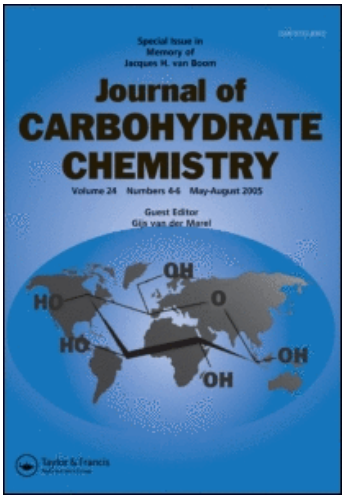

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SYNTHESIS, CONFORMATIONAL ANALYSIS, AND THE GLYCOSIDIC COUPLING REACTION OF SUBSTITUTED 2,7-DIOXABICYCLO[4.1.0]HEPTANES: 1,2-ANHYDRO-3,4-DI-*O*-BENZYL-β-L-ARABINOPYRANOSE•

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ABSTRACT

The title 1,2-anhydro sugar (**8**) was synthesized from L-arabinose. The key intermediate for the synthesis was 2-*O*-acetyl-3,4-di-*O*-benzyl-α-L-arabinopyranosyl fluoride (**7**) which was transformed into the target compound by ring closure with potassium *tert*-butoxide. Comparison of the observed vicinal coupling constants with the results obtained from calculations by molecular mechanics for **8** suggested that the conformation of the pyranose ring was close to a half chair $^5H_4$. The 1,2-anhydro sugar **8** was highly reactive; its condensation with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose in the absence of any Lewis catalysts afforded disaccharide derivatives in a reasonable yield, and in the presence of molecular sieves gave a quantitative yield of disaccharides, in which α-linked disaccharide predominated.

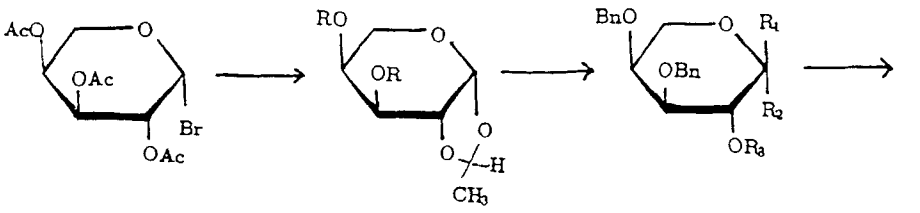
INTRODUCTION

1,2-Anhydro sugar derivatives are novel monomers for the synthesis of the corresponding stereoregular (1→2) linked polysaccharides,[1] important model

compounds for immunological research. The 1,2-anhydro sugar derivatives are also valuable glycosyl donors for the stereospecific synthesis of oligosaccharides[2] and other useful glycosyl derivatives.[3] The synthesis of 1,2-anhydro-3,4-di-*O*-benzyl-β-L-arabinopyranose is of interest, as its stereoregular polymerization and subsequent deprotection could lead to α-(1→2) linked L-arabinopyranan. Coupling of this 1,2-anhydro sugar with a suitable glycosyl acceptor could afford α-linked oligosaccharides containing an arabinopyranose moiety that are important model substances for polysaccharide structural analysis. Here we report the synthesis, conformational analysis, and the glycosidic coupling reaction of 1,2-anhydro-3,4-di-*O*-benzyl-β-L-arabinopyranose.

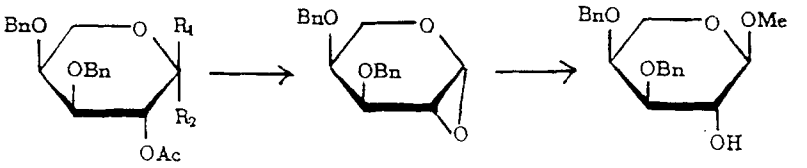
RESULTS AND DISCUSSION

3,4-Di-*O*-acetyl-1,2-*O*-[(*R,S*)-ethylidene]-β-L-arabinopyranose (**2**) was prepared from L-arabinose via the intermediate 2,3,4-tri-*O*-acetyl-β-L-arabinopyranosyl bromide (**1**) by a reported method.[4] Benzylation of compound **2** with potassium hydroxide and benzyl chloride in toluene yielded 3,4-di-*O*-benzyl-1,2-*O*-[(*R,S*)-ethylidene]-β-L-arabinopyranose (**3**). Hydrolytic removal of the ethylidene group from **3** with sulfuric acid in dioxane afforded 3,4-di-*O*-benzyl-L-arabinopyranose (**4**), and subsequent acetylation of **4** with acetic anhydride in pyridine furnished the diacetate **5**. Chlorination of **5** with hydrogen chloride in diethyl ether gave 2-*O*-acetyl-3,4-di-*O*-benzyl-β-L-arabinopyranosyl chloride (**6**) which was fluorinated with silver fluoride to afford 2-*O*-acetyl-3,4-di-*O*-benzyl-α-L-arabinopyranosyl fluoride (**7**) in high yield. Epoxide formation from **7** was readily carried out at room temperature with potassium *tert*-butoxide in oxolane to give 1,2-anhydro-3,4-di-*O*-benzyl-β-L-arabinopyranose (**8**) in high yield (80%). The 1,2-anhydro sugar ether **8** was characterized from ^{1}H NMR spectrometric, mass spectrometric, and optical rotation measurements. The ^{1}H NMR spectrum of **8** showed an upfield peak for H-2 at δ 3.17, characteristic of an epoxide methine C-H. The mass spectrum of **8** gave a molecular ion (m/z 312) of low intensity together with some fragmentation peaks, characteristic of a per-*O*-benzylated 1,2-anhydropyranose.[5]



	R
1	
2	Ac
3	Bn

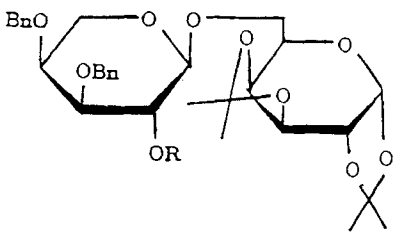
	R_1	R_2	R_3
4	H	OH	H
5	H(OAc)	OAc(H)	Ac



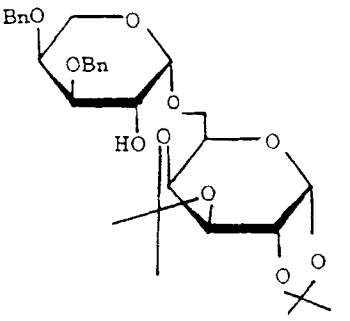
	R_1	R_2
6	H	Cl
7	F	H

8

9



	R
10	H
12	Ac



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Conformational analysis of **8** was carried out by ^{1}H NMR spectrometry in conjunction with calculations using molecular mechanics.[6] The ^{1}H NMR spectrum of **8** was fully assigned by the use of single frequency decoupling. The anomeric proton signal appeared as a doublet of doublets at δ 4.94 with $J_{1,2}$ = 2.9 Hz and $J_{1,3}$ = 1.0 Hz. The signals at δ 3.96, 3.90, 3.72, and 3.53 were assigned as H-3, H-5, H-4, and H-5′ respectively. For a close inspection

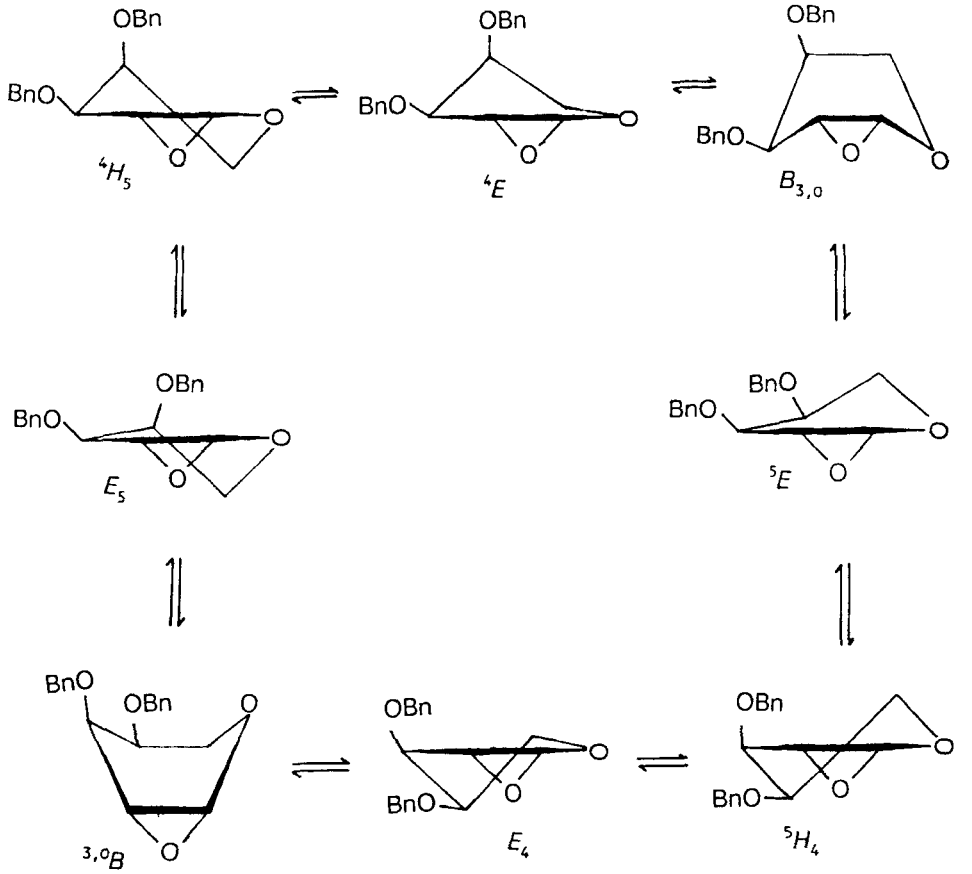
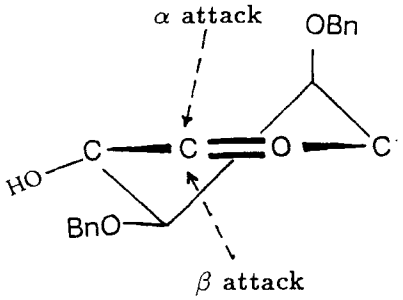


Figure. Possible conformations for pseudorotation of compound **8**.

of the conformation of **8**, molecular mechanics calculations for the conformations $^4H_5$, ^4E, $B_{3,O}$, ^5E, $^5H_4$, E_4, $^{3,O}B$, E_5 of **8**, involved in the pseudorotation,[7] were carried out. It was found that the $^5H_4$ form has the lowest energy (45.87 kcal/mol) and the E_4, ^5E, $^4H_5$, and ^4E forms have similar energies (0.2, 0.5, 0.6, and 0.8 kcal/mol higher than the lowest, respectively), and the other forms have relatively high energies (1.3 to 2.5 kcal/mol higher than that of the $^5H_4$ form). The energy differences described for the conformations of **8** suggested that **8** has an average conformation with the dynamic equilibrium containing large amounts of the low energy forms and lesser amounts of the higher energy forms. The torsional angles for the

pyranose and epoxide rings of **8** obtained from the calculations, and the corresponding calculated vicinal coupling constants are listed in the Table. As the modified Karplus equation[8] is not valid for the planar portion of the pyranose ring, evaluation of the conformation of **8** was mainly based on $J_{3,4}$, $J_{4,5}$, and $J_{4,5'}$ values. Comparison of the calculated vicinal coupling constants with the observed ones showed that none of the listed forms has coupling constants exactly the same as the observed values. Further calculation with two fixed torsional angles for H3-C3-C4-H4 ($\phi_{3,4}$) and H4-C4-C5-H5 ($\phi_{4,5}$) at the values, correlated to the observed coupling constants, gave a deduced conformation (**Exp**) that is nearly $^5H_4$ in terms of the corresponding torsional angles of the pyranose and epoxide rings (see the Table).

Methanolysis of **8** at room temperature gave quantitatively methyl 3,4-di-*O*-benzyl-α-L-arabinopyranoside (**9**). The coupling reaction of **8** with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose in dry oxolane without adding any catalysts gave a fair yield (60%) of disaccharides **10** and **11**, despite a similar coupling of 1,2-anhydro-3,4,6-tri-*O*-benzyl-β-D-mannopyranose[9] did not take place. When the same coupling reaction was conducted in the presence of 4A molecular sieves, a mixture of **10** and **11** was obtained in 94% yield. Either in the absence or in the presence of 4A molecular sieves, the reaction gave a mixture of α (**10**) and β isomer (**11**) in a ratio of 2:1. It seems that the first formed intermediate for **8** in the coupling reaction is a delocalized cation (**13**). The coupling reaction afforded in the presence of zinc chloride as catalyst, the disaccharides in high yield (90%) with a similar stereochemical outcome.



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The α-linked disaccharide **10** was identified further from the ^{1}H NMR spectrum of the acetylated disaccharide **12**. Characteristic peaks were a

TABLE. Selected torsional angles (°) and vicinal coupling constants obtained from calculation by MMX.

Angle	Magnitude (°)								
	$^4H_5$	$^5H_4$	Exp[a]	^4E	E_4	^5E	E_5	$B_{3,O}$	$^{3,O}B$
energy (Kcal/mol)	46.5	45.9	46.9	46.7	46.1	46.4	47.2	48.3	48.5
O5-C1-C2-C3	0.2*	-0.1*	4.9	-0.1*	0.3*	0.3*	-0.1*	0.1*	0.2*
C1-C2-C3-C4	-17.7*	18.0*	11.1	-31.0	28.1	0.3*	-0.4*	-53.9	46.9
C2-C3-C4-C5	50.9	-50.6	-50	61.3	-55.9	-31.5	29.6	54.1	-47.5
C3-C4-C5-O5	-70.1	69.4	80.1	-63.5	57.8	65.9	-60.3	-0.1*	0.1*
C4-C5-O5-C1	53.2	-51.5	-64.9	32.1	-29.9	-64.9	61.1	-55.4	49.6
C5-O5-C1-C2	-18.9	17.5	22.8	-0.1*	0.3*	32.9	-31.6	56.9	-51.3
C1-O2-C2-C3	107	100	109	107	107	110	107	99.8	100
O2-C2-C3-C4	-82.9	-47.4	-54	-95.7	-37.4	-64.7	-66.3	-118	-17.9
$J_{3,4}$(Hz)	3.2	3.4	3.3	2.3	3.1	5.5	5.5	2.7	3.7
$\phi_{3,4}$ (°)	52	-50	-51*	60	-53	-34	34	56	-48
$J_{4,5'}$(Hz)	0.5	3.7	1.2	0.8	5.2	4.1	1.0	8.5	9.0
$\phi_{4,5'}$(°)	-67	68	93	-61	59	66	-59	-2	4
$J_{4,5}$(Hz)	3.7	10.4	6.3	3.2	10.7	10.5	2.8	3.6	4.6
$\phi_{4,5}$(°)	52	-170	-136*	56	177	-172	60	116	123

a. The data were calculated for reproducing the observed conformation with two fixed torsional angles at the values that were closely correlated to the observed $J_{4,5}$(6.3 Hz) and $J_{3,4}$(2.7 Hz) values.
*Fixed torsional angle during energy minimization.

doublet of doublets at δ 5.30 ($J_{1',2'}$ = 5.4 Hz, $J_{2',3'}$ = 7.6 Hz) for H-2 of the arabinose moiety, a singlet at δ 2.08, indicating that the original disaccharide had only one free hydroxyl group, and the doublet at δ 4.48 ($J_{1',2'}$ = 5.4 Hz) for H-1 of the α-linked L-arabinopyranoside. The β-linked disaccharide **11** was identified in a similar way.

EXPERIMENTAL

General Methods. Optical rotations were determined at 20 °C with a Perkin-Elmer Model 241-MC automatic polarimeter. Melting points were

determined with a "Mel-Temp" apparatus and are reported uncorrected. ^1H NMR spectra were recorded with Varian XL-400 and Varian XL-200 spectrometers for solutions in $CDCl_3$. Chemical shifts are given in ppm downfield from the internal Me_4Si. For conformational analysis, ^1H NMR spectra were measured in the pulsed Fourier-transform mode at 20 °C. Mass spectra were recorded with a JMS-3005 mass spectrometer, using a direct sample introduction technique. Analytical LC was carried out in stainless steel columns packed with silica gel (10 x 150 mm or 4.6 x 250 mm) or Lichrosorb-NH_2 (4.6 x 250 mm) with peak detection by a differential refractometer (Perkin-Elmer LC-25 RI Detector). Ethyl acetate-petroleum ether (bp 60-90 °C) was used as the eluent at a flow rate of 1 to 4 mL min^{-1}. TLC was performed on silica gels G and HF, detection being affected either by charring with 30% (v/v) H_2SO_4 in MeOH or by UV light. Preparative chromatography was performed on columns (16 x 240, 18 x 300, and 35 x 400 mm) of silica gel (120-200 mesh). Solutions were concentrated at a temperature <50 °C under diminished pressure. Calculations by molecular mechanics were carried out using the MMX program[10] embedded in PCMODEL-386 on an AST-386 computer. The dielectric constant used throughout the calculations was 1.5. Each calculated total energy consisted of stretching, bending, stretching-bending, torsional, van der Waals, and dipole-dipole contributions. Calculations of each individual conformation involved in the pseudorotation from $^4H_5$ to $^5H_4$, and the reproduced conformation **Exp** were carried out with two fixed torsional angles that were different for *H*, *E*, *B*, and **Exp** forms.

3,4-Di-*O*-acetyl-1,2-*O*-[(*R,S*)-ethylidene]-β-L-arabinopyranose (2). To a solution of 2,3,4-tri-*O*-acetyl-β-L-arabinopyranosylbromide (11.6 g, 34.3 mmol, prepared by a standard method[11]) in dry acetonitrile (70 mL) was added at 0 °C tetrabutylammonium iodide (5 g, 13.6 mmol) and sodium borohydride (2.1 g, 56.8 mmol). Then the mixture was stirred for 18 h at room temperature, at which time TLC (2:1 petroleum ether-EtOAc) indicated that the reaction was complete. Filtration and concentration of the filtrate gave a residue that was diluted with dichloromethane (50 mL), washed with water (3 x 30 mL), and then concentrated. Column chromatography (3:1 petroleum ether-EtOAc) of the

syrup afforded **2** as a mixture (7.6 g, 85%) consisting of the *R* and *S* isomers in a ratio of 3:1: $[\alpha]_D$ +60.2° (*c* 7.0, $CHCl_3$); ^1H NMR for the *R* isomer: δ 5.40 (d, 1H, $J_{1,2}$ = 4.0 Hz, H-1), 5.31 (t, 1H, $J_{2,3}$ = 4.0 Hz, $J_{3,4}$ = 4.0 Hz, H-3), 5.27 (dd, 1H, $J_{3,4}$ = 4.0 Hz, $J_{4,5}$ = 6.5 Hz, H-4), 5.22 (q, 1H, J = 4.9 Hz, CH_3CH), 4.03 (dd, 1H, $J_{4,5}$ = 3.8 Hz, $J_{5,5'}$ = 13.0 Hz, H-5), 4.02 (t, 1H, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 4.0 Hz, H-2), 3.79 (dd, 1H, $J_{4,5'}$ = 6.5 Hz, $J_{5,5'}$ = 13 Hz, H-5'), 2.12, 2.07 (2s, 6H, CH_3CO), 1.49 (d, 3H, J = 4.9 Hz, CH_3CH); for the *S* isomer: δ 5.52 (q, 1H, J = 4.3 Hz, CH_3CH), 5.49 (d, 1H, $J_{1,2}$ = 4.3 Hz, H-1), 1.40 (d, 3H, J = 4.3 Hz, CH_3CH).

Anal. Calcd for $C_{11}H_{16}O_7$: C, 50.77; H, 6.15. Found: C, 51.19; H, 6.09.

3,4-Di-*O*-benzyl-1,2-*O*-[(*R,S*)-ethylidene]-β-L-arabinopyranose (3). To a solution of compound **2** (7.2 g, 27.7 mmol) in toluene (60 mL) was added, with vigorous stirring, finely powdered potassium hydroxide (12 g). The mixture was boiled under reflux, and benzyl chloride (12 mL, 104 mmol) was added dropwise within 10 min. The mixture was stirred and boiled under reflux for 2 h, when TLC (3:1 petroleum ether-EtOAc) indicated that the reaction was complete. The mixture was directly subjected to steam distillation to remove the excess benzyl chloride and the by-product dibenzyl ether, and then extracted with dichloromethane. The organic layer was concentrated to a syrup that was purified by column chromatography with 4:1 petroleum ether-EtOAc to give **3** (9.2 g, 93%): $[\alpha]_D$ +19.4° (*c* 3.3, $CHCl_3$); ^1H NMR for the *R* isomer: δ 7.36-7.25 (m, 10H, 2 Ph-H), 5.35 (d, 1 H, $J_{1,2}$ = 3.0 Hz, H-1), 5.19 (q, 1 H, J = 4.9 Hz, CH_3CH), 4.74, 4.64 (2s, 4H, 2 CH_2Ph), 4.08 (dd, 1H, $J_{1,2}$ = 3.0 Hz, $J_{2,3}$ = 3.8 Hz, H-2), 3.91 (dd, 1H, $J_{2,3}$ = 3.8 Hz, $J_{3,4}$ = 3.0 Hz, H-3), 3.87 (d, 2H, $J_{4,5}$ = 6.5 Hz, H-5), 3.83 (m, 1H, $J_{3,4}$ = 3.0 Hz, $J_{4,5}$ = 6.5 Hz, H-4), 1.37 (d, 3H, J = 4.9 Hz, CH_3CH). for the *S* isomer: δ 5.48 (d, 1H, $J_{1,2}$ = 3.0 Hz, H-1), 5.45 (q, 1H, J = 6.8 Hz, CH_3CH), 4.28 (dd, 1H, $J_{1,2}$ = 3.0 Hz, $J_{2,3}$ = 5.3 Hz, H-2), 1.26 (d, 3H, J = 6.8 Hz, CH_3CH).

Anal. Calcd for $C_{21}H_{24}O_5$: C, 70.79; H, 6.74. Found: C, 70.75; H, 6.52.

3,4-Di-*O*-benzyl-β-L-arabinopyranose (4). To a solution of **3** (9 g, 25.3 mmol) in dioxane (50 mL) was added 1 M sulfuric acid (5 mL), and the mixture

was boiled under reflux with stirring for 5 h, at which time TLC (2:1 petroleum ether-EtOAc) indicated that the reaction was complete. The mixture was carefully neutralized with powdered sodium bicarbonate, concentrated and partitioned between water and dichloromethane. The organic layer was dried over sodium sulfate and concentrated. Purification of the residue by column chromatography with 2:1 petroleum ether-EtOAc furnished syrupy **4** (6.8 g, 81%): $[\alpha]_D$ +87.8° (*c* 0.5, $CHCl_3$); ^1H NMR δ 7.40-7.26 (m, 10H, 2 Ph-H), 5.30 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1), 4.78-4.52 (m, 4H, 2 CH_2Ph), 4.20-3.40 (m, 5H, H-2,3,4,5).

Anal. Calcd for $C_{19}H_{22}O_5.0.5H_2O$: C, 67.26; H, 6.73. Found: C, 67.70; H, 6.66.

1,2-Di-*O*-acetyl-3,4-di-*O*-benzyl-L-arabinopyranose(5). Acetylation of **4** (1 g, 3 mmol) with pyridine (5 mL) and acetic anhydride (4 mL) at room temperature for 4 h gave compound **5** in a quantitative yield as a syrup consisting of α and β anomers in a ratio of 1:2: $[\alpha]_D$ +16° (*c* 1.5, $CHCl_3$); ^1H NMR for the β anomer: δ 7.37-7.26 (m, 10H, 2 Ph-H), 6.40 (d, 1H, $J_{1,2}$ = 3.9 Hz, H-1), 5.40 (dd, 1H, $J_{1,2}$ = 3.9 Hz, $J_{2,3}$ = 10 Hz, H-2), 4.72 (s, 2H, CH_2Ph), 4.65, 4.61 (2d, 2H, J = 11.6 Hz, CH_2Ph), 3.95 (dd, 1H, $J_{2,3}$ = 10 Hz, $J_{3,4}$ = 3.2 Hz, H-3), 3.93 (d, 2H, $J_{4,5}$ = 1.7 Hz, H-5), 3.82 (m, 1H, H-4), 2.11, 2.05 (2s, 6H, 2 CH_3CO); for the α-anomer: δ 5.68 (d, 1H, $J_{1,2}$ = 5.5 Hz, H-1), 5.29 (t, 1 H, $J_{1,2}$ = 5.5 Hz, $J_{2,3}$ = 5.5 Hz, H-2), 4.68-4.58 (m, 4H, 2 CH_2Ph), 4.12 (dd, 1H, $J_{4,5}$ = 3.9 Hz, $J_{5,5'}$ = 11.5 Hz, H-5), 3.78 (m, 1H, H-4), 3.70 (dd, 1H, $J_{2,3}$ = 5.5 Hz, $J_{3,4}$ = 2.8 Hz, H-3), 3.55 (dd, 1H, $J_{4,5}$ = 3.1 Hz, $J_{5,5'}$ = 11.5 Hz, H-5), 2.08, 2.03 (2s, 6H, 2 CH_3CO).

Anal. Calcd for $C_{23}H_{26}O_7$: C, 66.67; H, 6.28. Found: C, 66.86; H, 6.60.

2-*O*-Acetyl-3,4-di-*O*-benzyl-β-L-arabinopyranosyl chloride (6). A solution of compound **5** (828 mg, 2 mmol) in dry diethyl ether (20 mL) was saturated 0 °C with hydrogen chloride gas under a nitrogen atmosphere. Then the solution was kept at room temperature in a sealed bottle for 2 h, at which time TLC (3:1 petroleum ether-EtOAc) indicated that the reaction was complete. The solution was concentrated under reduced pressure to a syrupy residue which

was dissolved in dichloromethane (2 mL), and the solution was concentrated. This procedure was repeated several times to remove the hydrogen chloride. Purification of the product by column chromatography (3:1 petroleum ether-EtOAc) gave **6** as a syrup (680 mg, 87.1%): $[\alpha]_D$ +59.8° (*c* 2.3, $CHCl_3$); ^1H NMR δ 7.37-7.26 (m, 10H, 2 Ph-H), 6.40 (d, 1H, $J_{1,2}$ = 4.5 Hz, H-1), 5.41 (dd, 1 H, $J_{1,2}$ = 4.5 Hz, $J_{2,3}$ = 10 Hz, H-2), 4.72 (s, 2H, CH_2Ph), 4.66, 4.62 (2d, J = 11.6 Hz, CH_2Ph), 3.96 (dd, 1H, $J_{2,3}$ = 10 Hz, $J_{3,4}$ = 3.9 Hz, H-3), 3.93 (d, 2H, $J_{4,5}$ = 2.0 Hz, H-5), 3.82 (m, 1H, H-4), 2.11 (s, 3H, CH_3CO).

Anal. Calcd for $C_{21}H_{23}ClO_5$: C, 64.53; H, 5.89. Found: C, 64.59; H,6.10.

2-*O*-Acetyl-3,4-di-*O*-benzyl-α-L-arabinopyranosylfluoride (7). To a solution of **6** (650 mg, 1.7 mmol) in 2:5 acetonitrile-benzene (15 mL) was added silver fluoride (300 mg, 2.4 mmol). The mixture was stirred vigorously for 16 h in the dark at room temperature, then centrifugated, and the filter cake was washed repeatedly with dichloromethane. The supernatant liquor and combined washings were concentrated. Purification of the syrup by column chromatography (4:1 petroleum ether-EtOAc) yielded **7** as a syrup (500 mg, 80%): $[\alpha]_D$ -28.7° (*c* 0.8, $CHCl_3$); ^1H NMR δ 7.40-7.28 (m, 10H, 2 Ph-H), 5.34 (dd, 1H, $J_{1,F}$ = 54 Hz, $J_{1,2}$ = 1.0 Hz, H-1), 5.20 (m, 1H, H-2), 4.78, 4.72 (2d, 2H, J = 12.6 Hz, CH_2Ph), 4.53 (s, 2H, CH_2Ph), 4.24 (t, 1H, $J_{4,5}$ = $J_{5,5'}$ = 9.8 Hz, H-5), 3.83-3.64 (m, 3H, H-3,4,5'), 2.04 (s, 3H, CH_3CO).

Anal. Calcd for $C_{21}H_{23}FO_5$: C, 67.38; H, 6.15. Found: C, 67.32; H, 6.28.

1,2-Anhydro-3,4-di-*O*-benzyl-β-L-arabinopyranose (8). To a solution of **7** (450 mg, 1.2 mmol) in dry oxolane was added potassium *tert*-butoxide (280 mg, 2.5 mmol), and the mixture was stirred at room temperature for 6 h, at which time TLC (3:1 petroleum ether-EtOAc) indicated that the starting material disappeared. The mixture was concentrated to dryness, and the residue was repeatedly extracted with 3:1 petroleum ether-EtOAc. Concentration of the combined extracts yielded **8** as a syrup (300 mg, 80%): $[\alpha]_D$ -8.3° (*c* 1.4, $CHCl_3$); ^1H NMR δ 7.43-7.28 (m, 10H, 2 Ph-H), 4.94 (dd, 1H, $J_{1,2}$ = 2.9 Hz, $J_{1,3}$ = 1.0 Hz, H-1), 4.77, 4.70 (2d, 2H, J = 11.0 Hz, CH_2Ph), 4.75, 4.68 (2d, 2H, J = 10.8 Hz, CH_2Ph), 3.96 (dt, 1H, $J_{1,3}$ = 1.0 Hz, $J_{2,3}$ = 1.0 Hz, $J_{3,4}$ =

2.7 Hz, H-3), 3.90 (dd, 1H, $J_{4,5}$ = 6.3 Hz, $J_{5,5'}$ = 11.3 Hz, H-5), 3.72 (m, 1H, H-4), 3.53 (dd, 1H, $J_{4,5'}$ = 1.7 Hz, $J_{5,5'}$ = 11.3 Hz, H-5'), 3.17 (m, 1H, H-2). *m/z*: 312 (M^+), 221 (M^+ - Bn), 149, 107, 91.

Methyl 3,4-di-*O*-benzyl-α-L-arabinopyranoside (9). Compound **8** (20 mg, 0.064 mmol) was dissolved in anhyd methanol (2 mL) and kept for 20 min at room temperature. TLC (2:1 petroleum ether-EtOAc) indicated that the reaction was complete. The solution was concentrated to afford **9** quantitatively as white crystals: mp 109-110 °C; $[\alpha]_D$ -40.2° (*c* 0.5, $CHCl_3$); ^1H NMR δ 7.34-7.24 (m, 10H, 2 Ph-H), 4.68, 4.60 (2d, 2H, J = 12.3 Hz, CH_2Ph), 4.63, 4.46 (2d, 2H, J = 12.3 Hz, CH_2Ph), 4.12 (d, 1H, $J_{1,2}$ = 7.3 Hz, H-1), 4.10 (dd, 1H, $J_{4,5}$ = 2.2 Hz, $J_{5,5'}$ = 12.7 Hz, H-5), 3.95 (dd, 1H, $J_{1,2}$ = 7.3 Hz, $J_{2,3}$ = 9.1 Hz, H-2), 3.71 (m, 1H, H-4), 3.56 (s, 3H, CH_3O), 3.40 (dd, 1H, $J_{2,3}$ = 9.1 Hz, $J_{3,4}$ = 2.2 Hz, H-3), 3.31 (d, 1H, $J_{5,5'}$ = 12.7 Hz, H-5').

Anal Calcd for $C_{20}H_{24}O_5$: C,69.77; H, 6.98. Found: C, 70.14; H, 7.23.

O-(3,4-Di-O-benzyl-α-L-arabinopyranosyl)-(1→6)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (10) and O-(3,4-di-O-benzyl-β-L-arabinopyranosyl)-(1→6)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (11). (a) The 1,2-anhydro sugar **8** (20 mg, 0.064 mmol) was dissolved in anhyd oxolane (1.5 mL) containing molecular sieves (0.3 g). To the mixture was added a solution of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (28 mg, 0.11 mmol) in oxolane (1 mL) in one portion. The mixture was stirred at room temperature for 16 h, at which time TLC (2:1 petroleum ether-EtOAc) indicated that **8** disappeared. The solution was concentrated to a syrup that was subjected to separation by analytical LC with 2:1 petroleum ether-EtOAc as the eluent. Compound **10** was obtained as a syrup (23 mg, 62%): $[\alpha]_D$ -36.9° (*c* 0.3, $CHCl_3$); ^1H NMR δ 7.40-7.28 (m, 10H, 2 Ph-H), 5.55 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1), 4.76, 4.64 (2d, 2H, J = 12.5 Hz, CH_2Ph), 4.66 (s, 2H, CH_2Ph), 4.60 (dd, 1H, $J_{2,3}$ = 2.4 Hz, $J_{3,4}$ = 7.6 Hz, H-3), 4.32 (dd, 1H, $J_{1,2}$ = 5.0 Hz, $J_{2,3}$ = 2.4 Hz, H-2), 4.28 (d, 1H, $J_{1',2'}$ = 7.8 Hz, H-1'), 4.23 (dd, 1H, $J_{3,4}$ = 7.8 Hz, $J_{4,5}$ = 1.5 Hz, H-4), 4.12-3.95 (m, 4H, H-5,6, H-2'), 3.75 (dd, 1H, $J_{4',5'}$ = 9.0 Hz, $J_{5',5''}$ = 12.3 Hz, H-5'), 3.70-3.66 (m, 1H, H-4'), 3.45 (d, 1H, $J_{2',3'}$ = 9.5 Hz,

$J_{3',4'}$ = 3.2 Hz, H-3'), 3.30 (dd, 1H, $J_{4',5''}$ = 0.7 Hz, $J_{5',5''}$ = 12.3 Hz, H-5''), 2.28 (bs, 1H, O*H*), 1.52, 1.45, 1.35, 1.35 (4s, 12H, 4 CH_3).

Anal. Calcd for $C_{31}H_{40}O_{10}$: C,65.02; H, 6.99. Found: C, 64.53; H, 7.28.

Compound **11** was obtained as a syrup (12 mg, 32%): ^{1}H NMR δ 7.40-7.28 (m, 10H, 2 Ph-H), 5.53 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1), 4.94 (d, 1H, $J_{1',2'}$ = 3.4 Hz, H-1'), 4.72, 4.64 (2d, 2H, J = 11.2 Hz, CH_2Ph), 4.67 (s, 2H, CH_2Ph), 4.61 (dd, 1H, $J_{2,3}$ = 2.4Hz, $J_{3,4}$ = 8.0Hz, H-3), 4.31 (dd, 1H, $J_{1,2}$ = 5.0 Hz, $J_{2,3}$ = 2.4 Hz, H-2), 4.22 (dd, 1H, $J_{3,4}$ = 8.0Hz, $J_{4,5}$ = 1.7 Hz, H-4), 4.14 (dd, 1H, $J_{1',2'}$ = 3.4 Hz, $J_{2',3'}$ = 9.3 Hz, H-2'), 4.03-3.66 (m, 7H, H-5,6,3',4',5'), 2.10 (bs, 1H, OH), 1.52, 1.46, 1.36, 1.36 (4s, 12H, 4 CH_3).

(b) The coupling reaction in the absence of 4A molecular sieves was carried out in the same way as described in (a) to give a mixture of **10** and **11** in a ratio of 2:1 in a total yield 60%.

(c) To a solution of **8** (100 mg, 0.32 mmol) in oxolane (7 mL) was added a solution of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (140 mg, 0.54 mmol) and $ZnCl_2$ (0.04 mmol) in oxolane (3 mL). The mixture was stirred for 4 h at room temperature. The solution was concentrated to a syrup that was partitioned between water and dichloromethane. The organic layer was dried, concentrated and subjected to separation by analytical LC with 2:1 petroleum ether-EtOAc, to afford **10** (110 mg, 59%) and **11** (58mg, 31%).

***O*-(2-*O*-Acetyl-3,4-di-*O*-benzyl-α-L-arabinopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose(12).** Compound **10** (20 mg, 0.035 mmol) was acetylated with acetic anhydride (0.6 mL) in pyridine (1 mL) to afford **12** (21 mg, 98%) as a syrup: $[\alpha]_D$ -8.8° (*c* 0.8, $CHCl_3$); ^{1}H NMR δ 7.39-7.28 (m, 10H, 2 Ph-H), 5.52 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1), 5.30 (dd, 1H, $J_{1',2'}$ = 5.4 Hz, $J_{2',3'}$ = 7.6 Hz, H-2'), 4.66 (s, 2H, CH_2Ph), 4.64, 4.59 (2d, 2H, J = 12.2 Hz, CH_2Ph), 4.54 (dd, 1H, $J_{2,3}$ = 2.3 Hz, $J_{3,4}$ = 8.0 Hz, H-3), 4.48 (d, 1H, $J_{1',2'}$ = 5.4 Hz, H-1'), 4.20 (dd, 1H, $J_{1,2}$ = 5.0 Hz, $J_{2,3}$ = 2.3 Hz, H-2), 4.20 (dd, 1H, $J_{3,4}$ = 8.0 Hz, $J_{4,5}$ = 1.5 Hz, H-4), 4.11 (dd, 1H, $J_{5,6}$ = 5.6 Hz, $J_{6,6'}$ = 12.0 Hz, H-6), 4.00 (dd, 1H, $J_{5,6'}$ = 4.7 Hz, $J_{6,6'}$ = 12.0 Hz, H-6'), 3.96 (m, 1H, $J_{5,6}$ = 5.6 Hz, $J_{5,6'}$ = 4.7 Hz, $J_{4,5}$ = 1.5 Hz, H-5), 3.74(m, 1H, $J_{3',4'}$ = 3.2 Hz,

$J_{4',5'}$ = 2.4 Hz, $J_{4',5''}$ = 4.8 Hz, H-4'), 3.61 (dd, 1H, $J_{2',3'}$ = 7.7 Hz, $J_{3',4'}$ = 3.2 Hz, H-3'), 3.58 (dd, 1H, $J_{4',5''}$ = 4.8 Hz, $J_{5',5''}$ = 12.2 Hz, H-5''), 3.38 (dd, 1H, $J_{4',5'}$ = 2.4 Hz, $J_{5',5''}$ = 12.2 Hz, H-5'), 2.08 (s, 3H, CH_3CO), 1.53, 1.44, 1.34, 1.30 (4s, 12H, CH_3).

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