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Synthesis of regioisomeric methyl α-L-arabinofuranobiosides

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Abstract

The three regioisomers of methyl α-L-arabinofuranobioside, namely methyl *O*-α-L-arabinofuranosyl-(1→2)-α-L-arabinofuranoside, methyl *O*-α-L-arabinofuranosyl-(1→3)-α-L-arabinofuranoside, and methyl *O*-α-L-arabinofuranosyl-(1→5)-α-L-arabinofuranoside, were synthesized for use as substrates in studies of the specificity of α-L-arabinofuranosidase. The regiospecifically protected precursors, namely methyl 3,5-di-*O*-benzoyl-α-L-arabinofuranoside, methyl 2,5-di-*O*-benzyl-α-L-arabinofuranoside, and methyl 2,3-di-*O*-benzoyl-α-L-arabinofuranoside, were prepared from 2,3,5-tri-*O*-benzoyl-α-L-arabinofuranosyl chloride (**4**) and methyl 5-*O*-trityl-α-L-arabinofuranoside, respectively, and glycosylated with **4** in the presence of silver trifluoromethanesulfonate and *s*-collidine. ^{1}H and ^{13}C NMR data for all compounds are presented.

Keywords: Regioisomeric; Arabinofuranobiosides, methyl α-L-

1. Introduction

L-Arabinofuranose units are widely distributed in the cell-wall and intercellular-matrix polysaccharides, including arabinofuranans, of higher plants. The many α-L-arabinofuranans so far analyzed are highly branched, with (1→5)-links between the main-chain residues, which are partially substituted at O-2 and/or O-3 with single or two-unit side chains [1]. Recently, we reported the substrate specificity of α-L-arabinofuranosidase from *Aspergillus niger* 5-16 [2], but we did not show whether the enzyme can hydrolyze (1→2)- and (1→3)-α-L-arabinofuranosidic linkages. There are many papers on α-L-arabinofuranosidases [3], but no one seems to have elucidated the detailed substrate specificity of one of

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these enzymes. As for substrates, there is some work about the synthesis of α-L-arabinofurano-oligosaccharides, (1→5)- and (1→3)-α-L-arabinofuranans, for example, reported by Backinowsky et al. [4] and Nepogod'ev et al. [5], respectively. The regioisomeric methyl α-L-arabinofuranobiosides were also prepared, in the protected form, by Backinowsky et al. [6], but the free glycosides were not obtained. Therefore, we sought convenient syntheses of the regioisomeric methyl α-L-arabinofuranobiosides in order to determine the precise substrate specificity of the *Aspergillus* arabinofuranosidase and related enzymes. Herein we report the details of our syntheses.

2. Results and discussion

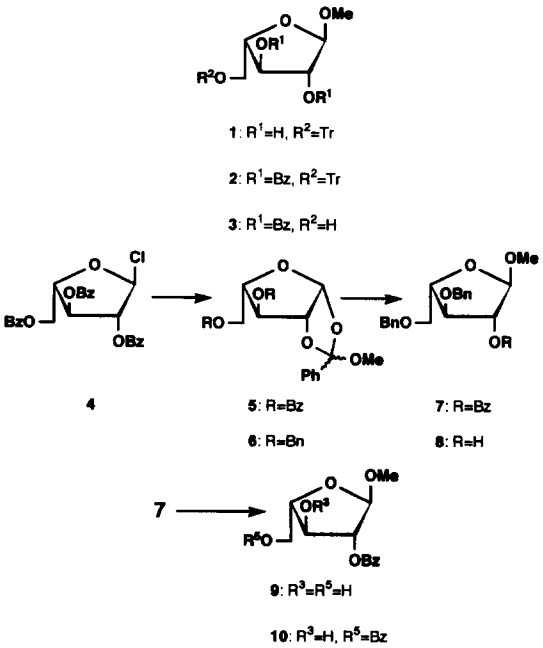
Our target compounds, the α-L-arabinofuranobioses, were prepared as the methyl glycosides. Since the methyl-glycosidic linkage is largely resistant to α-L-arabinofuranosidases [7], the hydrolysis of the intersugar linkage is easily followed by analysis for the reducing sugar, for example, by the Somogyi–Nelson method. And another advantage of anomeric protection with an *O*-methyl group is that the ^{1}H and ^{13}C NMR spectra are more easily assignable than those of disaccharides whose reducing ends are free.

The arabinose acceptor unsubstituted at the O-5 position was synthesized from methyl 5-*O*-trityl-α-L-arabinofuranoside (**1**) [8] in two steps (formulas **1–3**). Compound **1** was benzoylated, then detritylated with formic acid [9] to give methyl 2,3-di-*O*-benzoyl-α-L-arabinofuranoside (**3**) in 88% overall yield.

To prepare the acceptor (**8**) having O-2 unsubstituted, the known 2,3,5-tri-*O*-benzoyl-α-L-arabinofuranosyl chloride (**4**) [10] was converted [11] into the 1,2-orthoester **5** [12]. Sequential replacement of the benzoyl groups of **5** by benzyl groups [13] to give **6**, acid-catalyzed rearrangement of the orthoester function [14] to give **7**, and debenzoylation gave methyl 3,5-di-*O*-benzyl-α-L-arabinofuranoside (**8**) in 44% overall yield from **4**.

For the preparation of the arabinose acceptor unsubstituted at O-3, compound **7** was debenzylated by catalytic hydrogenolysis to give **9**. The primary hydoxyl group of **9** was then selectively benzoylated by a Mitsunobu reaction [15] to give crystalline methyl 2,5-di-*O*-benzoyl-α-L-arabinofuranoside (**10**, Scheme 1) in 78% overall yield from **7**. Although Helm et al. [16] advocated the use of the *tert*-butyldimethylsilyl group for the selective protection of O-5, we chose the benzoyl group because the deprotection of the eventual glycosylation product could then be accomplished in one step.

As the arabinofuranosyl donor, we chose the chloride **4** because of its superior stability, as compared with the corresponding bromide [10]. The coupling reactions between **4** and the acceptors **3**, **8**, and **10** were carried out in the presence of silver trifluoromethanesulfonate (AgOTf) and *s*-collidine [17], according to a published procedure [10] (Scheme 2). The glycosylation products **11**, **13**, and **15** were isolated by flash-column chromatography in yields of 81, 96, and 69%, respectively. The 1,2-*trans* disposition of their glycosidic linkages was indicated by the characteristic H-1,2 coupling constants (<1 Hz) and C-1 chemical shifts (**11**, 106.8; **13**, 105.5; **15**, 107.0 ppm) of their nonreducing L-arabinofuranosyl moieties [10]. The coupling reactions proceeded with remarkable α-selectivity as a result of neighboring group participation by the benzoyl substituent at position 2 of **4**. β-Anomeric glycosylation products were negligible on TLC. The yield in the (1→3)-glycosylation



Scheme 1. Synthesis of the acceptors **3**, **8**, and **10**.

(69%) was the lowest of the three reactions. This result may be explained by a lowering of the reactivity of O-3 for glycosylation by the two neighboring benzoyl groups at O-2 and O-5 of the acceptor **10**.

The disaccharide derivatives **11** and **15** were debenzoylated to give methyl α-L-arabinofuranobiosides **12** and **16**, respectively. The disaccharide derivative **13** was firstly debenzylated by catalytic hydrogenolysis and then debenzoylated to give **14**. The ^{1}H and ^{13}C NMR spectra of the three methyl α-L-arabinofuranobiosides are presented in Tables 1 and 2, respectively. These assignments were made from ^{1}H–^{1}H COSY and ^{1}H–^{13}C heteronuclear correlated spectroscopy experiments. Specific assignment of the H-5*proR* and H-5*proS* signals is based on their $J_{4,5}$ values ($J_{4,5proR} < J_{4,5proS}$) [18,19].

In conclusion, we synthesized the isomeric methyl α-L-arabinofuranobiosides by using regioselectively protected L-arabinofuranose derivatives as glycosyl acceptors, and the highly stereoselective glycosylation reaction, promoted by silver trifluoromethanesulfonate and *s*-collidine, of the arabinofuranosyl chloride **4**.

3. Experimental

General.—Melting points are uncorrected. Optical rotations were measured with a Jasco DIP-140 polarimeter at 24°C, unless noted otherwise. Solvents for reactions were purified before used. Traditional chromatography and flash chromatography were carried out on columns of Silica Gel (Merck, 240–400 mesh). TLC was conducted on plates coated with Silica Gel 60 F_{254} (Merck), and products were detected either by UV light or by charring

Table 1
^{1}H NMR data of α-L-arabinofuranobioside regioisomers **12**, **14**, and **16**

Compound		Chemical shifts in ppm [a] (*J* in Hz [b])						
		H-1	H-2	H-3	H-4	H-5*proR*	H-5*proS*	OMe
12	H	4.984	4.071	4.011	4.176	3.794	3.893	3.425
	J	d (1.5)	dd (1.6, 3.2)	dd (3.2, 5.7)	ddd (3.3, 5.7)	dd (3.3, 11.4)	dd (5.7, 11.4)	
	H′	5.090	4.136	3.961	4.100	3.838	3.723	
	J	d (1.3)	dd (1.4, 3.3)	dd (3.3, 6.0)	ddd (3.4, 5.9)	dd (3.4, 12.3)	dd (5.8, 12.3)	
14	H	5.048	4.087	4.064	4.11 [c]	3.834	3.720	3.429
	J	d (1.5)	dd (1.7, 3.3)	dd (3.3, 6.0)		dd (3.4, 12.4)	dd (5.7, 12.4)	
	H′	5.175	4.123	3.934	4.037	3.843	3.720	
	J	d (1.4)	dd (1.5, 3.3)	dd (3.3, 6.0)	ddd (3.2, 5.8)	dd (3.3, 12.4)	dd (5.7, 12.4)	
16	H	4.966	4.227	4.025	4.147	3.839	3.763	3.425
	J	br s	dd (1.2, 3.2)	dd (3.3, 5.7)	ddd (3.3, 5.6)	dd (3.0, 12.2)	dd (5.7, 12.3)	
	H′	5.157	4.127	3.943	4.04 [c]	3.869	3.714	
	J	d (1.3)	dd (1.5, 3.4)	dd (3.4, 6.3)		dd (3.2, 12.2)	dd (5.9, 12.3)	

[a] Measured at 500 MHz in D_2O with sodium 3-(trimethylsilyl)propionate-2,2,3,3-d_4 as internal standard.
[b] Observed first-order splittings.
[c] These signals were overlapped with other signals.

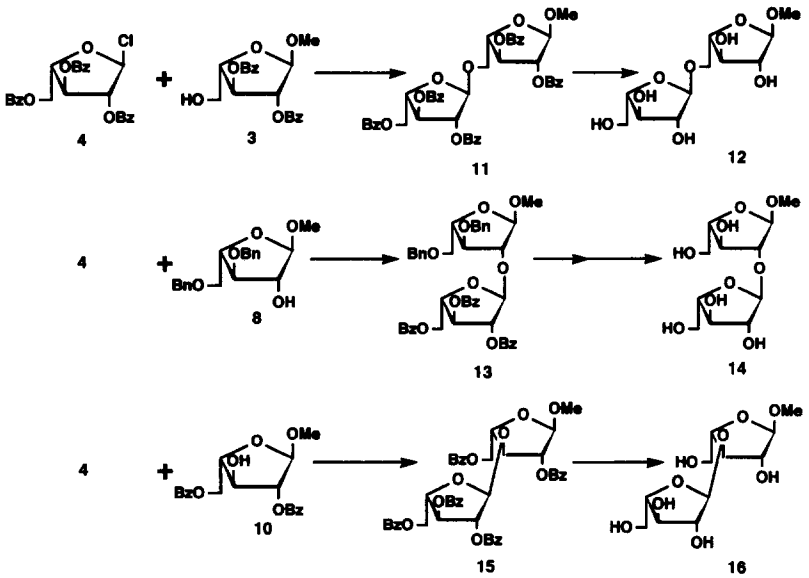
with H_2SO_4. NMR spectra were recorded with a Jeol JNM-EX270 or Bruker AM-500 NMR spectrometer for solutions in $CDCl_3$, C_6D_6, or D_2O. The values for δ_H and δ_C are referenced to internal tetramethylsilane for spectra taken in $CDCl_3$ and C_6D_6, and to sodium 3-(trimethylsilyl)propionate-2,2,3,3-d_4 for spectra taken in D_2O. Two-dimensional (2D) correlated spectroscopy (COSY) and 2D heteronuclear correlated spectropcopy were performed with a Jeol JNM-EX270 instrument, using standard Jeol software.

*Methyl 2,3-di-*O*-benzoyl-5-*O*-trityl-α-*L*-arabinofuranoside* (**2**).—Benzoyl chloride (2.4 g, 17 mmol) was added to a solution of methyl 5-*O*-trityl-α-L-arabinofuranoside (**1**, 1.30 g, 3.20 mmol) [8] in pyridine (20 mL), and the mixture was stirred at room temperature

Table 2
^{13}C NMR data of α-L-arabinofuranobioside regioisomers **12**, **14**, and **16**

Compound		Chemical shifts in ppm [a]					
		C-1	C-2	C-3	C-4	C-5	OMe
Methyl α-L-arabinofuranoside [b]		111.0	83.4	79.0	86.6	63.9	57.6
12	C	111.3	83.4	79.4	85.1	69.7	57.8
	C′	110.3	83.8	79.4	86.8	64.0	
14	C	110.1	89.9	77.7	85.8	63.6	57.8
	C′	110.0	84.1	79.4	86.9	64.0	
16	C	111.3	84.9 [c]	81.9	86.0	63.9 [d]	57.6
	C′	109.3	84.0 [c]	79.4	86.7	64.0 [d]	

[a] Measured at 67.8 MHz in D_2O with sodium 3-(trimethylsilyl)propionate-2,2,3,3-d_4 as internal standard.
[b] From [20].
[c,d] These assignments may be reversed.



Scheme 2. Synthesis of methyl α-L-arabinofuranobioside regioisomers **12**, **14**, and **16**.

for 24 h. The solution was diluted with $CHCl_3$ (200 mL), then washed with water and brine, dried ($MgSO_4$), and concentrated. The residue was purified by chromatography on silica gel (30 g, 3:1 hexane–EtOAc) to give **2** (1.78 g, 91%); $[\alpha]_D$ +24.8° (*c* 3.85, $CHCl_3$); R_f 0.35 (3:1 hexane–EtOAc); ^{1}H NMR ($CDCl_3$): δ 3.48 (s, 3 H, OMe), 4.11 (m, 2 H, H-5a,5b), 4.45 (q, 1 H, *J* 4.7 Hz, H-4), 5.14 (s, 1 H, H-1), 5.43 (d, 1 H, *J* 1.5 Hz, H-2), and 5.58 (dd, 1 H, *J* 1.5, 4.6 Hz, H-3); ^{13}C NMR: δ 54.9 (OMe), 63.4 (C-5), 77.9 (C-3), 81.4 (C-4), 82.2 (C-2), 86.8 (*tert*-C), 106.8 (C-1), 165.4, and 165.5 (C=O). Anal. Calcd for $C_{39}H_{34}O_7$: C, 76.21; H, 5.58. Found: C, 76.51; H, 5.62.

Methyl 2,3-di-O-benzoyl-α-L-arabinofuranoside (**3**).—Formic acid [9] (100 μL) was added to a solution of **2** (1.78 g, 2.90 mmol) in $CHCl_3$ (10 mL), and the solution was stirred at room temperature for 4 h. After the reaction was complete, the mixture was diluted with $CHCl_3$ (50 mL) and washed with aq $NaHCO_3$, water, and brine. The washed solution was dried ($MgSO_4$) and concentrated, and the residue was purified by silica gel column chromatography (60 g, 4:1 → 2:1 hexane–EtOAc) to give **3** (1.05 g, 97%); $[\alpha]_D$ +44.0° (*c* 2.78, $CHCl_3$); R_f 0.37 (3:1 hexane–EtOAc); ^{1}H NMR ($CDCl_3$): δ 3.47 (s, 3 H, OMe), 3.98 (dd, 1 H, *J* 4.0, 12.2 Hz, H-5a), 4.04 (dd, 1 H, *J* 3.6, 12.2 Hz, H-5b), 4.32 (m, 1 H, H-4), 5.14 (s, 1 H, H-1), 5.45 (dd, 1 H, *J* 1.2, 5.1 Hz, H-3), and 5.53 (d, 1 H, *J* 1.2 Hz, H-2); ^{13}C NMR: δ 55.0 (OMe), 62.3 (C-5), 77.8 (C-3), 81.9 (C-4), 83.4 (C-2), 106.7 (C-1), 165.4, and 166.2 (C=O). Anal. Calcd for $C_{20}H_{20}O_7$: C, 64.51; H, 5.41. Found: C, 64.61; H, 5.45.

3,5-Di-O-benzoyl-1,2-(α-methoxybenzylidene)-β-L-arabinofuranose (**5**).—A slurry of 2,3,5-tri-*O*-benzoyl-α-L-arabinofuranosyl chloride (**4**, 1.44 g, 3.00 mmol) [10] and activated, powdered 4A molecular sieves (0.5 g) in dry CH_2Cl_2 (10 mL) was stirred at room temperature for 30 min. Triethylamine (840 μL, 6.0 mmol), tetrabutylammonium bromide [11] (1.0 g, 3.0 mmol), and dry MeOH (150 μL, 4.5 mmol) were added to the mixture,

and it was stirred at room temperature for 24 h under Ar. The suspension was then filtered through a Celite pad, and insoluble materials were washed with CH_2Cl_2. The filtrate and washings were combined, washed with water and brine, dried ($MgSO_4$), and concentrated. The residue was purified by silica gel column chromatography (30 g, 2:1 hexane–EtOAc containing 0.5% Et_3N) to give **5** (1.15 g, 80%); $[\alpha]_D$ +17.6° (*c* 1.08, $CHCl_3$); lit. [12] $[\alpha]_D^{23}$ +18° (*c* 1, $CHCl_3$); R_f 0.35 (3:1 hexane–EtOAc); ^{1}H NMR ($CDCl_3$): δ 3.19 (s, 3 H, OMe), 4.19–4.31 (m, 2 H, H-5a,5b), 4.62 (m, 1 H, H-4), 5.11 (d, 1 H, *J* 4.3 Hz, H-2), 5.52 (d, 1 H, *J* 0.6 Hz, H-3), and 6.35 (d, 1 H, *J* 4.3 Hz, H-1); ^{13}C NMR ($CDCl_3$): δ 51.0 (OMe), 63.8 (C-5), 77.7 (C-3), 84.0 (C-4), 84.9 (C-2), 106.4 (C-1), 123.5 (*tert*-C), 165.3, and 165.8 (C=O).

*3,5-Di-*O*-benzyl-1,2-(α-methoxybenzylidene)-β-*L*-arabinofuranose* (**6**).—Powdered KOH [13] (1.4 g) was added to a solution of **5** (1.05 g, 2.20 mmol) and benzyl bromide (0.9 g, 4.6 mmol) in dry THF (20 mL), and the suspension was refluxed for 4 h with exclusion of moisture. It was then cooled and diluted with CH_2Cl_2 (150 mL) and water (150 mL). The CH_2Cl_2 layer was washed with water, aq $NaHCO_3$, water, and brine, dried ($MgSO_4$), and concentrated. The residue was purified by chromatography on silica gel (20 g, 5:1 → 3:1 hexane–EtOAc containing 0.5% Et_3N) to give **6** (0.76 g, 71%); $[\alpha]_D$ +10.7° (*c* 1.89, benzene); R_f 0.41 (15:1 benzene–EtOAc); ^{1}H NMR (C_6D_6): δ 2.99 (s, 3 H, OMe), 3.28 (dd, 1 H, *J* 8.6, 9.6 Hz, H-5a), 3.41 (dd, 1 H, *J* 3.6, 9.6 Hz, H-5b), 4.11 (br s, 1 H, H-3), 4.52 (m, 1 H, H-4), 4.82 (d, 1 H, *J* 4.3 Hz, H-2), and 6.11 (d, 1 H, *J* 4.3 Hz, H-1); ^{13}C NMR (C_6D_6): δ 50.9 (OMe), 71.9 (C-5), 77.9 (C-3), 85.6 (C-4), 86.3 (C-2), 107.3 (C-1), and 124.2 (*tert*-C). Anal. Calcd for $C_{39}H_{34}O_7$: C, 76.21; H, 5.58. Found: C, 76.51; H, 5.62.

*Methyl 2-*O*-benzoyl-3,5-di-*O*-benzyl-α-*L*-arabinofuranoside* (**7**).—A solution of **6** (0.76 g, 1.56 mmol) in dry CH_2Cl_2 (5 mL) was treated with 0.4 M trimethylsilyl trifluoromethanesulfonate [14] in CH_2Cl_2 (20 μL), and the mixture was kept at room temperature for 2 h under Ar. It was then diluted with CH_2Cl_2 (100 mL), washed with aq $NaHCO_3$, water, and brine, dried ($MgSO_4$), and concentrated. The residue was purified by chromatography on silica gel (25 g, 5:1 → 3:1 hexane–EtOAc) to give **7** (647 mg, 92%); $[\alpha]_D$ −48.4° (*c* 1.89, $CHCl_3$); R_f 0.38 (15:1 benzene–EtOAc); ^{1}H NMR ($CDCl_3$): δ 3.45 (s, 3 H, OMe), 3.58 (dd, 1 H, *J* 5.1, 10.7 Hz, H-5a), 3.65 (dd, 1 H, *J* 3.8, 10.7 Hz, H-5b), 4.00 (m, 1 H, *J* 1.1, 5.4 Hz, H-3), 4.32 (ddd, 1 H, *J* 3.8, 5.2 Hz, H-4), 5.08 (s, 1 H, H-1), and 5.36 (d, 1 H, *J* 1.2 Hz, H-2); ^{13}C NMR ($CDCl_3$): δ 55.0 (OMe), 69.4 (C-5), 81.8 (C-4), 82.1 (C-3), 83.2 (C-2), 107.2 (C-1), and 165.4 (C=O). Anal. Calcd for $C_{27}H_{28}O_6 \cdot 0.25\ H_2O$: C, 71.59; H, 6.34. Found: C, 71.63; H, 6.24.

*Methyl 3,5-di-*O*-benzyl-α-*L*-arabinofuranoside* (**8**).—A solution of **7** (547 mg, 1.21 mmol) in dry MeOH (5 mL) was treated with 0.1 N NaOMe in MeOH (2.0 mL), and the mixture was stirred at room temperature for 6 h. The solution was neutralized with Amberlite 200-C resin (H^+ form), and then the resin was filtered off and washed with MeOH. The filtrate and washings were combined and concentrated. The residue was purified by chromatography on silica gel (20 g, 5:1 → 2:1 hexane–EtOAc) to give **8** (350 mg, 91%); $[\alpha]_D$ −125° (*c* 1.38, $CHCl_3$); R_f 0.30 (2:1 hexane–EtOAc); ^{1}H NMR ($CDCl_3$): δ 3.41 (s, 4 H, OMe and O*H*), 3.43 (dd, 1 H, *J* 2.3, 10.5 Hz, H-5a), 3.65 (dd, 1 H, *J* 2.3, 10.5 Hz, H-5b), 3.89 (d, 1 H, *J* 2.6 Hz, H-3), 4.12 (s, 1 H, H-2), 4.27 (q, 1 H, *J* 2.5 Hz, H-4), and 4.90 (s, 1 H, H-1); ^{13}C NMR ($CDCl_3$): δ 55.2 (OMe), 69.6 (C-5), 77.8 (C-2), 83.5 (C-3), 84.8

(C-4), and 110.4 (C-1). Anal. Calcd for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.84; H, 7.09.

Methyl 2-O-benzoyl-α-L-arabinofuranoside (**9**).—A mixture of **7** (500 mg, 1.02 mmol) and 10% Pd–C (50 mg) in MeOH (5 mL) was stirred for 1 day at room temperature under H_2 at 1 atmosphere until the reaction was complete. The mixture was filtered, washed with water, and concentrated. The residue was purified by silica gel chromatography (20 g, 10:1 $CHCl_3$–MeOH) to give **9** (210 mg, 95%); $[\alpha]_D$ −81.2° (*c* 0.70, $CHCl_3$); R_f 0.40 (10:1 $CHCl_3$–MeOH); ^{1}H NMR ($CDCl_3$): δ 3.46 (s, 3 H, OMe), 5.08 (t, 1 H, *J* 1.2 Hz, H-2), and 5.15 (d, 1 H, *J* 1.1 Hz, H-1); ^{13}C NMR ($CDCl_3$): δ 55.1 (OMe), 61.9 (C-5), 76.4 (C-4), 84.0 (C-3), 86.0 (C-2), 106.4 (C-1), and 166.7 (C=O). Anal. Calcd for $C_{13}H_{16}O_6$: C, 58.20; H, 6.01. Found: C, 58.26; H, 6.06.

Methyl 2,5-di-O-benzoyl-α-L-arabinofuranoside (**10**).—A solution of diethyl azodicarboxylate (205 mg) [15] and benzoic acid (144 mg) in dry dioxane (5 mL) was added dropwise to a solution of **9** (210 mg, 0.78 mmol) and triphenylphosphine (308 mg) in dry dioxane (5 mL), with stirring at room temperature. The mixture was stirred for 2 h, and the solvent was evaporated. The residue was purified by chromatography on silica gel (30 g, 3:1→1:1 hexane–EtOAc) to give **10** (313 mg, 82%); mp 92–93°C (from hexane–EtOAc); $[\alpha]_D$ −42.9° (*c* 0.83, $CHCl_3$); R_f 0.53 (1:1 hexane–EtOAc); ^{1}H NMR ($CDCl_3$): δ 3.38 (br s, 1 H, O*H*), 3.48 (s, 3 H, OMe), 4.25 (br d, 1 H, *J* 4.0 Hz, H-3), 4.43 (ddd, 1 H, *J* 4.0, 5.4 Hz, H-4), 4.53 (dd, 1 H, *J* 5.3, 11.9 Hz, H-5a), 4.65 (dd, 1 H, *J* 3.6, 11.9 Hz, H-5b), 5.13 (dd, 1 H, *J* 0.7, 2.3 Hz, H-2), and 5.19 (s, 1 H, H-1); ^{13}C NMR ($CDCl_3$): δ 55.1 (OMe), 63.8 (C-5), 77.3 (C-4), 81.9 (C-3), 85.5 (C-2), 106.4 (C-1), 166.3, and 166.6 (C=O). Anal. Calcd for $C_{20}H_{20}O_7$: C, 64.51; H, 5.41. Found: C, 64.59; H, 5.39.

Methyl O-*(2,3,5-tri-O-benzoyl-α-L-arabinofuranosyl)-(1→5)-2,3-di-O-benzoyl-α-L-arabinofuranoside* (**11**).—A mixture of the acceptor **3** (200 mg, 0.54 mmol), dry CH_2Cl_2 (15 mL), and activated, powdered 4A molecular sieves (500 mg) was stirred under Ar. The mixture was cooled to 0°C, and the arabinofuranosyl donor **4** (306 mg, 0.64 mmol) was added to the mixture. After the dissolution of **4** was complete, silver trifluoromethanesulfonate (AgOTf) (327 mg, 1.27 mmol) and *s*-collidine (155 μL, 1.17 mmol) were rapidly added. The mixture was stirred for 30 min, and then filtered through a Celite pad. The filtrate was successively washed with aq $Na_2S_2O_3$, cold 3 N H_2SO_4, water, and brine, dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography on silica gel (50 g, 15:1 benzene–EtOAc) to give **11** (357 mg, 81%); $[\alpha]_D$ +11.5° (*c* 1.98, $CHCl_3$); R_f 0.34 (20:1 benzene–EtOAc); ^{1}H NMR ($CDCl_3$): δ 3.45 (s, 3 H, OMe), 3.99 (dd, 1 H, *J* 2.6, 11.2 Hz, H-5b), 4.24 (dd, 1 H, *J* 4.3, 11.2 Hz, H-5a), 4.46 (m, 1 H, H-4), 4.67 (dd, 1 H, *J* 4.6, 11.5 Hz, H-5′b), 4.75 (m, 1 H, *J* 3.0, 4.6 Hz, H-4′), 4.85 (dd, 1 H, *J* 3.0, 11.5 Hz, H-5′a), 5.13 (s, 1 H, H-1), 5.47 (s, 1 H, H-1′), 5.52 (d, 1 H, *J* 1.3 Hz, H-2′), 5.58 (br d, 1 H, *J* 4.6 Hz, H-3′), and 5.64 (m, 2 H, H-2,3); ^{13}C NMR ($CDCl_3$): δ 54.7 (OMe), 63.7 (C-5), 66.1 (C-5′), 77.3 (C-3′), 77.8 (C-3), 81.2 (C-4), 81.6 (C-4′), 81.9 (C-2′), 81.9 (C-2), 105.9 (C-1), 106.8 (C-1′), 165.2, 165.4, 165.7 (2 C), and 166.2 (C=O). Anal. Calcd for $C_{46}H_{40}O_{14}$: C, 67.64; H, 4.94. Found: C, 67.60; H, 4.91.

Methyl O-*α-L-arabinofuranosyl-(1→5)-α-L-arabinofuranoside* (**12**).—A solution of **11** (351 mg, 0.43 mmol) in MeOH (5 mL) was treated with 0.1 N NaOMe in MeOH (4 mL). The mixture was stirred at room temperature for 2 h, and neutralized with Amberlite 200-C resin (H^+ form). The resin was filtered off and washed with MeOH. The filtrate and

washings were concentrated, and the residue was dissolved in $CHCl_3$–water. The water layer was concentrated to dryness, and the residue was purified by chromatography on silica gel (20 g, 2:1 $CHCl_3$–MeOH) to give **12** (122 mg, 91%); $[\alpha]_D$ −137° (*c* 0.62, H_2O); R_f 0.43 (2:1 $CHCl_3$–MeOH); for ^1H and ^{13}C NMR data, see Tables 1 and 2. Anal. Calcd for $C_{11}H_{20}O_9 \cdot H_2O$: C, 42.04; H, 7.06. Found: C, 42.28; H, 6.92.

Methyl O-*(2,3,5-tri*-O-*benzoyl*-α-L-*arabinofuranosyl)*-*(1→2)*-*3,5-di*-O-*benzyl*-α-L-*arabinofuranoside* (**13**).—The acceptor **8** (227 mg, 0.66 mmol) was condensed with the chloride **4** (476 mg, 0.99 mmol) in dry CH_2Cl_2 (15 mL) in the presence of AgOTf (340 mg, 1.33 mmol), *s*-collidine (150 μL, 1.14 mmol), and activated, powdered 4A molecular sieves (600 mg) under Ar at 0°C. After treatment as described for **11**, flash chromatography on silica gel (60 g, 15:1 benzene–EtOAc) gave **13** (498 mg, 96%); $[\alpha]_D$ −24.5° (*c* 0.39, $CHCl_3$); R_f 0.38 (15:1 benzene–EtOAc); ^1H NMR ($CDCl_3$): δ 3.38 (s, 3 H, OMe), 3.62 (d, 1 H, *J* 2.6 Hz, H-2), 3.64 (d, 1 H, *J* 1.4 Hz, H-3), 3.93 (dd, 1 H, *J* 3.2, 6.2 Hz, H-4), 4.23 (m, 2 H, H-5a,5b), 4.79 (dd, 1 H, *J* 3.5, 11.7 Hz, H-5′b), 5.04 (s, 1 H, H-1), 5.20 (s, 1 H, H-1′), 5.45 (d, 1 H, *J* 1.0 Hz, H-2′), and 5.55 (br d, 1 H, *J* 4.9 Hz, H-3′); ^{13}C NMR ($CDCl_3$): δ 55.1 (OMe), 63.7 (C-5′), 69.8 (C-5), 77.6 (C-3′), 80.8 (C-4′), 81.3 (C-3), 82.3 (C-2′), 83.1 (C-4), 86.5 (C-2), 105.5 (C-1′), 107.8 (C-1), 165.3, 165.7, and 166.1 (C=O). Anal. Calcd for $C_{46}H_{44}O_{12}$: C, 70.08; H, 5.62. Found: C, 69.79; H, 5.49.

Methyl O-α-L-*arabinofuranosyl*-*(1→2)*-α-L-*arabinofuranoside* (**14**).—The disaccharide derivative **13** (476 mg, 0.60 mmol) in MeOH (15 mL) was debenzylated by catalytic hydrogenolysis over 10% Pd–C (40 mg) at room temperature for 24 h, as described for **9**. The catalyst was removed by filtration and the filtrate was concentrated to dryness. The residue was dissolved in MeOH (10 mL), 0.1 N NaOMe in MeOH (1.0 mL) was added, and the solution was stirred at room temperature for 9 h. After treatment as described for **12** the residue was purified by silica gel chromatography (20 g, 2:1 $CHCl_3$–MeOH) to give **14** (163 mg, 86%); $[\alpha]_D$ −144° (*c* 0.37, H_2O); R_f 0.44 (2:1 $CHCl_3$–MeOH); for ^1H and ^{13}C NMR data, see Tables 1 and 2. Anal. Calcd for $C_{11}H_{20}O_9 \cdot H_2O$: C, 42.04; H, 7.06. Found: C, 42.05; H, 6.98.

Methyl O-*(2,3,5-tri*-O-*benzoyl*-α-L-*arabinofuranosyl)*-*(1→3)*-*2,5-di*-O-*benzoyl*-α-L-*arabinofuranoside* (**15**).—The acceptor **10** (226 mg, 0.61 mmol) was condensed with the chloride **4** (409 mg, 0.85 mmol) in CH_2Cl_2 (15 mL) in the presence of AgOTf (312 mg, 1.22 mmol), *s*-collidine (145 μL, 1.10 mmol), and activated, powdered 4A molecular sieves (600 mg) under Ar at 0°C. After treatment as described for **11**, flash chromatography on silica gel (60 g, 15:1 benzene–EtOAc) gave **15** (342 mg, 69%); $[\alpha]_D$ −11.1° (*c* 0.19, $CHCl_3$); R_f 0.35 (15:1 benzene–EtOAc); ^1H NMR ($CDCl_3$): δ 3.48 (s, 3 H, OMe), 5.17 (s, 1 H, H-1), 5.39 (s, 1 H, H-1′), 5.57 (br d, 1 H, *J* 3.3 Hz, H-3′), 5.66 (d, 1 H, *J* 1.0 Hz, H-2′), and 5.71 (s, 1 H, H-2); ^{13}C NMR ($CDCl_3$): δ 54.9 (OMe), 63.2 (C-5′), 63.8 (C-5), 77.6 (C-3), 81.0 (2 C, C-4 and C-4′), 81.7 (C-3′), 81.8 (C-2′), 82.4 (C-2), 105.3 (C-1), 107.0 (C-1′), 165.2, 165.3, 165.6, and 166.1 (2 C) (C=O). Anal. Calcd for $C_{46}H_{40}O_{14}$: C, 67.64; H, 4.94. Found: C, 67.94; H, 4.96.

Methyl O-α-L-*arabinofuranosyl*-*(1→3)*-α-L-*arabinofuranoside* (**16**).—The disaccharide derivative **15** (322 mg, 0.39 mmol) was debenzoylated as described for **12**. The residue was purified by silica gel chromatography (20 g, 2:1 $CHCl_3$–MeOH) to give **16** (99 mg, 79%); $[\alpha]_D$ −157° (*c* 0.83, H_2O); R_f 0.44 (2:1 $CHCl_3$–MeOH); for ^1H and ^{13}C NMR

data, see Tables 1 and 2. Anal. Calcd for $C_{11}H_{20}O_9 \cdot 1.5\ H_2O$: C, 40.87; H, 7.17. Found: C, 40.93; H, 7.20.

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