.6	60.3		63.0	61.6	66.0	68.0
C-1″			88.6	105.3	109.2	106.3	109.1
2″			84.7	81.1	82.3	81.3	82.3
3″			76.7	77.6	77.9	77.9	77.6
4″			85.7	81.8	85.1	82.2	84.8
5″			62.6	63.7	62.4	63.7	62.3
OMe	56.9	57.1		57.9	58.5	57.0	58.4

[a] For solutions of compound **3**, **5**, **6**, **7**, and **9** in $CDCl_3$, and for solutions of **8** and **10** in D_2O.

(2,3,5-tri-*O*-benzoyl-α-L-arabinofuranosyl)-(1→6)-*O*-(2,3-di-*O*-acetyl-α-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (**9**). Removal of the blocking groups with 50% methanolic triethylamine afforded methyl *O*-α-L-arabinofuranosyl-(1→6)-*O*-α-D-glucopyranosyl-(1→4)-β-D-glucopyranoside (**10**). The α-L configuration for the newly formed glycosidic bond in **10** was evident from the ^{13}C-n.m.r. spectrum[4] (C-1″ at δ 109.1). No anomeric impurities were observed by ^{1}H- and ^{13}C-n.m.r. spectrometry in all the compounds described. The ^{13}C shifts of the trisaccharide derivatives and related compounds are listed in Table I.

EXPERIMENTAL

General methods. — Melting points were determined with a Yanagimoto microapparatus and are uncorrected. ^{1}H-N.m.r. spectra were recorded with a JNM MH-100 spectrometer, and ^{13}C-n.m.r. spectra with a FX-100 instrument, tetramethylsilane being the internal standard in both cases. Optical rotations were measured with a JASCO DIP-4 digital polarimeter. Thin-layer chromatography was conducted on precoated Silica gel plates (Merck GF-254), and the detection of compounds was achieved by quenching of u.v. fluorescence and with 10% H_2SO_4 solution. Column chromatography was carried out on silica gel (Merck Kieselgel 60).

Materials. — 2,3,5-Tri-*O*-benzoyl-α-L-arabinofuranosyl bromide (**6**) {$[\alpha]_D^{18}$ −47.5° (*c* 0.57, chloroform)} was prepared from methyl 2,3,5-tri-*O*-benzoyl-α-L-arabinofuranoside according to the method of Fletcher[3]. Methyl 2,3,2′,3′,4′-penta-*O*-acetyl-6,6′-di-*O*-trityl-β-D-maltoside (**2**), methyl 2,3,6,2′,3′-penta-*O*-acetyl-4′,6′-*O*-benzylidene-β-D-maltoside (**4**), and methyl 2,3,6,2′,3′-penta-*O*-acetyl-β-D-maltoside (**5**) were obtained by the procedure of Koizumi and Utamura[5].

*Methyl 2,3-di-O-acetyl-4-O-(2,3,6-tri-O-acetyl-α-*D*-glucopyranosyl)-β-*D*-glucopyranoside* (**3**). — A solution of **2** (1 g) in 80% acetic acid (20 mL) was stirred at 60° for 8 h. It was then poured into ice–water and extracted with chloroform. Work-up in the usual manner gave a solid (500 mg, 92.8% yield), m.p. 86–88° (ethanol), $[\alpha]_D^{18}$ +31.1° (*c* 0.5, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 3.53 (3 H, OMe), 2.21–1.96 (15 H, 5 OAc).

Anal. Calc. for $C_{23}H_{34}O_{16}$: C, 48.76; H, 6.05. Found: C, 48.82; H, 6.11.

*Methyl 2,3-di-O-acetyl-4-O-(2,3,6-tri-O-acetyl-α-*D*-glucopyranosyl)-6-O-(2,3,5-tri-O-benzoyl-α-*L*-arabinofuranosyl)-β-*D*-glucopyranoside* (**7**). — A solution of 2,3,5-tri-*O*-benzoyl-α-L-arabinofuranosyl bromide (**6**) (788 mg, 1.5 mmol) in nitromethane (10 mL) was added to a mixture of methyl 2,3,2′,3′,6′-penta-*O*-acetyl-β-D-maltoside (**3**) (566 mg, 1 mmol), $Hg(CN)_2$ (4.5 g), and molecular sieve 4A (1.5 g) in the same solvent (10 mL). After being stirred for 6 h at 60°, the mixture was cooled and washed successively with saturated aqueous $NaHCO_3$, saturated aqueous NaCl, and water, dried (Na_2SO_4), and evaporated to give a syrup that contained, as shown by t.l.c. in 4:1 (v/v) benzene–acetone, a major product (R_F 0.49) and a hydrolysis product of **6** (R_F 0.25). The residue was chromatographed on a column of silica gel. The product, eluted with 4:1 (v/v) benzene–acetone, crystallized from ethanol (862 mg, yield 62.2%), m.p. 86–87°, $[\alpha]_D^{22}$ +16.8° (*c* 1.0, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 5.52 (s, 1 H, H-1″), 5.39 (d, 1 H, *J* 4 Hz, H-1′), 4.46 (d, 1 H, *J* 8 Hz, H-1), 3.41 (3 H, OMe), and 2.03–1.96 (15 H, 5 OAc).

Anal. Calc. for $C_{49}H_{54}O_{23}$: C, 58.22; H, 5.38. Found: C, 58.45; H, 5.43.

*Methyl 6-O-α-*L*-arabinofuranosyl-4-*O*-α-*D*-glucopyranosyl-β-*D*-glucopyranoside* (**8**). — Compound **7** (147 mg) was *O*-deacetylated and *O*-debenzoylated with triethylamine (0.5 mL) in 50% aqueous methanol (4 mL) and, after removal of the solvents, the residue crystallized from ethanol (64.3 mg, 90.5%), m.p. 102–104°, $[\alpha]_D^{22}$ +5.1° (*c* 1.0, water); t.l.c. (5:4:1, v/v, chloroform–methanol–water) R_F 0.33; ^{1}H-n.m.r. (D_2O): δ 5.35 (d, 1 H, *J* 4 Hz, H-1′), 5.11 (s, 1 H, H-1″), 4.40 (d, 1 H, *J* 8 Hz, H-1), and 3.57 (3 H, OMe).

Anal. Calc. for $C_{18}H_{32}O_{15}$: C, 44.26; H, 6.60. Found: C, 44.41; H, 6.66.

Methyl O-*(2,3,5-tri-*O*-benzoyl-α-*L*-arabinofuranosyl)-(1→6)-*O*-(2,3-di-*O*-acetyl-α-*D*-glucopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-*D*-glucopyranoside* (**9**). — Compound **5** (283 mg, 0.5 mmol) was condensed with **6** (525 mg, 1 mmol) as described for the synthesis of **7**. The dried solution was evaporated to give a syrup, which was chromatographed on a column of silica gel with 4:1 (v/v) benzene–acetone as eluent. Compound **9** was obtained as a white powder (313 mg, 62%), m.p. 85–86°, $[\alpha]_D^{22}$ +20.1° (*c* 1.62, chloroform); t.l.c. (4:1, v/v, benzene–acetone) R_F 0.49; ^{1}H-n.m.r. ($CDCl_3$): δ 8.10–7.84 (m, 6 H, arom. H), 7.60–7.16 (m, 9 H, arom. H), 5.48 (s, 1 H, H-1″), 5.32 (d, 1 H, *J* 4 Hz, H-1′), 4.40 (d, 1 H, *J* 8 Hz, H-1), 3.38 (3 H, OMe), and 2.12–1.80 (15 H, 5 OAc).

Anal. Calc. for $C_{49}H_{54}O_{23}$: C, 58.22; H, 5.38. Found: C, 58.18; H, 5.43.

Methyl O-*α-*L*-arabinofuranosyl-(1→6)-*O*-α-*D*-glucopyranosyl-(1→4)-β-*D*-glucopyranoside* (**10**). — Compound **9** (150 mg) was *O*-deacylated with triethylamine (0.5 mL). The solution was evaporated to give a white powder (65.5 mg, 90.3%), $[\alpha]_D^{22}$ +4.0° (*c* 3.0, water); t.l.c. (5:4:1, v/v, chloroform–methanol–water) R_F 0.38; ^{1}H-n.m.r. (D_2O): δ 5.32 (d, 1 H, *J* 4 Hz, H-1′), 5.08 (s, 1 H, H-1″), 4.36 (d, 1 H, *J* 8 Hz, H-1), and 3.55 (3 H, OMe).

Anal. Calc. for $C_{18}H_{32}O_{15}$: C, 44.26; H, 6.60. Found: C, 44.36; H, 6.72.

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