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Synthesis, conformation and glycosylation reaction of substituted 2,6-dioxabicyclo[3.1.1]heptanes: 1,3-anhydro-2,4-di-*O*-benzyl-α-L-arabinopyranose

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Abstract

The title 1,3-anhydro sugar (**10**) was obtained as crystals by the ring closure of 3-*O*-acetyl-2,4-di-*O*-benzyl-α,β-L-arabinopyranosyl chloride (**9**) which was prepared from methyl β-L-arabinopyranoside via a sequence of reactions involving initial selective 3-*O*-allylation. Methanolysis of **10** gave 1,3-*cis* arranged methyl 2,4-di-*O*-benzyl-α-L-arabinopyranoside as the major product. Glycosylation of **10** with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose or with serine derivatives resulted in the same stereochemical outcome, while glycosylation of the 1,3-anhydro galacto- (**19**) and manno-pyranose (**24**) analogues afforded predominantly 1,3-*trans* ring opening products. Conformational analysis of **10, 19** and **24** revealed that the C-5 head of **10** is flexible. The conformation of **10** in solution is close to E_2 while **19** and **24** prefer the $B_{2,5}$ form.

Keywords: 2,6-Dioxabicyclo[3.1.1]heptanes; Synthesis; Conformation

1. Introduction

As part of an ongoing research-effort on 2,6-dioxabicyclo[3.1.1]heptane derivatives, we have synthesized 1,3-anhydro-β-L-rhamno- [1], -β-D-galacto- [2], -6-deoxy-β-D-gluco- [3], -6-azido-6-deoxy-β-D-manno- [4], -β-D-fuco- [5], and -β-D-talo-pyanose [6] benzyl ethers. The synthesis of 1,3-anhydro-β-D-gluco- [7,8] and -β-D-manno-pyranose [9,10] analogues had been reported earlier by Schuerch's group. We report here on the

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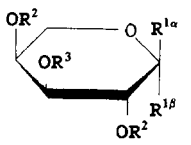
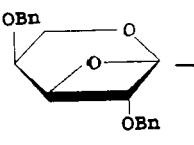
synthesis, conformation, and glycosylation reaction of 1,3-anhydro-2,4-di-*O*-benzyl-α-L-arabinose whose stereoregular polymerization could afford 1 → 3-linked arabinopyranan, a useful model compound for polysaccharide research.

2. Results and discussion

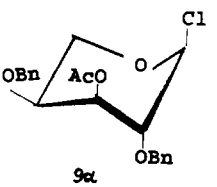
L-Arabinopyranose (**1**) was converted to methyl β-L-arabinopyranoside (**2**) with strongly acidic resin (H^+ form) as catalyst [11]. Compound **2** was selectively allylated at C-3 using the method for 3-*O*-alkylation of methyl α-D-galactopyranoside [2] *via* a stannylene complex, and methyl 3-*O*-allyl-β-L-arabinopyranoside (**3**) was obtained in satisfactory yield. Removal of most of the tetrabutylammonium iodide used in the monoallylation from the reaction mixture was helpful for the further purification of **3** by column chromatography, and the recovered tetrabutylammonium iodide from ethyl acetate or diethyl ether could be reused. The structure of **3** was confirmed by acetylation to afford methyl 2,4-di-*O*-acetyl-3-*O*-allyl-β-L-arabinopyranoside (**4**) whose ^{1}H NMR spectrum showed H-2 and H-4 shifted downfield. Benzylation of **3** with benzyl bromide and sodium hydride in oxolane afforded methyl 3-*O*-allyl-2,4-di-*O*-benzyl-β-L-arabinopyranoside (**5**). Acid hydrolysis of **5** (→ **6**) followed by deallylation with tris(triphenylphosphine)rhodium(I) chloride as the catalyst yielded 2,4-di-*O*-benzyl-L-arabinopyranose (**7**). Acetylation of **7** with acetic anhydride in pyridine gave the 1,3-diacetate **8**. Both compounds **7** and **8** were obtained as a mixture of α and β anomers as indicated by their ^{1}H NMR spectra. Compound **8** was reacted with hydrogen chloride in diethyl ether to furnish the key intermediates 3-*O*-acetyl-2,4-di-*O*-benzyl-α-(**9α**) and -β-L-arabinopyranosyl chloride (**9β**), which were separated in pure form by analytical LC, in a ratio of about 1:1. Compound **9α** assumes a conformation close to $^1C_4$ as indicated from its ^{1}H NMR spectrum which yielded small values for $^3J_{H1,H2}$ (1.1 Hz), $^3J_{H2,H3}$ (2.9 Hz), and a relatively large value for $^3J_{H4,H5}$ (6.7 Hz), while **9β** exists in a $^4C_1$ form as shown from $^3J_{H1,H2}$ (3.7 Hz), a large value of $^3J_{H2,H3}$ (10.3 Hz), and a small $^3J_{H4,H5}$ (2.0 Hz). Similar conformation flipping was observed for compound **4** ($^3J_{H2,H3} = 2.0$ Hz). An alternative method for the preparation of 3-*O*-acetyl-2,4-di-*O*-benzyl-L-arabinopyranosyl chloride was also examined. Deallylation of **5** with palladium dichloride as the catalyst in methanol furnished methyl 2,4-di-*O*-benzyl-β-L-arabinopyranoside (**11β**) in good yield. Chlorination of **11β** with hydrogen chloride in 1:1 HOAc–CH_2Cl_2 gave the chloride compound in low yield (40%), together with some by-products, and product purification was difficult. Similar treatment of methyl 3-*O*-acetyl-2,4-di-*O*-benzyl-β-L-arabinopyranoside (**12β**) was also troublesome, and so the alternative method was not used. Compound **9β** contains a *trans*-oriented C-3-*O*-acetate as a potential alkoxide and C-1-Cl as a leaving group, fulfilling the requirement for a backside attack in a ring closure reaction, whereas **9α** does not have such a relation between C-1 and C-3. However, it was found that treatment of either **9α** or **9β** with potassium *tert*-butoxide in anhydrous oxolane yielded 1,3-anhydro-2,4-di-*O*-benzyl-α-L-arabinopyranose (**10**), a crystalline compound, as the major product, indicating that isomerization of **9α** to **9β** occurred easily during the ring closure reaction. This behavior is different from the 1,2-ring closure reaction [12,13] in which the precursor for



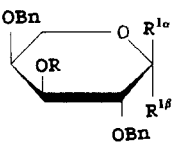
	$R^{1\alpha}$	$R^{1\beta}$	R^2	R^3
1	H, OH		H	H
2	H	OCH_3	H	H
3	H	OCH_3	H	All
4	H	OCH_3	Ac	All
5	H	OCH_3	Bn	All
6	H, OH		Bn	All
7	H, OH		Bn	H
8	H, OAc		Bn	Ac
9α	Cl	H	Bn	Ac
9β	H	Cl	Bn	Ac



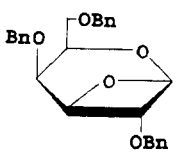
10



9α

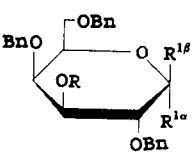


	$R^{1\alpha}$	$R^{1\beta}$	R
11α	OCH_3	H	H
11β	H	OCH_3	H
12α	OCH_3	H	Ac
12β	H	OCH_3	Ac
13α	Gal	H	H
13β	H	Gal	H
14α	Ser^1	H	H
14β	H	Ser^1	H
15α	Ser^1	H	Ac
15β	H	Ser^1	Ac



19

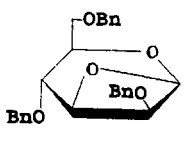
16 or 17



$HOCHR^1CH(NHR^2)COOCH_3$

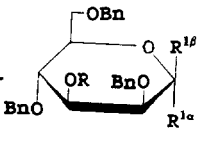
	R^1	R^2
16	H	Cbz
17	H	Ts
18	Me	Cbz

	$R^{1\alpha}$	$R^{1\beta}$	R
20α	Ser^1	H	H
20β	H	Ser^1	H
21α	Ser^1	H	Ac
21β	H	Ser^1	Ac
22α	Ser^2	H	H
22β	H	Ser^2	H
23α	Ser^3	H	Ac
23β	H	Ser^3	Ac



24

16, 17 or 18



	$R^{1\alpha}$	$R^{1\beta}$	R
25α	Ser^1	H	H
25β	H	Ser^1	H
26α	Ser^1	H	Ac
26β	H	Ser^1	Ac
27α	Ser^2	H	H
27β	H	Ser^2	H
28α	Ser^3	H	Ac
28β	H	Ser^3	Ac
29	H, Thr		H

Ser^1=$OCH_2CH(NHCbz)COOCH_3$
Ser^2=$OCH_2CH(NHTs)COOCH_3$
Ser^3=$OCH_2CH(NAcTs)COOCH_3$
Thr=$OCH(CH_3)CH(NHCbz)COOCH_3$
Gal=6-*O*-1,2:3,4-di-*O*-isopropylidine-α-D-galactopyranos-6-yl

the ring closure must have C-2-*O*-acetate and C-1-halide in a *trans*-relation. As either **9**α or **9**β was readily converted to the anhydro sugar **10**, a practical preparation of **10** was carried out with the mixture of **9**α and **9**β. The ^{1}H NMR spectrum of **10** showed a characteristic triplet at δ 5.58 for H-1 with $^3J_{H1,H2} = J_{H1,H3} = 3.4$ Hz, a similar pattern to the spectrum of 1,3-anhydro-2,4,6-tri-*O*-benzyl-β-D-galactopyranose [2] (δ 5.58 for H-1, $^3J_{H1,H2} = J_{H1,H3} = 3.5$ Hz). It was reported that treatment of 3-*O*-acetyl-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl chloride [8] and 3-*O*-acetyl-2,4-di-*O*-benzyl-6-deoxy-α-D-glucopyranosyl chloride [3] with potassium *tert*-butoxide in oxolane yielded the corresponding glucal derivatives as the main products, by *trans*-diaxial elimination of hydrogen chloride from C-1 and C-2. This behavior was not observed during similar treatment of 3-*O*-acetyl-2,4,6-tri-*O*-benzyl-α-D-galactopyranosyl chloride and 3-*O*-acetyl-2,4-di-*O*-benzyl-6-deoxy-α-D-galactopyranosyl chloride [5]. In the present study of 3-*O*-acetyl-2,4-di-*O*-benzyl-L-arabinopyranosyl chloride treated with potassium *tert*-butoxide in dry oxolane, 1,3-anhydro sugar was formed as the main product (77%) while the glycal derivative was obtained as a by-product (15%; its ^{1}H NMR spectrum gave H-1 as a singlet at δ 6.25 ppm).

For investigation of the conformation of **10** calculations by molecular mechanics [14] were carried out. MMX is a new program recently made available [15] for performing molecular mechanics calculations on an IBM 386 or equivalent, and a detailed description of this method of operation has appeared [16]. This program, based on the MM2

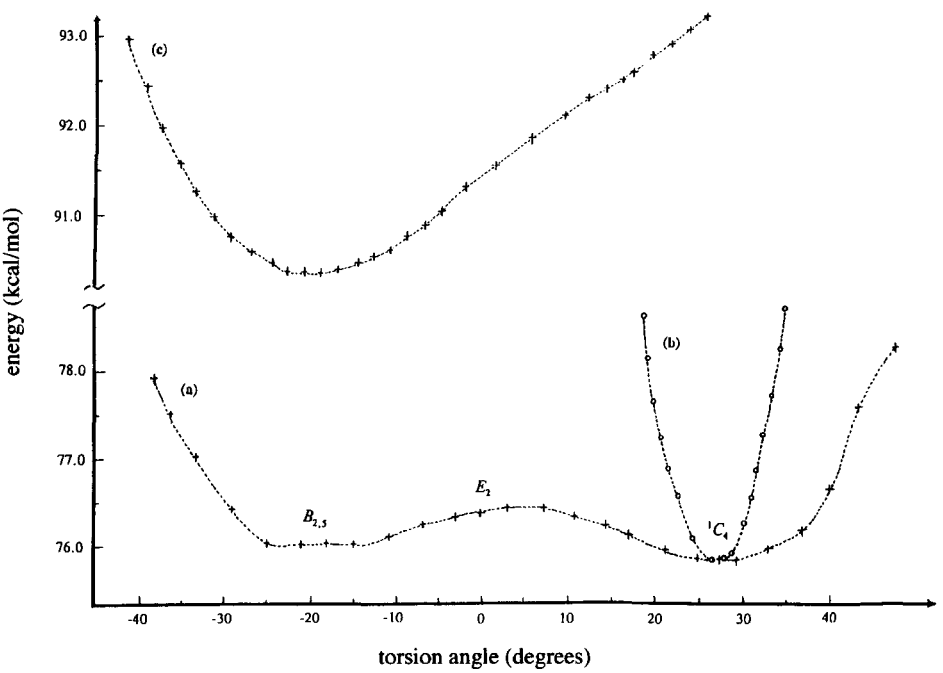


Fig. 1. Plots of energy (kcal/mol) versus the torsion angle (deg). (a) C-3–C-4–C-5–O-5 for **10**. (b) C-3–C-2–C-1–O-3 for **10**. (c) C-3–C-4–C-5–O-5 for **19**.

force field of Allinger, has already gained considerable acceptance [17–19]. Previously we found that the conformational properties of per-*O*-benzylated 1,2-anhydro-D-talopyranose in the solid state [20], and per-*O*-benzylated 1,2-anhydro-D-xylopyranose in the solution state [21], could be reproduced satisfactorily using MMX. Here we conducted calculations for description of the conformational properties of **10** and **19** as shown in Fig. 1. In Fig. 1, plot **a** represents the relationship between total energy and the C-3–C-4–C-5–O-5, torsion angle which indicates the energy changes upon pseudorotation from the $B_{2,5}$ form to the $^1C_4$ form for the pyranose ring of **10**. It was found that a conformation close to $^1C_4$ had the lowest energy (75.82 kcal/mol), and a conformation close to $B_{2,5}$ had a similar energy (76.00 kcal/mol), while the E_2 form had an energy of 76.40 kcal/mol. When the C-3–C-4–C-5–O-5 torsion angle changed over a wide range ($-25°$ to $+37°$, accompanied by a symmetrical change in the C-4–C-5–O-5–C-1 torsion angle) the energy fluctuation was relatively small (75.82–76.42 kcal/mol), thus revealing that the C-4–C-5–O-5 moiety (C-5 head) of the pyranose ring is flexible. Plot **b** describes the rigidity of the four membered ring part in **10**. A sharp increment of the total energy was observed when the C-3–C-2–C-1–O-3 torsion angle assumed a value outside the 29°–25° range, indicating that the four membered ring is considerably rigid. Plot **c** indicates the conformational properties of **19**, which are different from those of **10**. There is only one energy well for the C-3–C-4–C-5–O-5 torsion angle at about 19°, corresponding to the $B_{2,5}$ conformation; the E_2 and $^1C_4$ forms had 1 kcal/mol and 2.8 kcal/mol higher energies, respectively, than that of $B_{2,5}$. The calculated torsional angles and coupling constants for the conformations corresponding to $^1C_4$, E_2, and $B_{2,5}$ of **10**, and also for the conformation (**Exp**) having coupling constants close to the experimental values, are shown in Table 1. We suggest from the data that the actual conformation of **10** in the solution state is close to E_2. For comparison, the reproduced conformations, being close to $B_{2,5}$ for **19** and **24** calculated according to the observed coupling constants, are also shown in Table 1 (**19 Exp, 24 Exp**).

Methanolysis of the 1,3-anhydropyranose **10** was conducted to investigate its reactivity. No reaction occurred when a methanol solution of **10** was stirred at room temperature for 16 h. However, when freshly fused $ZnCl_2$ was added as the catalyst, all of the starting material disappeared and two compounds formed in a ratio of 3.5:1 as indicated by analytical LC. The major product was identified by ^{1}H NMR as methyl 2,4-di-*O*-benzyl-α-L-arabinopyranoside (**11**α), and the minor one was methyl 2,4-di-*O*-benzyl-β-L-arabinopyranoside (**11**β) which was identical to the product obtained from deallylation of **5**. Thus, an unexpected ring opening of the 1,3-anhydro sugar produced mainly the 1,3-*cis* glycoside. Further study of the glycosidic coupling reaction of **10** with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose as the acceptor gave a similar result, i.e. α-linked disaccharide **13**α was the major product. The $^4C_1$ conformation and α (1,2-*trans*) anomeric configuration of the arabinose moiety of **13**α were established from its ^{1}H NMR spectrum, which yielded an upfield shift for H-1′ (δ 4.30, axial H), and large values for $^3J_{H1',H2'}$ (8.3 Hz) and $^3J_{H2',H3'}$ (9.2 Hz). The structural assignment of **13**β was also achieved from its ^{1}H NMR spectrum, which yielded a downfield H-1′ (δ 4.89, equatorial H), a small $^3J_{H1',H2'}$ (3.8 Hz), and a large $^3J_{H2',H3'}$ (9.0 Hz,$^4C_1$ form). The structure of **14**α was assigned by the same method (δ 4.38 for H-1, α-linkage; $^3J_{H1,H2} = 5.4$ Hz, $^3J_{H2,H3} = 7.1$ Hz for a $^4C_1$ conformation), and the assignment was

Table 1
Selected torsion angles and $^1H-^1H$ vicinal coupling constants obtained by MMX for **10**, **19**, and **24**

Angle	Magnitude (°)					
	10				**19**	**24**
	$^1C_4$	$B_{2,5}$	E_2	**Exp**	**Exp**	**Exp**
O-5–C-1–C-2–C-3	−87.6	−82.6	−87.8	−87.3	−80.2	−86.4
C-1–C-2–C-3–C-4	82.5	79.2	83.4	83.3	77.0	83.2
C-2–C-3–C-4–C-5	−63.9	−34.6	−50.5	−49.3	−32.3	−38.2
C-3–C-4–C-5–O-5	27.8	−28.8	0	−3.0	−21.8	−35.3
C-4–C-5–O-5–C-1	−31.1	29.9	−0.6	3.1	23.6	37.4
C-5–O-5–C-1–C-2	71.5	34.2	53.5	51.0	30.5	35.5
C-5–O-5–C-1–O-3	−28.5	−64.9	−47.5	−50.0		
O-5–C-1–O-3–C-3	85.3	88.3	88.6	88.9		
C-1–O-3–C-3–C-4	−84.1	−85.2	−85.6	−85.4		
O-3–C-3–C-4–C-5	33.5	61.9	47.4	48.6		
C-1–O-3–C-3–C-2	28.5	30.0	27.2	27.4		
O-3–C-3–C-2–C-1	−26.5	−27.9	−25.4	−25.6		
C-3–C-2–C-1–O-3	26.6	28.0	25.5	25.7		
C-2–C-1–O-3–C-3	−28.5	−30.0	−27.3	−27.5		
Coupling constants (Hz, modified Karplus) for indicated torsion angles (°)						
$J_{1,2}$ / $\phi_{1,2}$	5.5 / 31	5.5 / 31	5.6 / 30	5.6 / 30	5.6 / 29	1.1 / 101
$J_{2,3}$ / $\phi_{2,3}$	8.2 / 26	8.0 / 28	8.2 / 26	8.2 / 26	7.6 / 33	1.6 / 106
$J_{3,4}$ / $\phi_{3,4}$	0.9 / 79	2.9 / 55	1.9 / 65	1.9 / 64	3.8 / 48	3.6 / 62
$J_{4,5}$ / $\phi_{4,5}$	8.9 / 29	5.6 / 24	8.8 / 1	8.5 / 1	1.8 / 49	6.6 / 145
$J_{4,5'}$ / $\phi_{4,5'}$	8.4 / 148	1.5 / 92	3.8 / 118	3.4 / 115		
Observed coupling constants (Hz) for **10**, **19**, and **24**						
				10	**19**	**24**
$J_{1,2}$				3.4	3.5	0
$J_{2,3}$				6.1	5.5	0
$J_{3,4}$				1.2	2.3	3.4
$J_{4,5}$				7.2	1.2	6.6
$J_{4,5'}$				3.4	–	–

further confirmed from its acetylated derivative **15**α (δ 4.40 for H-1, $^3J_{H1,H2}$ = 5.1 Hz). The ^{1}H NMR of **14**β was not easily assigned due to overlap of some signals, whereas its acetylated derivative **15**β gave a clear spectrum (δ 4.80 for H-1, β-linkage; $^3J_{H1,H2}$ = 4.0 Hz, $^3J_{H2,H3}$ = 11.8 Hz for the $^4C_1$ form). The stereochemical outcome for the glycosylation of **10** slightly changed as the reaction temperature was varied ($\alpha:\beta$ = 2:1 at −10°C, and 3:1 at 30°C). It was also found that, with boron trifluoride etherate or silver triflate as the catalyst at room temperature, both the stereochemical outcome and the total yield were somewhat different (BF_3Et_2O, $\alpha:\beta$ = 1.5:1, yield 63%; $ZnCl_2$, $\alpha:\beta$ = 3:1, total yield 84%; AgOTf, $\alpha:\beta$ = 3.2:1, yield 88%).

To rationalize the 1,3-*cis* ring opening of **10**, further studies on the glycosylation of **10**, 1,3-anhydro-2,4,6-tri-*O*-benzyl-β-D-galacto- (**19**) [2], and -β-D-mannopyranose (**24**) (prepared from methyl α-D-mannopyranoside through selective 3-*O*-allylation, then benzylation followed by the same procedures as reported in [10]) with *N*-benzyloxycarbonyl- (**16**) and *N*-tosyl-L-serine (**17**) or *N*-benzyloxycarbonyl-L-threonine (**18**)

methyl ester derivatives were carried out. Compounds **19** and **24** gave normal 1,3-*trans* glycopeptides predominantly, while **10** still gave the 1,3-*cis* arranged product as the major one. The assignment of anomeric configuration of mannopyranosyl derivatives was based upon the chemical shift of H-1, i.e. the α anomers gave an H-1 signal at downfield (δ 4.85 for **25**α, δ 4.81 for **27**α) whereas the β anomers gave an H-1 signal upfield (δ 4.47 for **25**β, δ 4.38 for **27**β). The difference in the chemical shift of H-1 between **25**α and **25**β (0.38 ppm), or between **27**α and **27**β (0.43 ppm) is close to that (0.46 ppm) between allyl 3-*O*-allyl-2,4,6-tri-*O*-benzyl-α-D-mannopyranoside (δ 4.92 for H-1) [22] and allyl 3,4,6-tri-*O*-benzyl-β-D-mannopyranoside (δ 4.46 for H-1) [23]. The detailed mechanism for the ring opening of 1,3-anhydro sugars remains to be elucidated.

3. Experimental

General methods.—Melting points were determined with a "Mel-Temp" apparatus. Optical rotations were determined with a Perkin–Elmer model 241-MC automatic polarimeter for solutions in a 1-dm, jacketed cell. ^{1}H and ^{13}C NMR spectra were recorded with Varian XL-400 and Varian XL-200 spectrometers, for solutions in $CDCl_3$ with tetramethylsilane (Me_4Si) as the internal standard. Chemical shifts are expressed in ppm downfield from the internal Me_4Si absorption. Mass spectra were recorded with a JDS-D 3005 mass spectrometer using a direct-insertion technique to introduce the sample. Analytical LC was performed with a pump (model YSB-2, made in China), stainless-steel columns packed with silica gel (10 × 150 mm, or 4.6 × 250 mm) or Lichrosorb-NH_2 (4.6 × 250 mm), a differential refractometer (Perkin–Elmer LC-25 RI Detector), and ethyl acetate–petroleum ether (bp 60–90°C) as the eluent at a flow rate of 1–4 mL/min. Thin-layer chromatography (TLC) was performed on silica gel HF, detection being affected by charring with 30% (v/v) sulfuric acid in methanol or sometimes by UV detection. Column chromatography was conducted by elution of a column (16 × 240 mm, 18 × 300 mm, 35 × 400 mm) of silica gel (100–200 mesh). Solutions were concentrated at a temperature < 60°C under diminished pressure.

Molecular mechanics calculations [14] were carried out using the MMX program [15] 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 were carried out with one fixed torsion angle (C-3–C-4–C-5–O-5 for evaluation of the flexibility of the pyranose moiety C-4–C-5–O-5 of **10** and **19**; and C-3–C-2–C-1–O-3 for evaluation of the rigidity of the four membered ring C-3–C-2–C-1–O-3 of **10**). Calculations with the two torsion angles H-3–C-3–C-4–H-4 ($\Phi_{3,4}$) and H-4–C-4–C-5–H-5 ($\Phi_{4,5}$) fixed at values correlated to the observed coupling constants $^3J_{H3,H4}$ and $^3J_{H4,H5}$ gave the deduced conformation for **19** and **24** (**Exp** in Table 1).

Methyl 3-O-allyl-β-L-arabinopyranoside (**3**).—A mixture of methyl β-L-arabinopyranoside (**2**) [11] (3.28 g, 20 mmol) and dibutyltin oxide (5.5 g, 22.0 mmol) in absolute methanol (160 mL) was boiled under reflux. After the mixture became transparent, heating was continued for 2 h, and the solution was concentrated to give a

white foamy residue (8.8 g). Tetrabutylammonium iodide (7.4 g, 20 mmol), allyl bromide (20.4 mL, 240 mmol) and toluene (200 mL) were added to the residue and the mixture was stirred for 1 day at 60°C. TLC (EtOAc) showed the presence of major product **3** together with small amounts of the di-*O*-allylated compound and methyl 4-*O*-allyl-β-L-arabinopyranoside as by-products. After evaporation of the solvent, most of the tetrabutylammonium iodide was recovered from the residue by precipitation with ethyl acetate or diethyl ether. The brownish residue was purified by chromatography on a column of silica gel (1:1 petroleum ether–EtOAc) to afford yellowish syrupy **3** (2.81 g, 69%); ^{1}H NMR: δ 6.00–5.70 (m, 1 H, CH_2=C*H*–CH_2), 5.25–5.15 (m, 2 H, CH_2=CH–CH_2–), 4.85 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1), 4.72 (dd, 1 H, $J_{1,2}$ 3.4, $J_{2,3}$ 2.8 Hz, H-2), 4.45–4.38 (m, 3 H, H-4 and CH_4=CH–CH_2–), 3.98 (dd, 1 H, $J_{2,3}$ 2.8, $J_{3,4}$ 4.1 Hz, H-3), 3.95–3.87 (m, 2 H, H-5,5′), 3.40 (s, 3 H, OCH_3). Methyl 4-*O*-allyl-β-L-arabinopyranoside was the minor product and not isolated in a pure form; its ^{1}H NMR gave OCH_3 as a singlet at δ 3.38, and its ^{13}C NMR gave O*C*H$_3$ at δ 55.10. After acetylation, the ^{1}H NMR spectrum of methyl 2,3-di-*O*-acetyl-4-*O*-allyl-β-L-arabinopyranoside showed two CH_3CO signals at δ 2.09 and 2.08.

Compound **3** was acetylated by standard methods and compound **4** was obtained in a quantitative yield as a syrup; [α]$_D$ +181° (*c* 4.7, $CHCl_3$); ^{1}H NMR: δ 5.95–5.70 (m, 1 H, CH_2=C*H*–CH_2), 5.30 (dd, 1 H, $J_{1,2}$ 3.7, $J_{2,3}$ 2.0 Hz, H-2), 5.25–5.17 (m, 1 H, H-4), 5.15–5.05 (m, 2 H, CH_2=CH–CH_2), 4.91 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.10–4.00 (m, 2 H, CH_2=CH–CH_2–), 3.87 (dd, 1 H, $J_{2,3}$ 2.0, $J_{3,4}$ 4.2 Hz, H-3), 3.82–8.67 (m, 2 H, H-5,5′), 3.39 (s, 3 H, OCH_3), 2.15, 2.12 (2 s, 6 H, CH_3CO); ^{13}C NMR: δ 170.0 (CH_3*C*O), 134.2 (CH_2=*C*H–CH_2), 116.6 (CH_2=CH–CH_2–), 96.8 (C-1), 72.0, 70.4, 70.0 (C-3,2, and 4), 68.1 (CH_2=CH–*C*H_2–), 60.2 (C-5), 55.2 (O*C*H$_3$) Anal. Calcd for $C_{13}H_{20}O_7$: C, 54.17; H, 6.94. Found: C, 54.28; H, 6.89.

*Methyl 3-*O*-allyl-2,4-di-*O*-benzyl-β-*L*-arabinopyranoside* (**5**).—To a solution of **3** (2.5 g, 11.0 mmol) in dry oxolane (50 mL) cooled in an ice bath was added sodium hydride (80% in oil; 1.05 g, 35 mmol) with stirring. Benzyl bromide (2.93 mL, 24.2 mmol) was added dropwise to the mixture and the mixture was boiled under reflux with vigorous agitation for 4 h. TLC (4:1 petroleum ether–EtOAc) indicated that the reaction was complete. The remaining sodium hydride was filtered off and the filtrate was concentrated. The residue was partitioned between water and dichloromethane, and the organic layer was dried (Na_2SO_4) and concentrated. Column chromatography (5:1 petroleum ether–EtOAc) gave pure compound **5** as a yellowish syrup (4.5 g, 95%); [α]$_D$ +57.5° (*c* 3.8, $CHCl_3$); ^{1}H NMR: δ 7.40–7.20 (m, 10 H, Ph), 6.02–5.82 (m, 1 H, CH_2=C*H*–CH_2–), 5.38–5.12 (m, 2 H, CH_2=CH–CH_2–), 4.82, 4.67 (2 d, 2 H, *J* 12.2 Hz, PhCH_2), 4.74, 4.73 (2 d, 2 H, *J* 10.0 Hz, PhCH_2), 4.64 (d, 1 H, $J_{1,2}$ 3.2 Hz, H-1), 4.20–4.10 (m, 2 H, H-2,4), 3.80–3.55 (m, 3 H, H-3,5, and 5′), 3.39 (s, 3 H, OCH_3). Anal. Calcd for $C_{23}H_{28}O_5$: C, 71.87; H, 7.29. Found: C, 71.66; H, 7.32.

*3-*O*-Allyl-2,4-di-*O*-benzyl-*L*-arabinopyranose* (**6**).—A mixture of **5** (4.0 g, 10.4 mmol), acetic acid (80%, 24 mL) and hydrochloric acid (1 N, 6 mL) was boiled under reflux for 2 h, at the end of which time TLC (2:1 petroleum ether–EtOAc) showed that all of the starting material had disappeared. Solid sodium bicarbonate was added to neutralize the mixture. The mixture was extracted with CH_2Cl_2 (3 × 20 mL), the extract was washed with saturated sodium bicarbonate and then water, dried (Na_2SO_4) and

concentrated to a syrup. Purification of the syrup by column chromatography (2:1 petroleum ether–EtOAc) yielded crystalline **6** consisting of β and α anomers in a ratio of 2.5:1 (3.18 g, 82.7%); mp 32–34°C, $[\alpha]_D$ +25° (*c* 4.7, $CHCl_3$); ^{13}C NMR: δ 134.2 ($CH_2=CHI-CH_2-$ of β anomer), 134.0 ($CH_2=CH-CH_2$ of α anomer), 128.1, 127.7 (Ph–C of β anomer), 127.8, 127.6 (Ph–C of α anomer), 116.6 ($CH_2=CH-CH_2-$ of α anomer), 116.2 ($CH_2=CH-CH_2-$ of β anomer), 94.2 (C-1 of α anomer), 91.8 (C-1 of β anomer), 77.0, 76.1, 75.8, 73.2, and 71.9 (2 $PhCH_2$, C-2,3, and 4 of β anomer), 77.8, 76.9, 76.2, 72.8, and 71.6 (2 $PhCH_2$, C-2,3, and 4 of α anomer), 71.4 ($CH_2=CH-CH_2-$ of α anomer), 71.1 ($CH_2=CH-CH_2-$ of β anomer), 60.4 (C-5 of α anomer), 59.5 (C-5 of α anomer). Anal. Calcd for $C_{22}H_{26}O_5 \cdot 0.5H_2O$: C, 69.65; H, 7.12. Found: C, 69.78; H, 7.16.

*2,4-Di-*O*-benzyl-*L*-arabinopyranose* (**7**).—Compound **6** (2.04 g, 5.5 mmol) was dissolved in ethanol (90%, 50 mL) and tris(triphenylphosphine)rhodium(I) chloride (100 mg, 0.11 mmol) was added to the solution. The mixture was refluxed and the reaction was monitored by TLC (1:1 petroleum ether–EtOAc) until all of the starting material was consumed (about 5 h). The mixture was filtered and the filtrate was concentrated to give a yellowish solid; recrystallization from EtOAc–petroleum ether afforded **7** as white crystals consisting of β and α anomers in a ratio of 1.5:1 (1.53 g, 84%); mp 104–105.5°C; $[\alpha]_D$ +39° (*c* 0.6, $CHCl_3$); ^1H NMR: δ 4.60 (d, H-1 of α anomer), 5.16 (d, H-1 of β anomer). Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.09; H, 6.67. Found: C, 69.16; H, 6.66.

*1,3-Di-*O*-acetyl-2,4-di-*O*-benzyl-*L*-arabinopyranose* (**8**).—Compound **7** (1.06 g, 3.2 mmol) was treated with acetic anhydride (2 mL) in pyridine (3 mL) by a standard method. Compound **8** was obtained in quantitative yield as a syrupy mixture of α and β anomers in a ratio of 2:1; $[\alpha]_D$ +64° (*c* 2.7, $CHCl_3$); ^1H NMR: δ 7.38–7.18 (m, 10 H, Ph), 6.35 (d, 0.33 H, $J_{1,2}$ 3.4 Hz, H-1 of β anomer), 5.68 (d, 0.66 H, $J_{1,2}$ 5.6 Hz, H-1 of α anomer), 5.15 (dd, 0.33 H, $J_{1,2}$ 3.4, $J_{2,3}$ 6.2 Hz, H-3 of β anomer), 5.05 (dd, 0.66 H, $J_{1,2}$ 5.6, $J_{2,3}$ 10.2 Hz, H-3 of α anomer), 4.70–4.43 (m, 4 H, 2 $PhCH_2$), 4.18–3.58 (m, 4 H, H-2,4,5, and 5'), 2.10, 2.04 (2 s, 1.98 H, 2 CH_3CO of β anomer), 2.09, 2.01 (2 s, 3.76 H, 2 CH_3CO of α anomer). Anal. Calcd for $C_{23}H_{26}O_7$: C, 66.67; H, 6.28. Found: C, 66.69; H, 6.20.

Compound **8** was also prepared by acetolysis of methyl 2,4-di-*O*-benzyl-β-L-arabinopyranoside (**11**β). Compound **11**β (170 mg, 0.49 mmol) was treated with acetic anhydride (3 mL) containing acetic acid (1 mL) and concentrated H_2SO_4 (0.03 mL) for 1.5 h. The reaction mixture was neutralized with ice-cooled aqueous potassium carbonate and extracted with CH_2Cl_2. The organic layer was concentrated to a syrup, which was purified by column chromatography (with 4:1 petroleum ether–EtOAc as the eluent) to give syrupy **8** (96 mg, 47%, $\alpha:\beta = 2:3$).

*3-*O*-Acetyl-2,4-di-*O*-benzyl-α-* (**9**α) *and -β-*L*-arabinopyranosyl chloride* (**9**β).—A solution of compound **8** (400 mg, 0.97 mmol) in dry diethyl ether (35 mL) was saturated with hydrogen chloride gas under a nitrogen atmosphere at 0°C and the solution was kept at room temperature in a sealed bottle for 1 h. TLC (3:1 petroleum ether–EtOAc) indicated that the reaction was complete. The solution was concentrated to a syrup, which was dissolved in CH_2Cl_2 (1 mL) and the solvent evaporated. This procedure was repeated 6 times. The product was then purified by analytical LC (5:1 petroleum

ether–EtOAc) to give the chlorides **9**α and **9**β in a ratio of about 1:1 with a total yield of 91%; For **9**α, $[\alpha]_D$ +68.8° (*c* 2.2, $CHCl_3$); ^{1}H NMR: δ 7.41–7.22 (m, 10 H, Ph), 5.80 (d, 1 H, $J_{1,2}$ 1.1 Hz, H-1), 5.26 (t, 1 H, $J_{2,3} = J_{3,4} = 2.9$ Hz, H-3), 4.65, 4.64 (2 d, 2 H, *J* 12.0 Hz, PhCH_2), 4.59, 4.51 (2 d, 2 H, *J* 11.8 Hz, PhCH_2), 4.11 (d, 1 H, $J_{4,5}$ 0, $J_{5,5'}$ 12.5 Hz, H-5), 3.98 (dd, 1 H, $J_{1,2}$ 1.1, $J_{2,3}$ 2.9 Hz, H-2), 3.93 (dd, 1 H, $J_{3,4}$ 2.9, $J_{4,5}$ 6.7 Hz, H-4), 3.68 (dd, 1 H, $J_{4,5'}$ 6.7, $J_{5,5'}$ 12.5 Hz, H-5), 2.13 (s, 3 H, CH_3CO). Anal. Calcd for $C_{21}H_{23}ClO_5$: C, 64.53; H, 5.89. Found: C, 64.48; H, 6.06. For **9**β, $[\alpha]_D$ +151.8° (*c* 2.5, $CHCl_3$). ^{1}H NMR: δ 7.37–7.22 (m, 10 H, Ph), 6.14 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 5.21 (dd, 1 H, $J_{2,3}$ 10.3, $J_{3,4}$ 3.2 Hz, H-3), 4.69, 4.68 (2 d, 2 H, *J* 12.9 Hz, PhCH_2), 4.62, 4.53 (2 d, 2 H, *J* 12.3 Hz, PhCH_2, 4.19 (dd, 1 H, $J_{1,2}$ 3.7, $J_{2,3}$ 10.3 Hz, H-2), 4.06 (dd, 1 H, $J_{4,5}$ 0.9, $J_{5,5}$ 12.7 Hz, H-5), 3.98–3.93 (m, 1 H, H-4), 3.86 (dd, 1 H, $J_{4,5}$ 2.0, $J_{5,5}$ 12.7 Hz, H-5′), 2.02 (s, 3 H, CH_3CO).

*1,3-Anhydro-2,4-di-*O*-benzyl-*α*-*L*-arabinopyranose* (**10**).—To a 1:1 mixture of **9**α and **9**β (101 mg, 0.26 mmol) in dry oxolane (5 mL) was added potassium *tert*-butoxide (90 mg, 0.8 mmol), and the mixture was stirred at room temperature for 2 h, at the end of which time TLC (3:1 petroleum ether–EtOAc) indicated that the starting material had 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 **10** as a syrup, which crystallized upon standing in a refrigerator for several days (62.2 mg, 77%); mp 31°C; $[\alpha]_D$ +25° (*c* 1, $CHCl_3$); ^{1}H NMR: δ 7.40–7.22 (m, 10 H, Ph), 5.58 (t, 1 H, $J_{1,2} = J_{1,3} = 3.4$ Hz, H-1), 4.85–4.72 (m, 1 H, $J_{1,3}$ 3.4, $J_{2,3}$ 6.1, $J_{3,4}$ 1.2 Hz, H-3), 4.60, 4.47 (2 d, 2 H, *J* 11.7 Hz, PhCH_2), 4.58 (dd, 1 H, $J_{4,5}$ 7.2, $J_{5,5'}$ 10.7 Hz, H-5), 4.51, 4.50 (2 d, 2 H, *J* 11.6 Hz, PhCH_2), 4.42 (dd, 1 H, $J_{1,2}$ 3.4, $J_{2,3}$ 6.1 Hz, H-2), 4.30 (dd, 1 H, $J_{4,5'}$ 3.4, $J_{5,5'}$ 10.7 Hz, H-5′), 3.95–3.84 (m, 1 H, $J_{3,4}$ 1.2, $J_{4,5}$ 7.2, $J_{4,5'}$ 3.4 Hz, H-4). Anal. Calcd for $C_{19}H_{20}O_4$: C, 73.08; H, 6.41. Found: C, 72.97; H, 6.42.

*Methyl 2,4-di-*O*-benzyl-*α- (**11**α) *and -*β*-*L*-arabinopyranoside* (**11**β).—Compound **10** (50 mg, 0.16 mmol) was dissolved in anhyd MeOH (5.0 mL) in the presence of freshly fused $ZnCl_2$ (23.0 mg, 0.17 mmol) and the solution was kept for 1 h at room temperature. TLC (2:1 petroleum ether–EtOAc) indicated that the reaction was complete. The solvent was evaporated and water (6 mL) was added to the residue. The mixture was extracted with CH_2Cl_2 (3 × 2 mL), and the combined extracts were dried (Na_2SO_4), and concentrated. Analytical LC (3:1 petroleum ether–EtOAc) of the syrup gave **11**α (37.7 mg, 68.4%) and **11**β (10.7 mg, 19.6%); For **11**α, ^{1}H NMR: δ 7.40–7.20 (m, 10 H, Ph), 4.76, 4.60 (2 d, 2 H, *J* 11.7 Hz, PhCH_2), 4.68, 4.62 (2 d, 2 H, *J* 12.0 Hz, PhCH_2), 4.39 (d, 1 H, $J_{1,2}$ 4.4 Hz, H-1), 3.95 (dd, 1 H, $J_{4,5}$ 6.4, $J_{5,5'}$ 12.0 Hz, H-5), 3.89 (dd, 1 H, $J_{2,3}$ 6.6, $J_{3,4}$ 3.4 Hz, H-3), 3.78 (ddd, 1 H, $J_{3,4}$ 3.4, $J_{4,5}$ 6.4, $J_{4,5'}$ 2.9 Hz, H-4), 3.59 (dd, 1 H, $J_{1,2}$ 4.4, $J_{2,3}$ 6.6 Hz, H-2), 3.48 (dd, 1 H, $J_{4,5'}$ 2.9, $J_{5,5'}$ 12.0 Hz, H-5′), 3.47 (s, 3 H, OCH_3), 2.40 (bs, 1 H, OH). Acetylation of **11**α gave **12**α as a syrup; $[\alpha]_D$ +42.5° (*c* 0.6, $CHCl_3$); ^{1}H NMR: δ 7.40–7.22 (m, 10 H, Ph), 4.95 (dd, 1 H, $J_{2,3}$ 8.5, $J_{3,4}$ 3.4 Hz, H-3), 4.82, 4.52 (2 d, 2 H, *J* 11.7 Hz, PhCH_2), 4.64, 4.62 (2 d, 2 H, *J* 12.2 Hz, PhCH_2), 4.35 (d, 1 H, $J_{1,2}$ 6.1 Hz, H-1), 4.10 (dd, 1 H, $J_{4,5}$ 4.2, $J_{5,5'}$ 12.5 Hz, H-5), 3.82 (ddd, 1 H, $J_{3,4}$ 3.4, $J_{4,5}$ 4.2, $J_{4,5'}$ 2.0 Hz, H-4), 3.76 (dd, 1 H, $J_{1,2}$ 6.1, $J_{2,3}$ 8.5 Hz, H-2), 3.52 (s, 3 H, OCH_3), 3.44 (dd, 1 H, $J_{4,5'}$ 2.0, $J_{5,5'}$ 12.5 Hz, H-5′), 2.05 (s, 3 H, CH_3CO). Anal. Calcd for $C_{22}H_{26}O_6$: C, 68.39; H, 6.74. Found:

C, 68.21; H, 6.73. For **11β**, ^{1}H NMR: δ 7.38–7.25 (m, 10 H, Ph), 4.82–4.59 (m, 5 H, H-1, 2 PhCH_2), 4.03 (dd, 1 H, H-2), 3.82–3.74 (m, 2 H, H-3,4), 3.72–3.66 (m, 2 H, H-5,5′), 3.38 (s, 3 H, OCH_3), 2.18 (bs, 1 H, O*H*). Acetylation of **11β** gave **12β** as a syrup; $[\alpha]_D$ +112° (*c* 4.6, $CHCl_3$); ^{1}H NMR: δ 7.40–7.20 (m, 10 H, Ph), 5.20 (dd, 1 H, $J_{2,3}$ 10.3, $J_{3,4}$ 3.4 Hz, H-3), 4.72, 4.52 (2 d, 2 H, *J* 12.2 Hz, PhCH_2), 4.70 (d, 1 H, $J_{1,2}$ 3.1 Hz, H-1), 4.63, 4.62 (2 d, 2 H, *J* 12.5 Hz, PhCH_2), 4.00 (dd, 1 H, $J_{1,2}$ 3.1, $J_{2,3}$ 10.3 Hz, H-2), 3.93–3.86 (m, 1 H, H-4), 3.73 (dd, 1 H, $J_{4,5}$ 1.2, $J_{5,5'}$ 12.0 Hz, H-5), 3.64 (dd, 1 H, $J_{4,5}$ 2.2, $J_{5,5'}$ 12.0 Hz, H-5′), 3.41 (s, 3 H, OCH_3), 2.05 (s, 3 H, CH_3CO).

O-*(2,4-Di-*O*-benzyl-α-*L*-arabinopyranosyl)-(1 → 6)-1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranose* (**13α**) *and* O-*(2,4-di-*O*-benzyl-β-*L*-arabinopyranosyl)-(1 → 6)-1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranose* (**13β**).—The 1,3-anhydro sugar **10** (50 mg, 0.16 mmol) was dissolved in anhydrous oxolane (5.0 mL) containing freshly fused $ZnCl_2$ (20 mg) as the promoter. To the mixture was added a solution of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (70 mg, 0.27 mmol) in oxolane (2 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 **10** disappeared. The solution was concentrated to a syrup which was subjected to separation by analytical LC with 2:1 petroleum ether–EtOAc as eluent. Compound **13α** was obtained as a syrup (57.8 mg, 63.0%); $[\alpha]_D$ −53° (*c* 0.4, $CHCl_3$); ^{1}H NMR δ 7.40–7.20 (m, 10 H, Ph), 5.54 (d, 1 H, $J_{1,2}$ 5.1 Hz, H-1), 4.80, 4.65 (2 d, 2 H, *J* 11.8 Hz, PhCH_2), 4.67, 4.66 (2 d, 2 H, *J* 12.6 Hz, PhCH_2), 4.61 (dd, 1 H, $J_{2,3}$ 2.3, $J_{3,4}$ 7.8 Hz, H-3), 4.30 (dd, 1 H, $J_{1,2}$ 5.1, $J_{2,3}$ 2.3 Hz, H-2), 4.30 (d, 1 H, $J_{1',2'}$ 8.3 Hz, H-1′), 4.23 (dd, 1 H, $J_{3,4}$ 8.1, $J_{4,5}$ 1.7 Hz, H-4), 4.20 (dd, $J_{1',2'}$ 8.3 Hz, $J_{2',3'}$ 9.2 Hz, H-2′), 4.16–4.00 (m, 3 H, H-5, 6a, 6b), 3.75 (dd, 1 H, $J_{4',5'}$ 9.2 Hz, $J_{5',5''}$ 12.5 Hz, H-5′), 3.70–3.65 (m, 1 H, H-4′), 3.45–3.38 (m, 1 H, H-3′), 3.35 (dd, 1 H, $J_{4',5''}$ 1.8 Hz, $J_{5',5''}$ 12.5 Hz, H-5″), 1.80 (bs, 1 H, O*H*), 1.52, 1.44, 1.35, 1.34 (4 s, 12 H, 4 CH_3). Anal. Calcd for $C_{31}H_{40}O_{10}$: C, 65.05; H, 6.99. Found: C, 65.14; H, 7.23. Compound **13β** was obtained as a syrup (19.3 mg, 21.1%); $[\alpha]_D$ −8.2° (*c* 0.1, $CHCl_3$); ^{1}H NMR: δ 7.40–7.20 (m, 10 H, Ph), 5.53 (d, 1 H, $J_{1,2}$ 5.0 Hz, H-1), 4.89 (d, 1 H, $J_{1',2'}$ 3.8 Hz, H-1′), 4.79, 4.64 (2 d, 2 H, *J* 11.6 Hz, PhCH_2), 4.63, 4.62 (2 d, 2 H, *J* 12.8 Hz, PhCH_2), 4.61 (dd, 1 H, $J_{2,3}$ 2.4, $J_{3,4}$ 7.8 Hz, H-3), 4.30 (dd, 1 H, $J_{1,2}$ 5.0, $J_{2,3}$ 2.4 Hz, H-2), 4.22 (dd, 1 H, $J_{3,4}$ 7.8 Hz, $J_{4,5}$ 1.9 Hz, H-4), 4.20 (dd, 1 H, $J_{1',2'}$ 3.8, $J_{2',3'}$ 9.0 Hz, H-2′), 4.09–3.70 (m, 7 H, H-5,6a,6b,3′,4′,5′ and 5″), 2.03 (bs, 1 H, O*H*), 1.55, 1.46, 1.35, 1.35 (4 s, 12 H, 4 CH_3).

General procedure for glycopeptide preparation.—Amino acid methyl ester (1.2 equiv) was dissolved in dry CH_2Cl_2 (10 mL) in the presence of powdered 4 Å molecular sieves and the mixture was stirred for 10 min. Freshly fused $ZnCl_2$ (1 equiv) and 1,3-anhydo sugar (1 equiv) were then added with vigorous stirring. After 2 h the mixture was filtered and the filtrate was washed with water (3 × 10 mL), dried with Na_2SO_4, and evaporated to dryness. The crude product was purified by analytical LC on silica gel with 2:1 petroleum ether–EtOAc as the eluent. The following products were obtained starting from 100 mg of 1,3-anhydro sugars **10**, **19** and **24** respectively.

O-*(2,4-Di-*O*-benzyl-α-* (**14α**) *and -β-*L*-arabinopyranosyl)-*N*-benzyloxycarbonyl-*L*-serine methyl ester* (**14β**).—Pure **14α** (122.1 mg, 70%) and **14β** (52.9 mg, 20%) were obtained in a ratio of 3.5:1; For **14α**, ^{1}H NMR: δ 7.40–7.20 (m, 15 H, Ph), 5.71 (d, 1

H, *J* 8.1 Hz, N*H*), 5.12 (s, 2 H, PhCH_2OCO), 4.73, 4.56 (2 d, 2 H, *J* 11.5 Hz, PhCH_2), 4.69, 4.63 (2 d, 2 H, *J* 10.8 Hz, PhCH_2), 4.58–4.50 (m, 1 H, CH_2CH), 4.38 (d, 1 H, $J_{1,2}$ 5.4 Hz, H-1), 4.27, 3.89 (2 dd, 2 H, *J* 10.3, $J_{CH',CH}$ 3.2 Hz, $J_{CH'',CH}$ 4.7 Hz, CH_2CH), 3.80 (s, 3 H, OCH_3), 3.80–3.60 (m, 3 H, H-3,4 and 5), 3.54 (dd, 1 H, $J_{1,2}$ 5.4, $J_{2,3}$ 7.1 Hz, H-2), 3.38 (dd, 1 H, $J_{4,5'}$ 2.2, $J_{5,5'}$ 12.5 Hz, H-5'), 2.2 (bs, 1 H, O*H*). For **14**β, ^{1}H NMR: δ 7.40–7.16 (m, 15 H, Ph), 5.80 (d, 1 H, *J* 8.7 Hz, N*H*), 5.10 (s, 2 H, PhCH_2OCO), 4.80 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.67, 4.53 (2 d, 2 H, *J* 12.5 Hz, PhCH_2), 4.60–4.52 (m, 3 H, *J* 11.5 Hz, PhCH_2, CH_2CH), 4.09, 3.92 (2 dd, 2 H, *J* 10.8, $J_{CH',CH}$ 4.5 Hz, $J_{CH'',CH}$ 2.1 Hz, CH_2CH), 3.90–3.83 (m, 2 H, H-2,4), 3.70–3.56 (m, 6 H, H-3,5,5', and OCH_3).

Acetylation of **14**α and **14**β furnished **15**α and **15**β, respectively, as syrups. For **15**α, $[\alpha]_D$ +25.7° (*c* 2.2, $CHCl_3$); ^{1}H NMR: δ 7.40–7.20 (m, 15 H, Ph), 5.65 (d, 1 H, *J* 8.2 Hz, N*H*), 5.18 (s, 2 H, PhCH_2OCO), 5.02–4.97 (m, 1 H, H-3), 4.70, 4.50 (2 d, *J* 11.3 Hz, PhCH_2), 4.65–4.52 (m, 3 H, *J* 12.1 Hz, PhCH_2, CH_2CH), 4.40 (d, 1 H, $J_{1,2}$ 5.1 Hz, H-1), 4.30–4.25 (m, 1 H, one proton of CH_2CH), 4.09–4.01 (m, 1 H, one proton of CH_2CH), 3.90–3.80 (m, 2 H, H-2,4), 3.74 (s, 3 H, OCH_3), 3.70–3.60 (m, 1 H, $J_{5,5'}$ 10.4 Hz, H-5), 3.47–3.40 (m, 1 H, $J_{5,5'}$ 10.4 Hz, H-5'), 2.01 (s, 3 H, CH_3CO). Anal. Calcd for $C_{33}H_{37}NO_{10}$: C, 65.24; H, 6.10. Found: C, 64.92; H, 6.14. For **15**β, $[\alpha]_D$ +60.8° (*c* 2.0, $CHCl_3$); ^{1}H NMR: δ7.40–7.20 (m, 15 H, Ph), 5.82 (d, 1 H, *J* 8.9 Hz, N*H*), 5.11 (s, 2 H, P*HC*H_2CO), 5.08 (dd, 1 H, $J_{2,3}$ 11.8, $J_{3,4}$ 3.9 Hz, H-3), 4.80 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 4.61, 4.55 (2 d, 2 H, *J* 11.9 Hz, PhCH_2), 4.59, 4.58 (2 d, 2 H, *J* 12.0 Hz, PhCH_2), 4.54–4.46 (m, 1 H, CH_2CH), 4.03, 3.97 (2 dd, 2 H, *J* 9.1, $J_{CH',CH}$ 2.5 Hz, $J_{CH'',CH}$ 2.8 Hz, CH_2CH), 3.88–3.78 (m, 2 H, H-2,4), 3.66 (s, 3 H, OCH_3), 3.65–3.62 (m, 2 H, H-5,5'), 2.02 (s, 3 H, CH_3CO).

O-*(2,4,6-Tri*-O-*benzyl-*α- (**20**α) *and* -β-D-*galactopyranosyl)*-N-*benzyloxycarbonyl*-L-*serine methyl ester* (**20**β).—Assignment of compound **20**α (106.3 mg, 67%) and **20**β (33.2 mg, 20.9%) by ^{1}H NMR was difficult. Therefore, acetylation of **20**α, **20**β with Ac_2O in pyridine gave **21**α, **21**β, respectively. For **21**α, $[\alpha]_D$ +51° (*c* 6.7, $CHCl_3$); ^{1}H NMR: δ 7.40–7.20 (m, 20 H, Ph), 6.10 (d, 1 H, *J* 8.7 Hz, N*H*), 5.14 (dd, 1 H, $J_{2,3}$ 10.4, $J_{3,4}$ 3.4 Hz, H-3), 5.07 (s, 2 H, PhCH_2OCO), 4.79 (d, 1 H $J_{1,2}$ 3.7 Hz, H-1), 4.80, 4.52 (2 d, 2 H, *J* 12.0 Hz, PhCH_2), 4.61, 4.55 (2 d, 2 H, *J* 11.6 Hz, PhCH_2), 4.57–4.44 (m, 3 H, *J* 12.1 Hz, PhCH_2, CH_2CH), 4.14, 3.81 (2 dd, 2 H, *J* 10.7, $J_{CH',CH}$ 3.9, $J_{CH'',CH}$ 3.3 Hz, CHCH_2), 4.09–4.00 (m, 2 H, $J_{3,4}$ 3.4 Hz, H-4, H-5), 3.98 (dd, 1 H, $J_{1,2}$ 3.7, $J_{2,3}$ 10.4 Hz, H-2), 3.68 (s, 3 H, OCH_3), 3.55–3.45 (m, 2 H, $J_{5,6'}$ 6.6, $J_{5,6}$ 6.9 Hz, $J_{6,6'}$ 9.2 Hz, H-6,6'), 1.99 (s, 3 H, COCH_3). Anal. Calcd for $C_{41}H_{45}NO_{11}$: C, 67.68; H, 6.19. Found: C, 68.01; H, 6.27.

For **21**β, ^{1}H NMR: δ 7.38–7.15 (m, 20 H, Ph), 5.75 (d, 1 H, *J* 8.4 Hz, N*H*), 5.07 (s, 2 H, PhCH_2OCO), 4.85 (dd, 1 H, $J_{2,3}$ 10.1, $J_{3,4}$ 4.2 Hz, H-3), 4.50–4.45 (m, 3 H, *J* 11.3 Hz, PhCH_2, CH_2CH), 4.43, 4.37 (2 d, 2 H, *J* 12.3 Hz, PhCH_2), 4.41, 4.38 (2 d, 2 H, *J* 10.6 Hz, PhCH_2), 4.37 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 4.16, 3.75 (2 dd, 2 H, *J* 10.2, $J_{CH',CH}$ 5.9, $J_{CH'',CH}$ 3.0 Hz, CHCH_2), 4.14–4.00 (m, 2 H, $J_{3,4}$ 4.2 Hz, H-4,5), 3.93 (dd, 1 H, $J_{1,2}$ 8.4, $J_{2,3}$ 10.1 Hz, H-2), 3.75 (s, 3 H, OCH_3), 3.58–3.40 (m, 2 H, $J_{5,6'}$ 4.3, $J_{5,6}$ 7.2 Hz, $J_{6,6'}$ 10.1 Hz, H-6,6'), 1.90 (s, 3 H, COCH_3).

O-*(2,4,6-Tri*-O-*benzyl-*α- (**22**α) *and* -β-D-*galactopyranosyl)*-N-*tosyl*-L-*serine methyl ester* (**22**β).—For **22**α (95 mg, 58.4%), $[\alpha]_D$ +38° (*c* 4.2, $CHCl_3$); ^{1}H NMR: δ 7.70

(d, 2 H, Ph of Ts), 7.40–7.10 (m, 17 H, Ph), 6.10 (d, 1 H, *J* 8.4 Hz, N*H*), 4.78, 4.58 (2 d, 2 H, *J* 11.9 Hz, PhCH_2), 4.71 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1), 4.60 (s, 2 H, PhCH_2), 4.51, 4.45 (2 d, 2 H, *J* 10.8 Hz, PhCH_2), 3.50 (s, 3 H, OCH_3), 2.42 (s, 3 H, PhCH_3). Anal. Calcd for $C_{38}H_{43}NO_{10}S \cdot 0.5H_2O$: C, 63.86; H, 6.16. Found: C, 64.03; H, 6.09. For **22**β (35.6 mg, 21.8%), ^{1}H NMR: δ 7.60 (d, 2 H, Ph of Ts), 7.40–7.08 (m, 17 H, Ph), 5.65 (d, 1 H, *J* 8.8 Hz, N*H*), 4.79, 4.61 (2 d, 2 H, *J* 12.3 Hz, PhCH_2), 4.64, 4.63 (2 d, 2 H, *J* 12.4 Hz, PhCH_2), 4.28 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 3.60 (s, 2 H, OCH_3), 2.40 (s, 3 H, PhCH_3).

Acetylation of **22**α gave **23**α; $[\alpha]_D$ + 29° (*c* 2.2, $CHCl_3$); ^{1}H NMR: δ 8.95 (d, 2 H, Ph of Ts), 7.40–7.20 (m, 17 H, Ph), 5.33–5.25 (m, 1 H, H-3), 4.90 (d, 1 H, $J_{1,2}$ 2.9 Hz, H-1), 4.68–4.40 (m, 7 H, 3 PhCH_2, CH_2CH), 3.71 (s, 3 H, OCH_3), 2.40 (s, 3 H, PhCH_3), 2.20 (s, 3 H, NCOCH_3), 1.98 (s, 3 H, OCOCH_3). Acetylation of **22**β gave **23**β; ^{1}H NMR: δ 8.94 (d, 2 H, Ph of Ts), 7.40–7.25 (m, 17 H, Ph), 5.30–5.20 (m, 1 H, H-3), 4.60–4.45 (m, 7 H, 3 PhCH_2, CH_2CH), 4.40 (d, 1 H, $J_{1,2}$ 8.7 Hz, H-1), 3.68 (s, 3 H, OCH_3), 2.44 (s, 3 H, PhCH_3), 2.22 (s, 3 H, NCOCH_3), 1.98 (s, 3 H, OCOCH_3).

O-*(2,4,6-Tri*-O-*benzyl-*α- (**25**α) *and* -β-D-*mannopyranosyl)*-N-*benzyloxycarbonyl*-L-*serine methyl ester* (**25**β).—For **25**α (122.9 mg, 77.5%), $[\alpha]_D$ −19° (*c* 3.7, $CHCl_3$); ^{1}H NMR: δ 7.40–7.05 (m, 20 H, Ph), 5.75 (d, 1 H, *J* 9.1 Hz, N*H*), 5.09 (s, 2 H, PhCH_2OCO), 4.85 (d, 1 H, $J_{1,2}$ 1.3 Hz, H-1), 4.79, 4.46 (2 d, 2 H, *J* 10.8 Hz, PhCH_2), 4.71, 4.55 (2 d, 2 H, *J* 11.6 Hz, PhCH_2), 4.64, 4.48 (2 d, 2 H, *J* 11.8 Hz, PhCH_2), 4.53–4.45 (m, 1 H, OCH_2C*H*), 3.96–3.80 (m, 2 H, CHCH_2), 3.73 (s, 3 H, OCH_3), 3.72–3.58 (m, 6 H, H-2,3,4,5,6, and 6′), 2.17 (bs, 1 H, O*H*). Anal. Calcd for $C_{39}H_{43}NO_{10}$: C, 68.32; H, 6.28. Found: C, 68.21; H, 6.39. For **25**β (24.6 mg, 15.5%), $[\alpha]_D$ +11° (*c* 2.1, $CHCl_3$); ^{1}H NMR: δ 7.40–7.20 (m, 20 H, Ph), 5.72 (d, 1 H, *J* 8.6 Hz, N*H*), 5.12 (s, 2 H, PhCH_2OCO), 4.91, 51 (2 d, 2 H, *J* 11.7 Hz, PhCH_2), 4.84, 4.55 (2 d, 2 H, *J* 10.8 Hz, PhCH_2), 4.64, 4.54 (2 d, 2 H, *J* 12.0 Hz, PhCH_2), 4.53–4.45 (m, 1 H, OCH_2C*H*), 4.47 (bs, 1 H, H-1), 4.35, 3.97 (2 dd, 2 H, *J* 10.2, $J_{CH',CH}$ 3.8, $J_{CH'',CH}$ 7.1 Hz, CHCH_2), 3.80–3.40 (m, 6 H, H-2,3,4,5,6, and 6′), 3.61 (s, 3 H, OCH_3), 1.97 (bs, 1 H, O*H*).

Acetylation of **25**α gave **26**α as a syrup; $[\alpha]_D$ −25° (*c* 2.2, $CHCl_3$); ^{1}H NMR: δ 7.38–7.10 (m, 20 H, Ph), 5.87 (d, 1 H, *J* 8.5 Hz, N*H*), 5.19 (dd, 1 H, $J_{2,3}$ 3.2, $J_{3,4}$ 8.8 Hz, H-3), 5.10 (s, 2 H, PhCH_2OCO), 4.80 (d, 1 H, $J_{1,2}$ 2.2 Hz, H-1), 4.64–4.40 (m, 7 H, 3 PhCH_2, CH_2CH), 4.10–3.72 (m, 5 H, OCHCH_2, H-2,4, and 5), 3.68 (s, 3 H, OCH_3), 3.67–3.58 (m, 2 H, H-6,6′), 1.93 (s, 3 H, COCH_3).

Acetylation of **25**β gave **26**β as a syrup; $[\alpha]_D$ + 14° (*c* 4.9, $CHCl_3$); ^{1}H NMR: δ 7.40–7.10 (m, 20 H, Ph), 5.68 (d, 1 H, *J* 8.9 Hz, N*H*), 5.33 (dd, 1 H, $J_{2,3}$ 2.6, $J_{3,4}$ 6.8 Hz, H-3), 5.12 (s, 2 H, PhCH_2OCO), 4.80–4.50 (m, 6 H, 3 PhCH_2), 4.42 (s, 1 H, H-1), 4.35 (dd, 1 H, *J* 10.2, $J_{CH',CH}$ 2.7 Hz, one proton of OCHCH_2), 3.98–3.90 (m, 2 H, H-4, another proton of OCHCH_2), 3.80–3.70 (m, 2 H, H-2,5), 3.65 (s, 3 H, OCH_3), 3.50–3.35 (m, 2 H, H-6,6′), 1.90 (s, 3 H, OCOCH_3).

O-*(2,4,6-Tri*-O-*benzyl-*α- (**27**α) *and-*β-D-*mannopyranosyl)*-N-*tosyl*-L-*serine methyl ester* (**27**β).—For **27**α (102 mg, 62.5%); ^{1}H NMR: δ 7.69 (d, 2 H, Ph of Ts), 7.35–7.15 (m, 17 H, Ph), 5.68 (d, 1 H, *J* 8.9 Hz, N*H*), 4.81 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 4.73, 4.50 (2 d, 2 H, *J* 11.4 Hz, PhCH_2), 4.70, 4.63 (2 d, 2 H, *J* 10.6 Hz, PhCH_2), 4.58, 4.52 (2 d, 2H, *J* 11.6 Hz, PhCH_2), 4.40–4.15 (m, 2 H, CH_2CH and H-4),

3.85–3.60 (m, 5 H, H-2,3,5,6 and 6'),3.50 (s, 3 H, OCH_3), 2.38 (s, 3 H, PhCH_3), 2.20 (bs, 1 H, OH). Anal. Calcd for $C_{38}H_{43}NO_{10}S \cdot 0.5H_2O$: C, 63.86; H, 6.16. Found: C, 64.10; H, 6.21.

For **27**β (41 mg, 25.1%), ^{1}H NMR: δ 7.73 (d, 2 H, Ph of Ts), 7.40–7.15 (m, 17 H, Ph), 5.70 (d, 1 H, J 8.6 Hz, NH), 4.88–4.45 (m, 7 H, 3 PhCH_2, OCH$_2$CH), 4.38 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1), 4.25 (dd, 1 H, J 11.0, $J_{CH',CH}$ 5.0 Hz, one proton of OCHCH_2), 4.15–4.08 (m, 2 H, H-4 and another proton of OCHCH_2), 3.80–3.55 (m, 5 H, H-2,3,5,6, and 6'), 3.48 (s, 3 H, OCH_3), 2.37 (s, 3 H, PhCH_3), 1.70 (bs, 1 H, OH).

Acetylation of **27**α gave **28**α as a syrup in a quantitative yield; $[\alpha]_D$ −48° (*c* 2.3, $CHCl_3$); ^{1}H NMR: δ 7.90 (d, 2 H, Ph of Ts), 7.40–7.15 (m, 17 H, Ph), 5.20 (dd, 1 H, $J_{2,3}$ 3.7, $J_{3,4}$ 8.8 Hz, H-3), 4.90 (d, 1 H, J 1.7 Hz, H-1), 4.78–4.40 (m, 7 H, 3 PhCH_2 and OCH$_2$CH), 4.18–3.70 (m, 7 H, CHCH_2, H-2,4,5,6, and 6'), 3.60 (s, 3 H, OCH_3), 2.40 (s, 3 H, PhCH_3), 2.21 (s, 3 H, NCOCH_3), 1.95 (s, 3 H, OCOCH_3). Anal. Calcd for $C_{12}H_{17}NO_{12}S$: C, 63.88; H, 5.96; Found: C, 64.05; H, 6.11.

Acetylation of **27**β gave **28**β as a syrup in a quantitative yield; $[\alpha]_D$ −7.0° (*c* 2.5, $CHCl_3$); ^{1}H NMR: δ 8.01 (d, 2 H, Ph of Ts), 7.40–7.10 (m, 17 H, Ph), 5.43 (dd, 1 H, $J_{2,3}$ 3.6, $J_{3,4}$ 5.4 Hz, H-3), 4.90–4.60 (m, 7 H, 3 PhCH_2 and OCH$_2$CH), 4.58 (bs, 1 H, H-1), 4.45, 4.07 (2dd, 2 H, J 9.8, $J_{CH',CH}$ 4.7, $J_{CH',CH}$ 6.1 Hz, CHCH_2), 4.32–4.25 (m, 1 H, $J_{3,4}$ 5.0, $J_{4,5}$ 5.3 Hz, H-4), 3.82–3.67 (m, 2 H, H-2,5), 3.65 (s, 3 H, OCH_3), 3.60–3.43 (m, 2 H, H-6,6'), 2.30 (s, 3 H, PhCH_3), 2.19 (s, 3 H, NCOCH_3), 1.85 (s, 3 H, OCOCH_3).

O-*(2,4,6-Tri-*O*-benzyl-*D*-mannopyranosyl)*-N-*benzyloxycarbonyl-*L*-threonine methyl ester* (**29**).—Compound **29** was obtained as an α, β mixture (126 mg, 78%, α:β 3:1); $[\alpha]_D$ +9.4° (*c* 2.7, $CHCl_3$); ^{1}H NMR: δ 7.48–7.15 (m, 20 H, Ph), 5.48 (d, 0.25 H, J 8.3 Hz, NH of β anomer), 5.37 (d, 0.75 H, J 8.4 Hz, NH of α anomer), 5.12 (s, 1.5 H, PhCH_2OCO of α anomer), 5.11 (s, 0.5 H, PhCH_2OCO of β anomer), 4.91 (d, 0.75 H, $J_{1,2}$ 1.7 Hz, H-1 of α anomer), 4.75–4.45 (m, 9 H, 3 PhCH_2, H-2, OCHCH$_3$, CHNH), 4.36 (d, 0.25 H, $J_{1,2}$ 2.1 Hz, H-1 of β anomer), 3.70 (s, 2.25 H, OCH_3 of α anomer), 3.50 (s, 0.75 H, OCH_3 of β anomer), 2.25 (bs, 0.75 H, OH of α anomer), 1.61 (bs, 0.25 H, OH of β anomer), 1.35 (d, 2.25 H, J 4.3 Hz, OCHCH_3 of α anomer), 1.34 (d, 0.75 H, J 4.9 Hz, OCHCH_3 of β anomer). Anal. Calcd for $C_{40}H_{45}NO_{10}$: C, 68.67; H, 6.44. Found: C, 68.32; H, 6.51.

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