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Synthesis of specifically deoxygenated disaccharide derivatives of the *Shigella dysenteriae* type 1 O-antigen ☆

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Abstract

The synthesis of methyl *O*-α-L-rhamnopyranosyl-(1 → 2)-α-D-galactopyranosides specifically deoxygenated at position 2 (**31**), or 4 (**21**) of the rhamnopyranosyl residue was accomplished using methyl 3,4,6-tri-*O*-benzoyl-α-D-galactopyranoside (**18**) as the glycosyl acceptor. Phenyl thionocarbonate activation of the penta-*O*-benzoylated disaccharide precursor followed by Barton reduction and Zemplén transesterification gave **31**, while **21** was obtained via condensation of the deoxygenated monosaccharide donor with **18**, and subsequent debenzoylation of the product.

Keywords: Deoxygenated disaccharide derivatives; *Shigella dysenteriae*; O-Antigen

1. Introduction

A common feature of many Gram-negative pathogens is that their O-specific polysaccharide (O-SP) is essential for their virulence. For *Shigella dysenteriae* type 1, it has recently been suggested that antibodies to the organism's O-antigen can provide protective immunity to the host [2]. As part of a project aiming at a better understanding of antibody–O-antigen complexes at the molecular level, we are currently investigating the interaction between the antigenic determinant of the O-specific chain of *Shigella dysenteriae* type 1 lipopolysaccharide and its homologous antibodies.

Recently in our laboratory a short fragment (**I**) of the tetrasaccharidic repeating unit

☆ Part 9 of the series Synthesis of ligands related to the O-specific antigen of Shigella dysenteriae type 1. For Part 8 see ref. [1].

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[3,4] (**II**) of the bacterium's O-SP was identified [5] as an immunodeterminant for a monoclonal IgM elicited against this pathogen.

3)-α-L-Rha*p*-(1 → 2)-α-D-Gal*p*-(1 →
I

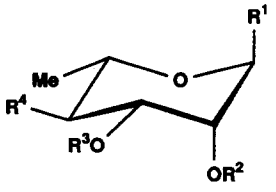
3)-α-D-Glc*p*NAc-(1 → 3)-α-L-Rha*p*-(1 → 3)-α-L-Rha*p*-(1 → 2)-α-D-Gal*p*-(1 →
II

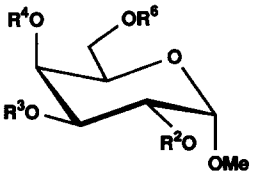
The use of specifically deoxygenated and deoxyfluorinated oligosaccharides as ligand probes to investigate the hydrogen bonding network stabilizing antibody–O-antigen complexes has been described [6]. Following this approach, methyl glycosides of **I** deoxygenated or deoxyfluorinated at position 3,4, or 6 of the galactose residue were prepared [1,7], and their affinity for the monoclonal IgM of reference studied [8]. As a continuation of this work, we describe here the preparation of analogues of methyl *O*-α-L-rhamnopyranosyl-(1 → 2)-α-D-galactopyranoside specifically deoxygenated at position 2 or 4 of the L-rhamnopyranose moiety, namely compounds **31** and **21**.

2. Results and discussion

For the preparation of methyl *O*-(4,6-dideoxy-α-L-*lyxo*-hexopyranosyl)-(1 → 2)-α-D-galactopyranoside (**21**), we used an already deoxygenated rhamnopyranosyl donor, **12**, bearing a participating group at C-2. Methyl 4,6-dideoxy-α-L-*lyxo*-hexopyranoside (**6**), required as an intermediate, was prepared from methyl α-L-rhamnopyranoside [9] (**1**) via a pathway employing a published strategy [10]. For deoxygenation, the *O*-(imidazol-1-ylthiocarbonyl) moiety was previously found satisfactory in our hands [7]. Therefore, instead of the *O*-(methylthio)thiocarbonyl derivative **3** [10], the 4-*O*-(imidazol-1-ylthiocarbonyl) intermediate **4**, prepared from methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside [11] (**2**) in 97% yield, was used as the activated precursor for the Barton–MacCombie reduction. Treatment [12] of **4** with tributyltin hydride in the presence of a catalytic amount of 2,2′-azobis(2-methylpropionitrile) (AIBN) afforded the dideoxy compound [10] **5** as the only product. In particular, contamination with the parent alcohol **2** was not detected. Subsequent hydrolysis of the isopropylidene acetal gave the target **6** (**4** → **6**, 85%).

In our first attempt towards the synthesis of **21**, the readily available [13] methyl 6-*O*-*tert*-butyldiphenylsilyl-3,4-*O*-isopropylidene-α-D-galactopyranoside (**13**) was used as the glycosyl acceptor. In order to limit the number of deprotection steps required at the disaccharide level, acetyl groups, regarded as acid labile, were preferred for the glycosyl donor. Therefore the diol **6** was converted into the corresponding diacetate **7**. When submitted to acetolysis, **7** gave the crystalline triacetate [14,15] **8**, which was treated [16] with dichloromethyl methyl ether (DCMME) and a catalytic amount of zinc chloride ($ZnCl_2 \cdot Et_2O$) to afford the glycosyl chloride **9** as an unstable intermediate. Condensation of **9** and **13**, achieved under base deficient conditions [17] using silver trifluoromethanesulfonate (AgOTf) as the promoter and 2,6-di-*tert*-butyl-4-methylpyridine as the acid scavenger, afforded the fully protected disaccharide **19** (71%). A one-step deprotection of **19** was attempted using anhydrous tetrafluoroboric acid (HBF_4) in methanol, but monosaccharides **14** and **6** were obtained as the sole products. This result confirmed the known high sensitivity [18] of deoxygenated sugars to acidic media, and this route was not pursued any further.





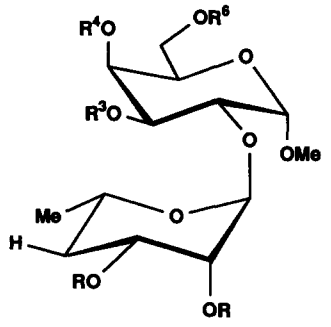
	R^1	R^2	R^3	R^4
1	OMe	H	H	OH
2	OMe	- CMe_2 -		OH
3	OMe	- CMe_2 -		OMtc
4	OMe	- CMe_2 -		OItc
5	OMe	- CMe_2 -		H
6	OMe	H	H	H
7	OMe	Ac	Ac	H
8	OAc	Ac	Ac	H
9	Cl	Ac	Ac	H
10	OMe	Bz	Bz	H
11	OAc	Bz	Bz	H
12	Cl	Bz	Bz	H

	R^2	R^3	R^4	R^6
13	H	- CMe_2 -		TBS
14	H	H	H	H
15	Bn	- CMe_2 -		$C(OMe)Me_2$
16	Bn	H	H	H
17	Bn	Bz	Bz	Bz
18	H	Bz	Bz	Bz

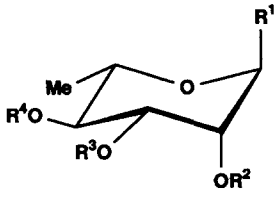
Mtc = (methylthio)thiocarbonyl
Ptc = phenoxythiocarbonyl
Itc = imidazol-1-ylthiocarbonyl
TBS = *tert*-butyl(diphenyl)silyl
Bz = benzoyl
Bn = benzyl

Next, we investigated the synthesis of the target disaccharide **21** via a pathway requiring a basic medium for the final one-step deprotection procedure. Methyl 3,4,6-tri-*O*-benzoyl-α-D-galactopyranoside (**18**), prepared from **14** via the known [7] **15**, was used as the glycosyl acceptor. Thus, selective acid hydrolysis of **15** gave the monobenzyl ether **16**, which was then fully benzoylated (→ **17**). Hydrogenolysis of the latter resulted in the tribenzoate **18** (96%). In order to avoid any possible transesterification side-reaction [19] during the condensation step, the dibenzoate **12** was chosen as the glycosyl donor, instead of the former diacetate **9**. Benzoylation of the diol **6**, followed by acetolysis (**6** → **10** → **11**, 96%) and subsequent treatment with DCMME–$ZnCl_2 \cdot Et_2O$ complex gave the chloride **12** (84%). Condensation of **12** and the acceptor **18** in the presence of silver trifluoromethanesulfonate gave the fully protected disaccharide **20** (66%), which was debenzoylated under Zemplén conditions (→ **21**, 96%). The α interglycosidic linkage in **20** and **21** was confirmed by measuring their C-1′, H-1′ coupling constants (170.8 Hz and 170.6 Hz, respectively).

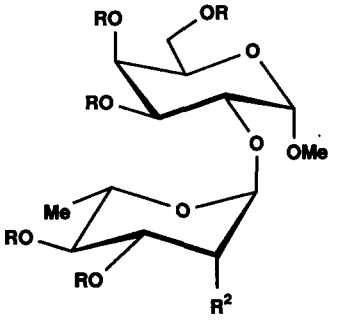
The lack of any participating group in a glycosylation reaction involving a donor deoxygenated at position C-2 renders the control of the stereoselectivity of the coupling problematic. In the following synthesis of **31**, the deoxygenation step was performed at



	R^3	R^4	R^6	R
19	- CMe_2 -		TBS	Ac
20	Bz	Bz	Bz	Bz
21	H	H	H	H



	R^1	R^2	R^3	R^4
22	OMe	- CMe(OMe) -		H
23	OMe	Ac	H	H
24	OMe	Ac	Bz	Bz
25	OAc	Ac	Bz	Bz
26	Cl	Ac	Bz	Bz



	R	R^2
27	Bz	OAc
28	Bz	OH
29	Bz	OPtc
30	Bz	H
31	H	H

the disaccharide level, thereby avoiding the problem. The key intermediate was the fully acylated **27**, bearing benzoyl groups save at C-2 of the rhamnopyranosyl subunit, which bore an acetyl group that could be selectively removed. Thus, reaction of **1** with trimethyl orthoacetate and partial acid hydrolysis of the resulting orthoester **22** afforded the monoacetate **23**, which was benzoylated to give the fully protected [20] **24**. Cleavage of the methyl glycoside **24** by acetolysis (Ac_2O, H_2SO_4) and treatment of the resulting [21] **25** with DCMME–$ZnCl_2 \cdot Et_2O$ complex then afforded the rhamnopyranosyl donor **26** (85%). The alcohol **18** was glycosylated with the chloride **26**, under promotion by silver trifluoromethanesulfonate, to give the disaccharide **27** (97%). The α interglycosidic linkage in **27** was demonstrated by the C-1′, H-1′ coupling constant (170.3 Hz).

The fully acylated disaccharide **27** was selectively deprotected at C-2′ when submitted to acid-catalyzed methanolysis [22] (→ **28**, 82%). Attempted activation by reaction of the hydroxyl group at C-2 of **28** with *N,N′*-thiocarbonyldiimidazole was sluggish. Consequently, the phenoxythiocarbonyl derivative **29** was prepared [23] (97%). Barton deoxygenation of the latter using tributyltin hydride and a catalytic amount of AIBN gave the fully protected **30** as the only detectable product (99%). A one-step deprotection of per-*O*-benzoylated **30**, by catalytic transesterification, afforded the target compound **31** (91%). Both disaccharides **21** and **31** were obtained crystalline. All new compounds were fully characterized by NMR spectroscopy.

3. Experimental

General methods.—Melting points were determined on a Kofler hot stage. Optical rotations were measured in $CHCl_3$ solution at 25°C, except where indicated otherwise, with a Perkin–Elmer automatic polarimeter, Model 241 MC. TLC on precoated slides of silica gel G F_{254} (Analtech) was performed with solvent mixtures of appropriately adjusted polarity consisting of *A*, dichloromethane–methanol; *B*, hexane–EtOAc; *C*, hexane–acetone; *D*, toluene–acetone; or *E*, toluene–EtOAc. Detection was effected, when applicable, with UV light and/or by charring with 5% H_2SO_4 in EtOH. Preparative chromatography was performed by elution from columns of silica gel 60 (particle size 0.04–0.063 mm). The NMR spectra were recorded at 25°C for solutions in $CDCl_3$, except when D_2O is specified, on a Varian Gemini-300 spectrometer (300 MHz for ^1H, 75 MHz for ^{13}C). Internal references for solutions in $CDCl_3$ were $CDCl_3$ (77.00 ppm for ^{13}C) and Me_4Si (0.00 ppm for ^1H); for solutions in D_2O, CD_3OD (49.00 ppm for ^{13}C) and HOD (4.78 ppm for ^1H). Proton-signal assignments were made by first-order analysis of the spectra, and were supported by homonuclear decoupling experiments. Of the two magnetically nonequivalent geminal protons at C-6, the one resonating at lower field is denoted H-6a and the one at higher field H-6b. The ^{13}C NMR assignments were made by two-dimensional ^{13}C-^1H correlation maps (HETCOR). In the listing of the assignments, atoms in the rhamnopyranosyl residue are indicated with a prime (′). Low resolution chemical ionization mass spectra (CIMS) were obtained using NH_3 as the ionizing gas. Before use, AgOTf was dried at 133 Pa/50°C for 2 h, and CH_2Cl_2 was dried over Drierite. Solutions in organic solvents were dried with anhydrous sodium sulfate.

Methyl 4-O-(imidazol-1-ylthiocarbonyl)-2,3-O-isopropylidene-α-L-rhamnopyranoside (**4**).—A solution of compound **2** [11] (3.79 g, 17.4 mmol) and *N,N′*-thiocarbonyldiimidazole (6.20 g, 34.8 mmol) in toluene (200 mL) was refluxed overnight. The solution was concentrated and the residue was taken up in dichloromethane, washed with aq 5% HCl, water, and satd aq NaCl. After concentration, the residue was chromatographed (solvent *B*, 4:1): to give **4** as a white solid (5.53 g, 97%), mp 101–102°C (diisopropyl ether); $[\alpha]_D$ − 41° (*c* 1.0); NMR: ^1H, δ 8.33, 7.63, 7.05, (3 s, 3 H, imidazole), 5.75 (dd, 1 H, $J_{3,4}$ 7.6, $J_{4,5}$ 9.8 Hz, H-4), 4.95 (s, 1 H, H-1), 4.38 (dd, 1 H, $J_{2,3}$ 5.4 Hz, H-3), 4.22 (d, 1 H, H-2), 3.95 (dq, 1 H, $J_{5,6}$ 6.3 Hz, H-5), 3.43 (s, 3 H, CH_3O), 1.62, 1.36 (2 s, 6 H, Me_2C), and 1.28 (d, 3 H, H-6); ^{13}C, δ 183.9, 136.9, 130.9 (3 C, imidazole),

118.1 (Me_2C), 98.0 (C-1), 83.1 (C-4), 75.9 (C-2), 75.2 (C-3), 63.7 (C-5), 55.1 (OCH_3), 27.5, 26.2 (Me_2C), and 17.1 (C-6); CIMS: m/z 346 $[(M + NH_4)^+]$ and 329 $[(M + H)^+]$. Anal. Calcd for $C_{14}H_{20}N_2O_5S$: C, 51.21; H, 6.14; N, 8.53; S, 9.76; Found: C, 50.98; H, 6.19; N, 8.39; S, 10.01.

*Methyl 4,6-dideoxy-α-*L-lyxo-*hexopyranoside* (**6**) *and methyl 2,3-di-*O*-acetyl-4,6-dideoxy-α-*L-lyxo-*hexopyranoside* (**7**).—AIBN (235 mg, 1.43 mmol) and tributyltin hydride (3.42 mL, 12.9 mmol) were added to a solution of **4** (2.35 g, 7.16 mmol) in toluene (180 mL). The solution was deoxygenated (N_2) for 20 min and heated at 110°C for 1.5 h, at which time all the starting material had been transformed into the less polar **5**. The solution was concentrated. Acetic acid (30 mL) and water (7 mL) were added to the residue and the mixture was stirred at room temperature for 16 h. Volatiles were evaporated and coevaporated with toluene. The residue was chromatographed (solvent *D*, 1.5:1) to give methyl 4,6-dideoxy-α-L-*lyxo*-hexopyranoside (**6**) as a white solid (982 mg, 85%), mp 100–100.5°C (EtOAc); $[\alpha]_D - 88°$ (c 1.0); lit. [10] mp 99–100.5°C, $[\alpha]_D - 83°$.

Acetic anhydride (4 mL, 42.4 mmol) was added at 0°C to a solution of the diol **6** (800 mg, 4.94 mmol) in pyridine (12 mL), and the solution was stirred at room temperature overnight. Methanol (10 mL) was added and stirring was continued for 1 h. The mixture was concentrated and the residue was partitioned between dichloromethane and water. After the usual workup, the organic phase was concentrated, and the residue was chromatographed (solvent *B*, 6:1). Compound **7** was obtained in theoretical yield as a colorless oil, $[\alpha]_D - 57°$ (c 0.9); NMR: ^{1}H, δ 5.21 (ddd, 1 H, $J_{2,3}$ 3.2, $J_{3,4ax}$ 10.3, $J_{3,4eq}$ 5.6 Hz, H-3), 4.38 (dd, 1 H, H-2), 4.22 (d, 1 H, $J_{1,2}$ 1.4 Hz, H-1), 3.94 (ddq, 1 H, $J_{4ax,5}$ 10.0, $J_{4eq,5}$ 4.0 Hz, H-5), 3.35 (s, 3 H, CH_3O), 2.12, 1.99 (2 s, 6 H, $COCH_3$), 1.76–1.65 (m, 2 H, H-4*ax*, 4*eq*), and 1.24 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6); ^{13}C, δ 170.3, 170.0 (2 C, $COCH_3$), 99.3 (C-1), 67.8 (C-2), 66.9 (C-3), 64.1 (C-5), 54.9 (OCH_3), 33.3 (C-4), and 20.0 (3 C, $COCH_3$, C-6); CIMS: m/z 264 $[(M + NH_4)^+]$. Anal. Calcd for $C_{11}H_{18}O_6$: C, 53.65; H, 7.37. Found: C, 53.41; H, 7.38.

Methyl O-*(2,3-di-*O*-acetyl-4,6-dideoxy-α-*L-lyxo-*hexopyranosyl)-(1 → 2)-6-*O-tert-*butyldiphenylsilyl-3,4-*O*-isopropylidene-α-*D-*galactopyranoside* (**19**).—Sulfuric acid (3 drops) was added to a solution of **7** (540 mg, 2.2 mmol) in acetic anhydride (5 mL) at 0°C. The solution was stirred at this temperature for 1 h and left in the refrigerator for 20 h. Solid $NaHCO_3$ (2 g) was added and the mixture was concentrated on the rotary evaporator. The residue was partitioned between dichloromethane and water. The organic phase was processed as usual and concentrated to give **8** as a white solid, mp 74.5–75°C (diisopropyl ether), $[\alpha]_D - 64°$ (c 1.0); lit. [15] mp 70.5–72.5°C, $[\alpha]_D - 58.1°$ (c 0.7).

Zinc chloride–diethyl ether complex (300 μL of a 2.2 M solution in dichloromethane) was added to a solution of the crude **8** and DCMME (4 mL) in dichloroethane (16 mL), and the mixture was stirred at room temperature for 2 h. Volatiles were evaporated and coevaporated with toluene. Finally, the residue was dissolved in toluene, filtered through a bed of Celite, and concentrated to a slightly orange solution. The product, 2,3-di-*O*-acetyl-4,6-dideoxy-α-L-*lyxo*-hexopyranosyl chloride (**9**) was found to be extremely unstable on TLC (solvent *B*, 4:1) and its isolation was not attempted. Characteristic NMR data for **9** are as follows: ^{1}H, δ 6.02 (s, 1 H, H-1), 5.51 (ddd, 1 H, $J_{2,3}$ 3.2, $J_{3,4ax}$

11.9, $J_{3,4eq}$ 5.1 Hz, H-3), 5.21 (bs, 1 H, H-2), 4.26 (ddq, 1 H, $J_{4ax,5}$ 10.9, $J_{4eq,5}$ 2.9 Hz, H-5), 2.14, 2.02 (2 s, 6 H, COCH_3), 1.90 (m, 1 H, H-4*eq*), 1.85 (m, 1 H, H-4*ax*), and 1.29 (d, 3H,$J_{5,6}$ 6.3 Hz, H-6); ^{13}C, δ 170.0 (2 C, $COCH_3$), 90.7 (C-1), 69.6 (C-3), 67.7 (C-2), 65.4 (C-5), 32.9 (C-4), 20.8, 20.6, and 20.5 (3 C, $COCH_3$, C-6).

A solution of crude **9**, prepared from **8** (442 mg, 1.72 mmol), the alcohol **13** [13] (700 mg, 1.32 mmol), and 2,6-di-*tert*-butyl-4-methylpyridine (346 mg, 1.69 mmol) in dichloromethane (10 mL) was added dropwise to a suspension of AgOTf (500 mg, 1.95 mmol) in dichloromethane (10 mL) at −15°C. The suspension was stirred for 1 h at this temperature and for 30 min at room temperature, at which time the mixture remained unchanged. Dichloromethane was added and the mixture was filtered through a bed of Celite. The organic phase was washed successively with 1:1 aq 5% sodium sulfite–aq 5% sodium bicarbonate, then water, and finally satd aq NaCl. Solvents were evaporated and the residue was chromatographed (solvent ***B***, gradient) to give **19** as an amorphous solid (630 mg, 71%), $[\alpha]_D$ + 19° (*c* 1.0); NMR: ^{1}H, δ 7.71–7.34 (aromatic), 5.25 (ddd, 1 H, $J_{2',3'}$ 3.4, $J_{3',4'ax}$ 11.7, $J_{3',4'eq}$ 4.9 Hz, H-3'), 5.21 (bs, 1 H, H-2'), 5.08 (d, 1 H, $J_{1',2'}$ 1.0 Hz, H-1'), 4.70 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.25 (m, 2 H, $J_{3,4}$ 5.3, $J_{2,3}$ 9.7 Hz, H-3,4), 3.99 (m, 2 H, $J_{4'ax,5'}$ 11.2, $J_{4'eq,5'}$ 2.4 Hz, H-5,5'), 3.93 (dd, 1 H, $J_{5,6a}$ 6.6, $J_{6a,6b}$ 9.5 Hz, H-6a), 3.85 (dd, $J_{5,6b}$ 6.3 Hz, H-6b), 3.70 (m, 1 H, H-2), 3.34 (3 H, O*Me*), 2.13, 1.99 (2 s, 6 H, COCH_3), 1.81 (m, 1 H, H-4'*eq*), 1.69 (m, 1 H, H-4'*ax*), 1.48, 1.31 (2 s, 6 H, CMe_2), 1.22 (d, 3 H, $J_{5',6'}$ 6.3 Hz, H-6'), and 1.05 (s, 9 H, *t*-Bu); ^{13}C, δ 170.1 (2 C, $COCH_3$), 135.8–127.6 (aromatic), 109.2 (CMe_2), 99.3 (C-1'), 99.1 (C-1), 76.6 (C-2), 75.4 (C-3), 73.3 (C-4), 67.7 (C-2'), 67.5 (C-5), 66.9 (C-3'), 64.4 (C-5'), 62.9 (C-6), 55.2 (O*Me*), 33.3 (C-4'), 28.2, 26.3 (CMe_2), 26.7 (*t*-Bu), and 20.9 (3 C, C-6', $COCH_3$); CIMS: *m/z* 704 [(M + NH_4) +]. Anal. Calcd for $C_{36}H_{50}O_{11}Si$: C, 62.95; H, 7.34. Found: C, 63.08; H, 7.39.

*Methyl 2,3-di-*O*-benzoyl-4,6-dideoxy-α-*L*-lyxo-hexopyranoside* (**10**).—Benzoyl chloride (3.2 mL, 27.5 mmol) was added dropwise to a solution of the diol **6** (1.5 g, 9.26 mmol) in pyridine (25 mL) at 0°C. Stirring was maintained at room temperature for 16 h. Methanol (10 mL) was added, and after 1 h the volatiles were evaporated. The residue was submitted to the usual workup and chromatographed (solvent *B*, 9:1) to give **10** as a colorless oil (3.32 g, 97%), $[\alpha]_D$ + 40° (*c* 1.1); NMR: ^{1}H, δ 8.12–7.29 (aromatic), 5.58 (ddd, 1 H, $J_{2,3}$ 3.3, $J_{3,4ax}$ 11.6, $J_{3,4eq}$ 5.3 Hz, H-3), 5.43 (bs, 1 H, H-2), 4.89 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 4.11 (ddq, 1 H, $J_{4ax,5}$ 12.5, $J_{4eq,5}$ 3.0 Hz, H-5), 3.43 (s, 3 H, O*Me*), 2.05–1.95 (m, 2 H, H-4*eq*, 4*ax*), and 1.34 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6); ^{13}C, δ 165.7, 165.4 (2 C, *C*OPh), 133.2–128.1 (aromatic), 99.3 (C-1), 68.49 (C-2), 67.9 (C-3), 64.1 (C-5), 55.0 (OMe), 33.9 (C-4), and 21.2 (C-6); CIMS: *m/z* 388 [(M + NH_4)$^+$]. Anal. Calcd for $C_{21}H_{22}O_6$: C, 68.09; H, 5.99. Found: C, 67.91; H, 5.97.

*1-*O*-Acetyl-2,3-di-*O*-benzoyl-4,6-dideoxy-α-*L*-lyxo-hexopyranose* (**11**).—Sulfuric acid (10 drops) was added to a solution of **10** (2.7 g, 7.30 mmol) in acetic anhydride (20 mL) at 0°C. The solution was stirred at this temperature for 2 h and left in the refrigerator for 20 h. Solid $NaHCO_3$ (~ 8 g) was added and the mixture was worked up as described for the preparation of **8**. Chromatography of the residue (solvent **B**, 9:1) gave **11** as a glassy solid (2.89 g, 100%), $[\alpha]_D$ + 17° (*c* 0.7); NMR; ^{1}H, δ 8.14–7.31 (aromatic), 6.27 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 5.62 (ddd, 1 H, $J_{2,3}$ 3.3, $J_{3,4ax}$ 10.8, $J_{3,4eq}$ 6.0 Hz, H-3), 5.45 (bs, 1 H, H-2), 4.20 (ddq, 1 H, $J_{4ax,5}$ 10.3, $J_{4eq,5}$ 3.3 Hz, H-5), 2.17 (s, 3 H, COCH_3),

2.17–1.98 (m, 2 H, H-4*eq*, 4*ax*), and 1.34 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6); ^{13}C, δ 168.5 ($COCH_3$), 165.6, 165.4 (2 C, COPh), 133.4–128.3 (aromatic), 91.9 (C-1), 67.5 (C-3), 67.2 (C-2), 66.8 (C-5), 33.6 (C-4), 21.3, and 21.1 (2 C, $COCH_3$, C-6); CIMS: *m/z* 416 [$(M + NH_4)^+$]. Anal. Calcd for $C_{22}H_{22}O_7$: C, 66.33; H, 5.57. Found: C, 66.13; H, 5.64.

*2,3-Di-*O*-benzoyl-4,6-dideoxy-α-*L*-lyxo-hexopyranosyl chloride* (**12**).—Zinc chloride–diethyl ether complex (670 μL of a 2.2 M solution in dichloromethane) was added to a solution of **11** (2.06 g, 5.20 mmol) and DCMME (8 mL) in dichloroethane (12 mL), and the mixture was stirred at room temperature for 4 h. Volatiles were evaporated and coevaporated with toluene. Finally, the residue was dissolved in toluene, filtered through a bed of Celite, and chromatographed (solvent *B*, 9:1) to give **12** as a colorless oil (1.63 g, 84%) together with some hydrolysis product, which was not further analyzed. Data for **12** are as follows: $[\alpha]_D$ − 23° (*c* 1.0); NMR: ^{1}H, δ 8.11–7.15 (aromatic), 6.25 (d, 1 H, $J_{1,2}$ 1.2 Hz, H-1), 5.87 (ddd, 1 H, $J_{2,3}$ 3.2, $J_{3,4ax}$ 11.9, $J_{3,4eq}$ 5.1 Hz, H-3), 5.59 (dd, 1 H, H-2), 4.26 (ddq, 1 H, $J_{4ax,5}$ 12.2, $J_{4eq,5}$ 2.4 Hz, H-5), 1.90 (ddd, 1 H, $J_{4eq,4ax}$ 12.6 Hz, H-4*eq*), 1.85 (dt, 1 H, H-4*ax*), and 1.37 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6); ^{13}C, δ 165.3 (2 C,COPh), 133.5–128.2 (aromatic), 90.8 (C-1), 70.3 (C-2), 67.7 (C-5), 66.4 (C-3), 33.6 (C-4), and 20.8 (C-6); CIMS: *m/z* 392 [$(M + NH_4)^+$]. Anal. Calcd for $C_{20}H_{19}ClO_5$: C, 64.09; H, 5.11. Found: C, 64.08; H, 5.27.

*Methyl 2-*O*-benzyl-α-*D*-galactopyranoside* (**16**).—Water (15 mL) was added to a solution of the mixed acetal [7] **15** (19.8 g, 50 mmol) in acetic acid (150 mL). The mixture was stirred at 70°C for 10 h, at which time one major polar product could be seen on TLC (solvent *E*, 1:1) together with partially acetylated ones. The volatiles were evaporated and coevaporated with toluene. The residue, in methanol, was treated with sodium methoxide under Zemplén conditions. When TLC showed that the deacetylation reaction was complete, the mixture was neutralized with Amberlite IR-120 (H^+) ion-exchange resin. After filtration, volatiles were evaporated to give crude **16** in quantitative yield. Chromatography of an analytical sample (solvent *D*, 1:1.2) gave **16** as a crystalline solid, mp 121.5–122°C (MeOH); $[\alpha]_D$ + 110° (*c* 1.0); NMR: ^{1}H, δ 7.35–7.27 (aromatic), 4.71 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1), 4.66 (s, 2 H, OCH_2Ph), 4.06 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-4), 3.96 (dd, 1 H, $J_{2,3}$ 9.8 Hz, H-3), 3.91–3,86 (m, 2 H, H-6a,6b), 3.77 (dd, 1 H, H-5), 3.73 (dd, 1 H, H-2), and 3.33 (s, 3 H, OCH_3); ^{13}C, δ 137.8–128.1 (aromatic), 97.9 (C-1), 76.5 (C-2), 72.9 (OCH$_2$Ph), 70.3 (C-4), 69.0, 68.9 (C-3,5), 63.0 (C-6), and 55.4 (OCH$_3$); CIMS: *m/z* 302 [$(M + NH_4)^+$]. Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 59.21; H, 7.13.

*Methyl 3,4,6-tri-*O*-benzoyl-2-*O*-benzyl-α-*D*-galactopyranoside* (**17**).—Benzoyl chloride (6 mL, 51.7 mmol) was added dropwise to a solution of the crude triol **16** (12.78 g, 45 mmol) in pyridine (200 mL) stirred at 0°C. The reaction mixture was stirred at room temperature overnight. Methanol (20 mL) was added and the mixture was stirred for 2 h. The solvents were evaporated and the residue, taken up in dichloromethane, was processed conventionally. Evaporation of the organic phase gave crude **17** in theoretical yield. Chromatography (solvent *B*, 4.5:1) provided an analytical sample as a colorless oil, $[\alpha]_D$ + 78° (*c* 1.4); NMR: ^{1}H, δ 8.05–7.29 (aromatic), 5.93 (bs, 1 H, H-4), 5.78 (bd, 1 H, $J_{2,3}$ 10.5 Hz, H-3), 4.93 (bs, 1 H, H-1), 4.71 (d, 1 H, J_{gem} 12.4 Hz, OCH_2Ph), 4.64 (d, 1 H, OCH_2Ph), 4.55 (dd, partially overlapped, 1 H, $J_{5,6a}$ 7.2 Hz, H-6a), 4.49 (m, overlapped, 1 H, H-5), 4.30 (dd, 1 H, $J_{5,6b}$ 3.8 Hz, $J_{6a,6b}$ 10.2 Hz, H-6b), 4.17 (dd,

1 H, $J_{1,2}$ 1.5 Hz, H-2), and 3.48 (s, 3 H, OCH_3); ^{13}C, δ 165.9–165.2 (3 C, 3 *C*O), 137.5–127.8 (aromatic), 98.5 (C-1), 73.3 (C-2), 73.1 (O*C*H_2Ph), 70.1 (C-3), 69.5 (C-4), 66.7 (C-5), 62.6 (C-6), and 55.6 (O*C*H_3); CIMS: *m/z* 614 [(M + NH_4)$^+$]. Anal. calcd for $C_{35}H_{32}O_9$: C, 70.46; H, 5.41. Found: C, 70.22; H, 5.77.

*Methyl 3,4,6-tri-*O*-benzoyl-α-*D*-galactopyranoside* (**18**).—A suspension of 10% Pd-C catalyst (3 g) and crude **17** (23.8 g, 40 mmol) in 2:1 ethanol–acetic acid (300 mL) was stirred overnight under an H_2 atmosphere. The catalyst was removed by filtration through a bed of Celite. The filtrate was concentrated and residual solvents were coevaporated with toluene. The residue was chromatographed (solvent *D*, 9:1) to give **18** as a white, amorphous solid (19.43 g, 96%), $[\alpha]_D$ + 102° (*c* 1.0); NMR: ^{1}H, δ 8.05–7.29 (aromatic), 5.91 (d, 1 H, H-4), 5.58 (bd, 1 H, $J_{3,4}$ 3.3, $J_{2,3}$ 10.3 Hz, H-3), 5.04 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 4.59 (dd, 1 H, $J_{5,6a}$ 7.0 Hz, H-6a), 4.49 (m, 1 H, H-5), 4.36 (dd, 1 H, $J_{5,6b}$ 5.4 Hz, $J_{6a,6b}$ 10.8 Hz, H-6b), 4.17 (bdt, 1 H, $J_{1,2}$ 3.7 Hz, H-2), 3.53 (s, 3 H, OCH_3), and 2.20 (d, 1 H, $J_{2,OH}$ 11.0 Hz, *H*O-2); ^{13}C, δ 166.2–165.5 (3 C, 3 *C* O), 133.5–128.1 (aromatic), 99.8 (C-1), 71.4 (C-3), 69.3 (C-4), 68.0 (C-2), 67.2 (C-5), 62.6 (C-6), and 55.8 (O*C*H_3); CIMS: *m/z* 524 [(M + NH_4)$^+$]. Anal. Calcd for $C_{28}H_{26}O_9$: C, 66.40; H, 5.17. Found: C, 66.43; H, 5.18.

Methyl O-*(2,3-di-*O*-benzoyl-4,6-dideoxy-α-*L*-lyxo-hexopyranosyl)-(1 → 2)-3,4,6-tri-*O*-benzoyl-α-*D*-galactopyranoside* (**20**).—A solution of the chloride **12** (386 mg, 0.99 mmol), the alcohol **18** (455 mg, 0.9 mmol) and 2,6-di-*tert*-butyl-4-methylpyridine (190 mg, 0.93 mmol) in dichloromethane (10 mL) was added dropwise to a suspension of AgOTf (347 mg, 1.35 mmol) in dichloromethane (5 mL) at −15°C. The suspension was stirred for 2 h at this temperature. TLC (solvent *D*, 9:1) showed that the donor had completely disappeared and that one major product was formed together with some minor ones. Stirring was continued for 30 min at 0°C, without any detectable change. The mixture was treated as for the preparation of **19** and the residue was chromatographed (solvent *B*, gradient) to give **20** as a white solid (500 mg, 66%) together with some unreacted glycosyl acceptor **18** (145 mg, 32%). Compound **20** had mp 180–181°C (ethyl acetate–hexane); $[\alpha]_D$ + 89° (*c* 1.0); NMR: ^{1}H, δ 8.01–7.25 (aromatic), 6.01 (d, 1 H, $J_{3,4}$ 3.2 Hz, H-4), 5.71 (dd, 1 H, $J_{2,3}$ 10.5 Hz, H-3), 5.52 (ddd, 1 H, $J_{2',3'}$ 3.4, $J_{3',4'ax}$ 11.9, $J_{3',4'eq}$ 4.6 Hz, H-3′), 5.25 (bd, 1 H, H-2′), 5.21 (bs, 1 H, H-1′), 5.13 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.59 (dd, 1 H, $J_{5,6a}$ 7.2, $J_{6a,6b}$ 10.0 Hz, H-6a), 4.55 (dd, 1 H, H-5), 4.32 (dd, 1 H, $J_{5,6b}$ 3.8 Hz, H-6b), 4.32 (dd, 1 H, partially overlapped, H-2), 4.27 (m, partially overlapped, 1 H, $J_{4'ax,5'}$ 9.4, $J_{4'eq,5'}$ 2.1 Hz, H-5′), 3.54 (s, 3 H, OCH_3), 2.14 (m, 1 H, H-4′*eq*), 1.93 (q, 1 H, H-4′*ax*), and 1.32 (d, 3 H, $J_{5',6'}$ 6.3 Hz, H-6′); ^{13}C, δ 165.7–165.2 (5 C, 5 *C*O), 133.2–128.6 (aromatic), 100.7 (C-1′, $^1J_{C,H}$ 170.8 Hz), 99.5 (C-1,$^1J_{C,H}$ 170.5 Hz), 77.2 (C-2), 69.8 (C-3), 69.3 (C-4), 68.3 (C-2′), 67.7 (C-3′), 66.7 (C-5), 64.9 (C-5′), 62.7 (C-6), 55.5 (O*C*H_3), 33.9 (C-4′), and 21.2 (C-6′); CIMS: *m/z* 862 [(M + NH_4)$^+$]. Anal. Calcd for $C_{48}H_{44}O_{14}$: C, 68.24; H, 5.25. Found: C, 68.48; H, 5.30.

Methyl O-*(4,6-dideoxy-α-*L*-lyxo-hexopyranosyl)-(1 → 2)-α-*D*-galactopyranoside* (**21**).—Sodium methoxide (1.5 mL of a 0.5 M solution in methanol) was added to **20** (1.04 g, 1.23 mmol) in methanol (15 mL), and the mixture was stirred at ambient temperature overnight. Amberlite IR-120 (H^+) ion-exchange resin was added to neutralize the reaction mixture. After filtration, volatiles were evaporated and the residue was

triturated in hexane. The hexane fraction was removed and the remaining material chromatographed (solvent *A*, 4:1) to give **21** as a crystalline solid (382 mg, 96%), mp 103–104°C (MeOH); $[\alpha]_D$ + 57° (*c* 0.7, MeOH); NMR (D_2O): ^1H, δ 4.94 (bs, 1 H, H-1′), 4.88 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.02 (m, 1 H, H-3′), 3.99 (m, 1 H, H-5′), 3.95 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-4), 3.85 (bs, 2 H, H-2′,5), 3.81 (dd, 1 H, H-3), 3.75 (dd, 1 H, $J_{2,3}$ 10.3 Hz, H-2), 3.70 (m, 2 H, H-6a,6b), 3.39 (s, 3 H, OCH_3), 1.73 (m, 1 H, H-4′*eq*), 1.54 (dt, 1 H, $J_{4'eq,4'ax}$ 12.2 Hz, H-4′*ax*), and 1.22 (d, 3 H, $J_{5',6'}$ 6.3 Hz, H-6′); ^{13}C, δ 104.6 (C-1′,$^1J_{C,H}$ 170.6 Hz), 99.9 (C-1, $^1J_{C,H}$ 170.2 Hz), 78.3 (C-2), 71.6 (C-2′), 70.3 (C-4), 69.5 (C-3), 68.6 (C-5), 66.8 (C-5′), 66.0 (C-3′), 62.2 (C-6), 55.67 (OCH_3), 35.6 (C-4′), and 21.2 (C-6′); CIMS; *m*/*z* 342 [$(M + NH_4)^+$]. Anal. Calcd for $C_{13}H_{24}O_9 \cdot H_2O$: C, 47.48; H, 7.51. Found: C, 47.40; H, 7.40.

Methyl 2-O-acetyl-α-L-rhamnopyranoside (**23**).—A mixture of methyl α-L-rhamnopyranoside [9] (**1**, 5.0 g, 28 mmol), *p*-toluenesulfonic acid monohydrate (300 mg), and trimethyl orthoacetate (7 mL) was stirred until dissolved in acetonitrile (100 mL, 5 min). After concentration, the residue was redissolved in acetonitrile (70 mL), and the solution was treated with aq 90% trifluoroacetic acid (3 mL) for 5 min, then concentrated. A solution of the residue in dichloromethane was washed with aq 5% $NaHCO_3$, and water, then dried and concentrated. Column chromatography (solvent *C*, 3:1) of the residue gave **23** (5.68 g, 92%) as a colorless oil, $[\alpha]_D$ − 39° (*c* 1.0); NMR: ^1H, δ 5.05 (dd, 1 H, $J_{2,3}$ 3.5, $J_{1,2}$ 1.5 Hz, H-2), 4.61 (d, 1 H, H-1), 3.89 (dd, 1 H, $J_{3,4}$ 9.5 Hz, H-3), 3.63 (dq, 1 H, $J_{4,5}$ 9.6 Hz, H-5), 3.43 (t, 1 H, H-4), 3.34 (s, 3 H, O*Me*), 2.11 (s, 3 H, $COCH_3$), and 1.31 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6); ^{13}C, δ 171.2 ($COCH_3$), 98.6 (C-1), 73.2 (C-4), 72.3 (C-2), 70.1 (C-3), 67.8 (C-5), 54.9 (O*Me*), 20.8 ($COCH_3$), and 17.4 (C-6); CIMS: *m*/*z* 238 [$(M + NH_4)^+$]. Anal. Calcd for $C_9H_{16}O_6 \cdot H_2O$: C, 47.15; H, 7.47. Found: C, 47.16; H, 7.24.

Methyl 2-O-acetyl-3,4-di-O-benzoyl-α-L-rhamnopyranoside (**24**).—Benzoyl chloride (3.5 mL, 30 mmol) was added dropwise to a solution of the monoacetate **23** (2.22 g, 10 mmol) in pyridine (30 mL) at 0°C. The mixture was stirred overnight at room temperature. Methanol (10 mL) was added and stirring was continued for 1 h. Volatiles were evaporated and the residue was processed as usual. Chromatography (solvent *B*, 6:1) gave **24** as a colorless oil that crystallized on standing (4.32 g, 100%), mp 107–108°C (diisopropyl ether); $[\alpha]_D$ + 42° (*c* 1.0); lit. [20] mp 94–96°C (ether–hexane), $[\alpha]_D$ + 46.5° (*c* 2.0); NMR: ^1H, δ 7.96–7.30 (aromatic), 5.70 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 10.1 Hz, H-3), 5.68 (dd, 1 H, H-4), 5.54 (dd, 1 H, $J_{1,2}$ 1.7 Hz, H-2), 4.76 (bs, 1 H, H-1), 4.40 (dq, 1 H, $J_{4,5}$ 9.7 Hz, H-5), 3.45 (s, 3 H, O*Me*), 2.15 (s, 3 H, $COCH_3$), and 1.33 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6); ^{13}C, δ 170.0 ($COCH_3$), 165.7, 165.4 (2 C, *C*OPh), 133.2–128.2 (aromatic), 88.6 (C-1), 71.6 (C-4), 70.1 (C-2), 69.8 (C-3), 66.5 (C-5), 55.2 (O*Me*), 20.8 ($COCH_3$), and 17.5 (C-6); CIMS: *m*/*z* 446 [$(M + NH_4)^+$]. Anal. Calcd for $C_{23}H_{24}O_8$: C, 64.48; H, 5.65. Found: C, 64.45; H, 5.72.

1,2-Di-O-acetyl-3,4-di-O-benzoyl-α-L-rhamnopyranose (**25**).—Sulfuric acid (10 drops) was added to a solution of crude **24** (from 5.4 g, 24.5 mmol of **23**) in acetic anhydride (40 mL) at 0°C. The solution was stirred at this temperature for 2 h and left in the refrigerator for 20 h. Solid $NaHCO_3$ (~ 4 g) was added and the mixture was processed as described for the preparation of **8**. TLC (solvent *B*, 5.6:1) showed the presence of one major compound contaminated by some minor ones. Chromatography of

the residue (solvent *B*, 9:1) gave **25** as a white foam (10.0 g, 90%), $[\alpha]_D$ + 30° (*c* 1.0); lit. [21], $[\alpha]_D$ + 35.7° (*c* 2.35); NMR: ^{1}H, δ 7.97–7.32 (aromatic), 6.13 (d, 1 H, $J_{1,2}$ 1.9 Hz, H-1), 5.70 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 10.1 Hz, H-3), 5.58 (dd, 1 H, H-4), 5.46 (dd, 1 H, H-2), 4.17 (dq, 1 H, $J_{4,5}$ 9.8 Hz, H-5), 2.22, 2.16 (2 s, 6 H, COCH_3), and 1.33 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6); ^{13}C, δ 169.8, 168.6 (2 C, *C*OCH$_3$), 165.7 (2 C, *C*OPh), 90.7 (C-1), 70.9 (C-4), 69.5 (C-3), 68.9 (2 C, C-2,5), 20.9, 20.6 (2 C, CO*C*H$_3$), and 17.5 (C-6); CIMS: *m/z* 474 [(M + NH_4)$^+$]. Anal. Calcd for $C_{24}H_{24}O_9$: C, 63.15; H, 5.30. Found: C, 63.15; H, 5.38.

*2-*O*-Acetyl-3,4-di-*O*-benzoyl-α-*L*-rhamnopyranosyl chloride* (**26**).—Zinc chloride–diethyl ether complex (200 μL of a 2.2 M solution in dichloromethane) was added to a solution of **25** (1.21 g, 2.65 mmol) and DCMME (3 mL) in dichloroethane (10 mL), and the mixture was stirred at ambient temperature for 1.5 h. Volatiles were evaporated and coevaporated with toluene. Finally, the residue was dissolved in toluene and chromatographed (solvent *B*, 7:1) to give **26** as a white solid (1.13 g, 98%), mp 99.5–100.5°C (diisopropyl ether–hexane); $[\alpha]_D$ + 4° (*c* 1.0); NMR: ^{1}H, δ 7.98–7.32 (aromatic), 6.05 (bs, 1 H, H-1), 5.94 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 10.2 Hz, H-3), 5.60 (t, partially overlapped, 1 H, H-4), 5.59 (dd, partially overlapped, 1 H, $J_{1,2}$ 1.7 Hz, H-2), 4.40 (dq, 1 H, $J_{4,5}$ 10.0, $J_{5,6}$ 6.1 Hz, H-5), 2.16 (s, 3 H, COCH_3), and 1.36 (d, 3 H, H-6); ^{13}C, δ 169.6–165.2 (3 C, *C*OCH$_3$, 2 *C*OPh), 89.1 (C-1), 72.2, 70.8 (C-2, 4), 69.7 (C-5), 68.5 (C-3), 20.8 (CO*C*H$_3$), and 17.2 (C-6); CIMS: *m/z* 450 [(M + NH_4)$^+$]. Anal. Calcd for $C_{22}H_{21}ClO_7$: C, 61.05; H, 4.89; Cl, 8.19. Found: C, 60.96; H, 4.98; Cl, 8.21.

Methyl O*-(2-*O*-acetyl-3,4-di-*O*-benzoyl-α-*L*-rhamnopyranosyl)-(1 → 2)-3,4,6-tri-*O*-benzoyl-α-*D*-galactopyranoside* (**27**).—A solution of crude **23** (from 2.92 g, 6.4 mmol of **25**), the alcohol **18** (2.49 g, 4.92 mmol) and 2,6-di-*tert*-butyl-4-methylpyridine (1.11 g, 5.41 mmol) in dichloromethane (30 mL) was added dropwise to a suspension of AgOTf (1.90 g, 7.39 mmol) in dichloromethane (20 mL) at −15°C. The suspension was stirred for 2 h at this temperature. More base was added (103 mg, 0.5 mmol) and the mixture was left stirring overnight in the cooling bath, reaching a final temperature of 15°C. Treatment proceeded as for the preparation of **19** and the residue was chromatographed (solvent *E*, 24:1) to give **27** as an amorphous solid (4.30 g, 97%), $[\alpha]_D$ + 125° (*c* 1.1); NMR: ^{1}H, δ 8.05–7.26 (aromatic), 6.04 (d, 1 H, $J_{3,4}$ 3.1 Hz, H-4), 5.71 (dd, 1 H, $J_{2,3}$ 10.4 Hz, H-3), 5.52 (dd, 1 H, $J_{2',3'}$ 3.2, $J_{3',4'}$ 10.0 Hz, H-3′), 5.49 (t, 1 H, $J_{4',5'}$ 9.8 Hz, H-4′), 5.26 (bs, 1 H, H-2′), 5.15 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1), 5.07 (s, 1 H, H-1′), 4.62 (dd, partially overlapped, 1 H, $J_{5,6a}$ 7.1, $J_{6a,6b}$ 10.2 Hz, H-6a), 4.57 (m, partially overlapped, 1 H, H-5), 4.36 (m, 2 H, $J_{5,6b}$ 4.7 Hz, H-6b, 2), 4.27 (dq, 1 H, $J_{4',5'}$ 9.7 Hz, H-5′), 3.55 (s, 3 H, OCH_3), 2.04 (s, 3 H, COCH_3), and 1.31 (d, 3 H, $J_{5',6'}$ 6.1 Hz, H-6′); ^{13}C, δ 169.6–165.1 (6 C, 5 *C*OPh, *C*OCH$_3$), 133.6–128.3 (aromatic), 99.7 (C-1′), 99.4 (C-1), 76.0 (C-2), 71.6 (C-4′), 70.1 (C-2′), 69.4, 69.3, 69.2 (C-3, 4, 3′), 67.3 (C-5′), 66.7 (C-5), 62.7 (C-6), 55.5 (O*C*H$_3$), 20.6 (CO*C*H$_3$), and 17.6 (C-6′); CIMS: *m/z* 920 [(M + NH_4)$^+$]. Anal. Calcd for $C_{50}H_{46}O_{16}$: C, 66.51; H, 5.14. Found: C, 66.28; H, 5.40.

Methyl O*-(3,4-di-*O*-benzoyl-α-*L*-rhamnopyranosyl)-(1 → 2)-3,4,6-tri-*O*-benzoyl-α-*D*-galactopyranoside* (**28**).—Tetrafluoroboric acid (3.0 mL of a 54% solution in diethyl ether) was added to a solution of compound **27** (3.16 g, 3.5 mmol) in methanol (70 mL), and the mixture was stirred at room temperature for 24 h or until TLC (solvent *D*, 9:1)

showed an optimal ratio of **28** versus **27** and extensively deacylated side-products. Solid $NaHCO_3$ was added until the solution was just neutral. Volatiles were removed by evaporation. The residue was partitioned between dichloromethane and water. The organic phase was concentrated and the residue chromatographed (solvent *D*, 9:1) to give **28** as an amorphous solid (2.27 g, 82%) together with unreacted starting material (**27**, 140 mg, 4%) and more polar, multiply deacylated byproducts (200 mg, 7%). Data for **28** are as follows: $[\alpha]_D$ + 130° (*c* 1.0); NMR: ^{1}H, δ 7.99–7.15 (aromatic), 5.95 (d, 1 H, H-4), 5.73 (dd, 1 H, $J_{3,4}$ 3.2, $J_{2,3}$ 10.5 Hz, H-3), 5.54 (dd, 1 H, $J_{2',3'}$ 2.9, $J_{3',4'}$ 9.9 Hz, H-3'), 5.48 (t, 1 H, $J_{4',5'}$ 9.8 Hz, H-4'), 5.10 (bs, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 5.07 (d, 1 H, $J_{1',2'}$ 1.4 Hz, H-1'), 4.56 (dd, partially overlapped, 1 H, $J_{5,6a}$ 7.1, $J_{6a,6b}$ 10.2 Hz, H-6a), 4.50 (m, partially overlapped, 1 H, H-5), 4.36 (dd, 2 H, $J_{5,6b}$ 3.8 Hz, H-6b,2), 4.19 (dq, 1 H,$J_{4',5'}$ 8.8 Hz, H-5'), 4.01 (bs, 1 H, H-2'), 3.50 (s, 3 H, OCH_3), 2.14 (d, 1 H, $J_{OH,2'}$ 4.0 Hz, O*H*), and 1.27 (d, 3 H, $J_{5',6'}$ 6.2 Hz, H-6'); ^{13}C, δ 166.0–165.1 (5 *C*OPh), 133.5–125.2 (aromatic), 102.0 (C-1'), 99.4 (C-1), 75.8 (C-2), 72.0 (C-3'), 71.4 (C-4'), 69.6, 69.5 (C-3,2'), 69.3 (C-4), 67.2 (C-5'), 66.7 (C-5), 62.6 (C-6), 55.5 (OCH_3), and 17.7 (C-6'); CIMS: *m/z* 878 [$(M + NH_4)^+$]. Anal. Calcd for $C_{48}H_{44}O_{15}$: C, 66.97; H, 5.15. Found: C, 67.03; H, 5.20.

Methyl O-*(3,4-di*-O-*benzoyl-2*-O-*phenoxythiocarbonyl-α*-L-*rhamnopyranosyl)-(1 → 2)-3,4,6-tri*-O-*benzoyl-α*-D-*galactopyranoside* (**29**).—Phenyl chlorothionocarbonate (210 μL, 1.5 mmol) was added to a solution of the alcohol **28** (1.0 g, 1.16 mmol) and 4-dimethylaminopyridine (368 mg, 3 mmol) in acetonitrile (30 mL). The mixture was stirred at ambient temperature for 20 h. Volatiles were evaporated and the residue was dissolved in dichloromethane. The solution was washed with water, then satd aq NaCl, dried, and evaporated to dryness. The residue was chromatographed (solvent *B*, 3:1) to give **29** as a white foam (1.12 g, 97%), $[\alpha]_D$ + 113° (*c* 1.0); NMR: ^{1}H, δ 8.05–7.21 (aromatic), 6.05 (d, 1 H, $J_{3,4}$ 3.2 Hz, H-4), 5.84 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-3), 5.80 (dd, partially overlapped, 1 H, $J_{2',3'}$ 2.9, $J_{3',4'}$ 9.9 Hz, H-3'), 5.77 (bs, 1 H, H-2'), 5.52 (t, 1 H, $J_{4',5'}$ 9.8 Hz, H-4'), 5.30 (d, 1 H, $J_{1',2'}$ 1.4 Hz, H-1'), 5.17 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.63 (dd, partially overlapped, 1 H, $J_{5,6a}$ 7.1, $J_{6a,6b}$ 10.3 Hz, H-6a), 4.58 (m, partially overlapped, 1 H, H-5), 4.38 (dd, 2 H, $J_{5,6b}$ 3.4 Hz, H-6b,2), 4.30 (dq, 1 H, $J_{4',5'}$ 9.8 Hz, H-5'), 3.58 (s, 3 H, OCH_3), and 1.34 (d, 3 H, $J_{5',6'}$ 6.1 Hz, H-6'); ^{13}C, δ 193.5 (*C*SPh), 165.4–164.9 (5 *C*OPh), 133.4–121.5 (aromatic), 99.3 (C-1'), 98.9 (C-1), 78.9 (C-2'), 76.2 (C-2), 71.6 (C-4'), 69.3, 69.1 (C-3,4,3'), 67.4 (C-5'), 66.7 (C-5), 62.6 (C-6), 55.6 (OCH_3), and 17.7 (C-6'); CIMS: *m/z* 1014 [$(M + NH_4)^+$]. Anal. Calcd for $C_{55}H_{48}O_{16}S$: C, 66.26; H, 4.85; S, 3.22. Found: C, 66.09; H, 4.91; S, 3.37.

Methyl O-*(3,4-di*-O-*benzoyl-2,6-dideoxy-α*-L-arabino-*hexopyranosyl)-(1 → 2)-3,4,6-tri*-O-*benzoyl-α*-D-*galactopyranoside* (**30**).—AIBN (64 mg, 0.39 mmol) and tributyltin hydride (880 μL, 3.30 mmol) were added to a solution of compound **29** (1.11 g, 1.11 mmol) in toluene (35 mL), and the reaction mixture was deoxygenated (N_2) for 20 min. The solution was heated at 110°C for 2 h, after which time all the starting material had disappeared and only one slightly less polar product could be seen on TLC (solvent *D*, 19:1). The solvent was evaporated, and the residue was chromatographed (solvent *E*, 32:1) to give **30** as an amorphous solid (935 mg, 99%), $[\alpha]_D$ + 109° (*c* 1.0); NMR: ^{1}H, δ 8.05–7.23 (aromatic), 6.00 (d, 1 H, $J_{3,4}$ 3.2 Hz, H-4), 5.76 (dd, 1 H, $J_{2,3}$ 10.5 Hz, H-3), 5.65 (ddd, 1 H, $J_{2'eq,3'}$ 5.4, $J_{2'ax,3'}$ 11.3, $J_{3',4'}$ 9.8 Hz, H-3'), 5.18 (t, 1 H, $J_{4',5'}$ 9.6

Hz, H-4′), 5.13 (d, 1 H, H-1), 5.11 (d, 1 H, $J_{1',2'ax}$ 3.6 Hz, H-1′), 4.61 (dd, partially overlapped, 1 H, $J_{5,6a}$ 7.1, $J_{6a,6b}$ 10.3 Hz, H-6a), 4.56 (m, partially overlapped, 1 H, H-5), 4.35 (dd, partially overlapped, 1 H, $J_{5,6b}$ 4.9 Hz, H-6b), 4.33 (dd, partially overlapped, 1 H, $J_{1,2}$ 3.5 Hz, H-2), 4.22 (dq, 1 H, $J_{4',5'}$ 9.8 Hz, H-5′), 3.56 (s, 3 H, OCH_3), 2.30 (dd, 1 H, $J_{2'eq,2'ax}$ 13.0 Hz, H-2′*eq*), 1.87 (ddd, 1 H, H-2′*ax*), and 1.27 (d, 3 H, $J_{5',6'}$ 6.3 Hz, H-6′); ^{13}C, δ 165.9–165.2 (5 *C*OPh), 133.4–128.0 (aromatic), 99.5 (2 C, C-1,1′), 75.1, 75.0 (C-2,4′), 69.8 (C-3), 69.4, 69.3 (C-4,3′), 66.6 (2 C, C-5,5′), 62.7 (C-6), 55.6 (OCH_3), 35.5 (C-2′), and 17.9 (C-6′); CIMS: m/z 862 $[(M + NH_4)^+]$. Anal. Calcd for $C_{48}H_{44}O_{14}$: C, 68.24; H, 5.25. Found: C, 68.51; H, 5.41.

Methyl O-*(2,6-dideoxy-α-*L-arabino-*hexopyranosyl)-(1 → 2)-α-*D-*galactopyranoside* (**31**).—Sodium methoxide (1.0 mL of a 0.5 M solution in methanol) was added to **30** (550 mg, 0.65 mmol) in methanol (10 mL) and the mixture was stirred at ambient temperature for 24 h. The solution was worked up as described for the preparation of **21**. After concentration, the residue was chromatographed (solvent *A*, 4:1) to give **31** as a crystalline solid (192 mg, 91%), mp 178.5–179.5°C (MeOH); $[\alpha]_D + 32°$ (*c* 0.7, MeOH); NMR (D_2O): ^1H, δ 5.07 (d, 1 H, $J_{1',2'ax}$ 3.4 Hz, H-1′), 4.88 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 3.99 (d, 1 H, $J_{3,4}$ 3.2 Hz, H-4), 3.90–3.82 (m, 3 H, H-3,5,5′), 3.79–3.67 (m, 4 H, H-2,6,5′), 3.42 (s, 3 H, OCH_3), 3.12 (t, 1 H, $J_{3',4'}$ 9.3, $J_{4',5'}$ 9.3 Hz, H-4′), 2.27 (dd, 1 H, $J_{2'eq,3'}$ 5.6, $J_{2'eq,2'ax}$ 13.2 Hz, H-2′*eq*), 1.71 (ddd, 1 H, $J_{2'ax,3'}$ 12.0 Hz, H-2′*ax*), and 1.30 (d, 3 H, $J_{5',6'}$ 6.3 Hz, H-6′); ^{13}C, δ 103.3 (C-1′), 99.9 (C-1), 78.0 (C-2), 77.5 (C-4′), 71.5 (C-3′), 70.2 (C-4), 69.6 (C-5′), 69.5 (C-3), 68.7 (C-5), 62.2 (C-6), 55.7 (OCH_3), 38.0 (C-2′), and 17.8 (C-6′); CIMS: m/z 342 $[(M + NH_4)^+]$. Anal. Calcd for $C_{13}H_{24}O_9 \cdot 0.75\ H_2O$: C, 46.21; H, 7.61. Found: C, 46.21; H, 7.78.

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