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Synthesis of α- and β-linked tyvelose epitopes of the *Trichinella spiralis* glycan: 2-Acetamido-2-deoxy-3-*O*-(3,6-dideoxy-D-*arabino*-hexopyranosyl)-β-D-galactopyranosides

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Abstract

The anomeric configuration of tyvelose, 3,6-dideoxy-D-*arabino*-hexopyranose, in the recently discovered glycan epitopes of the parasite *Trichinella spiralis* has not been established. Two 2-(trimethylsilyl)ethyl disaccharide glycosides, α- and β-Tyv-(1 → 3)-β-D-GalNAc (**4** and **5**), have been synthesized to provide model compounds that, together with the methyl 3,6-dideoxy-α- and β-D-*arabino*-hexopyranosides (**2** and **3**), aid the determination of the anomeric configuration of tyvelose residues in the parasite glycan, either indirectly by immunochemical inhibition data or directly by the technique of ^{1}H NMR spectroscopy. Methyl 3,6-dideoxy-β-D-*arabino*-hexopyranoside (**3**) was synthesized from methyl 2,3-anhydro-4,6-*O*-benzylidene-β-D-mannopyranoside (**9**) by a method previously used for the α anomer **2**. Benzylation of **2** provided a route to the glycosyl donor, 2,4-di-*O*-benzyl-3,6-dideoxy-α-D-*arabino*-hexopyranosyl chloride (**30**), that reacted with the selectively protected 2-acetamido-2-deoxy-D-galactopyranoside alcohol **18** in the presence of an insoluble silver zeolite catalyst to give the α- and β-linked disaccharides **31** and **32**. Glycosylation of the related 2-acetamido-2-deoxy-D-galactopyranoside alcohol **27** by **30** under similar conditions provided disaccharides **33** and **34** containing a tether. Deprotection of the saccharide and derivatization of the tether with 1,2-diaminoethane provided amide derivatives **35** and **36** suitable for the preparation of neoglycoconjugate antigens. Complete ^{1}H and ^{13}C NMR

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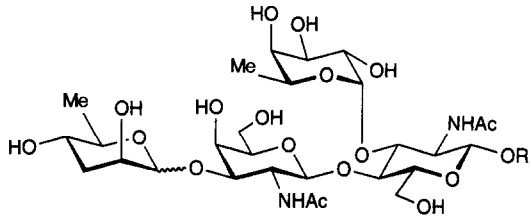
chemical shifts of the deprotected disaccharides and monosaccharides are reported. © 1996 Elsevier Science Ltd.

Keywords: Tyvelose; *Trichinella spiralis*; Glycan; Parasite; Glycosidation; Oligosaccharide

1. Introduction

Tyvelose (3,6-dideoxy-D-*arabino*-hexopyranose) is one of three 3,6-dideoxy-D-hexoses found in *Salmonella* O-antigens. Until recently these dideoxyhexoses were found only in Gram-negative bacteria, where they were shown to be immunodominant epitopes in the host response to bacterial infection [1]. Ascarylose, the L-enantiomer of tyvelose, was also found in ascaroside alcohols of *Ascaris* eggs [2]. The discovery of tyvelose as a major constituent of glycoconjugate antigens produced by the parasite *Trichinella spiralis* provides a novel and interesting example of this sugar as a terminal residue of N- and O-linked glycoprotein structures [3], where it also evokes a powerful in vivo antibody response [4]. Detailed characterization and analysis of the glycans by gas chromatography/mass spectrometry identified a terminal tetrasaccharide **1**; however, the configuration of the anomeric center of the tyvelose residue that caps the Lewis-x like structure was not determined [5]. To date 3,6-dideoxy-D-hexoses have been found exclusively as their respective α anomers in bacterial LPS; however, the much smaller quantities of parasite glycan available from the intact *Trichinella* antigen make analysis more challenging. Chemical synthesis of the antigenic determinants followed by immunochemical inhibition is one way to indirectly confirm structural features such as anomeric configuration, when direct NMR methods are precluded.



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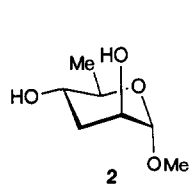
In order to aid the structural analysis of the *Trichinella* antigen by the immunochemical approach, it was desirable to obtain samples of both methyl 3,6-dideoxy-α-D-*arabino*-hexopyranoside **2** and methyl 3,6-dideoxy-β-D-*arabino*-hexopyranoside **3**. Since monoclonal antibodies to the glycan are available, hapten inhibition experiments, with monosaccharides **2** and **3** and disaccharide ligands **4** and **5**, should provide insight into the configuration of the tyvelose anomeric linkage in the native glycan. Similarly, neoglycoproteins bearing the α- and β-Tyv-(1 → 3)-β-D-GalNAc disaccharide epitopes would be valuable antigens with which to test specific *Trichinella* protective antibodies. Consequently, as a prelude to assembly of the complete tetrasaccharide epitope **1**, chemical synthesis of the known methyl glycosides **2** and **3**, the novel disaccharides **4**

and **5**, and the tether-linked analogues **6** and **7**, all suitable for neoglycoconjugate synthesis [6], was undertaken.



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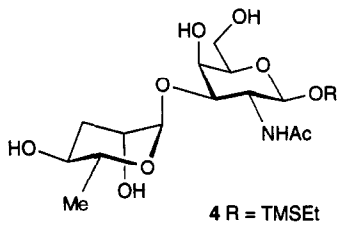
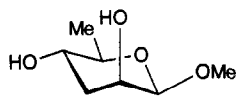


4 R = TMSEt
6 R = $(CH_2)_8CO_2Me$



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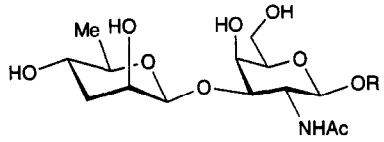
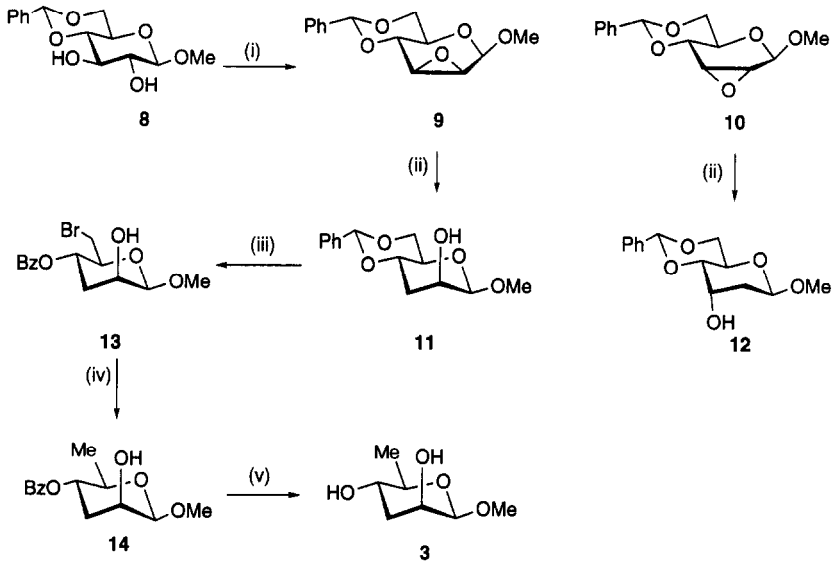


5 R = TMSEt
7 R = $(CH_2)_8CO_2Me$

2. Results

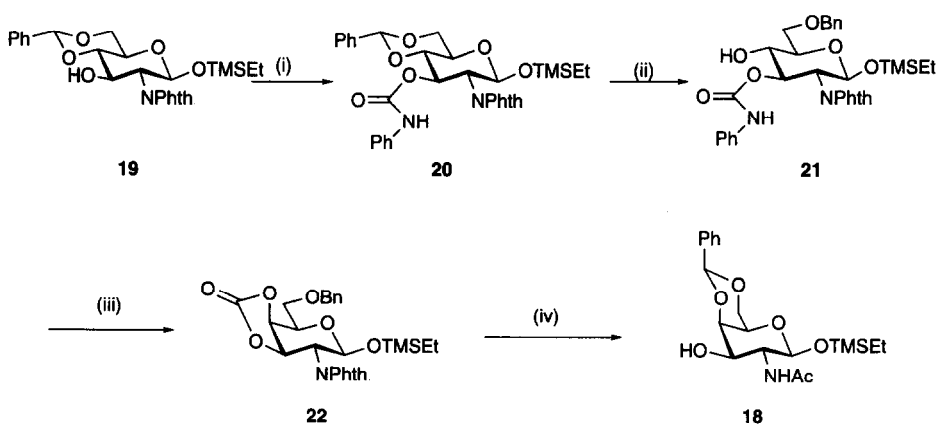
Methyl 3,6-dideoxy-α-D-*arabino*-hexopyranoside (**2**) was synthesized from methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-glucopyranoside as previously described [7,8]. The synthesis of methyl 3,6-dideoxy-β-D-*arabino*-hexopyranoside (**3**) has also been reported [9,10]. Here methyl 4,6-*O*-benzylidene-β-D-glucopyranoside [11] (**8**) was subjected to selective tosylation, followed by base-assisted displacement to form the epoxide **9** as described for the α anomer [7]; however, as reported by Stirm et al. [9], both 2,3-anhydro compounds **9** [12] and **10** [12,13] were produced (Scheme 1). Their respective configurations were confirmed by comparison with published physical constants [12,13] and by ring opening with lithium aluminum hydride to give the 3-deoxy-*arabino*-hexopyranoside **11** from **9** and 2-deoxy-*ribo*-hexopyranoside **12** from **10**. The target *arabino*-hexopyranoside **11** was reacted with *N*-bromosuccinimide [7,14] to give the 6-bromo-6-deoxy-hexopyranoside **13**. Hydrogenation over palladium-on-charcoal gave **14**, which was transesterified to give the target methyl glycoside **3**.

A low yield but convenient route to **3** was noted during the preparation of the α glycoside **2**. During workup of a transesterification reaction, it was observed that stirring a methanolic solution of **2** with Amberlite IR-120 (H^+) resin at room temperature for 2 h caused partial anomerization to **3** (6% yield). This procedure can represent a convenient, direct route to small quantities of **3** when gram amounts of **2** are being processed.



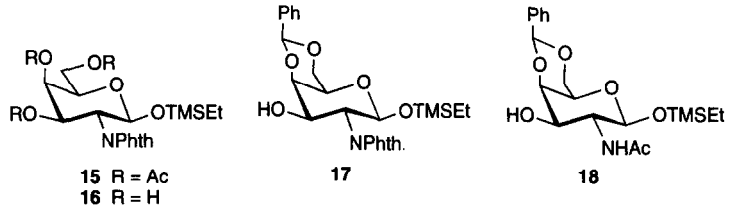
Scheme 1. *Reagents*: (*i*) NaH–DMF–*N*-tosylimidazole; (*ii*) $LiAlH_4$–Et_2O; (*iii*) NBS–CCl_4–$BaCO_3$; (*iv*) H_2–Pd/C–MeOH–Et_3N; (*v*) NaOMe–MeOH.

The synthesis of the α- and β-D-Tyv-(1 → 3)-β-D-GalNAc disaccharides was envisaged as involving 2-(trimethylsilyl)ethyl glycosides [15] **4** and **5**, as well as glycosides of the tether, methyl 9-hydroxynonanoate **6** and **7**. First, two distinct routes were employed to synthesize the glycosyl acceptor, 2-acetamido-2-deoxy-D-galactopyranoside (GalNAc) alcohol **16**. Either the protected monosaccharide glycoside **15** was prepared directly from galactosamine hydrochloride and then transformed **15** → **18**, or a method from



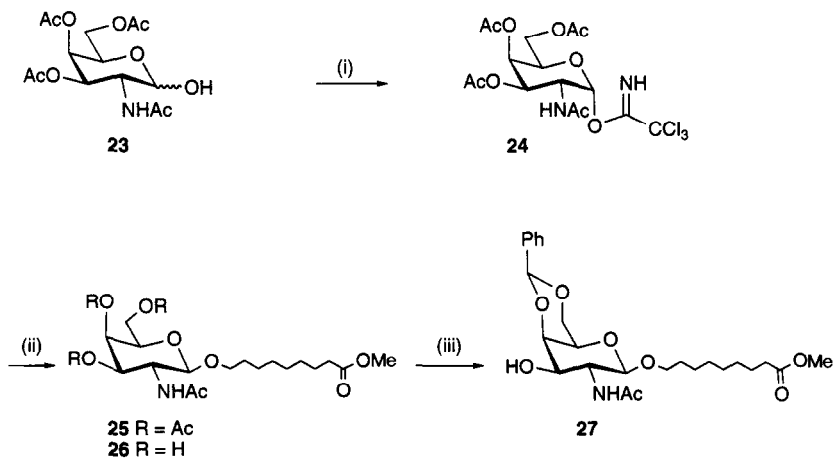
Scheme 2. *Reagents*: (*i*) PhCNO–DMAP; (*ii*) $NaCNBH_3$–HCl–Et_2O; (*iii*) DAST; (*iv*) (a) NaOMe–MeOH, (b) BuOH–$H_2NCH_2CH_2NH_2$, (c) pyridine–acetic anhydride, (d) NaOMe–MeOH, (e) H_2–Pd/C–AcOH, (f) $PhC(OMe)_2$–H^+.

Kunz and Günther [16], as adapted by Ogawa et al. [17] (Scheme 2), was used to transform glucosamine hydrochloride via an inversion at C-4.



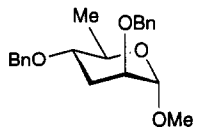
Zemplén deacetylation of the known triacetate **15** [15] gave the trihydroxy compound **16**, and this was converted to the benzylidene acetal **17** with α,α-dimethoxytoluene and *p*-toluenesulfonic acid. Removal of the phthaloyl protecting group was achieved with ethylenediamine in butanol [18], and the free amine produced was acetylated with acetic anhydride–pyridine. Zemplén deacetylation then gave the required aglycone **18**. The alternate route began with the glucosamine benzylidene acetal derivative **19**. Treatment with phenyl isocyanate gave carbamate **20**. Reductive ring opening of the benzylidene acetal with sodium cyanoborohydride led to **21**, which was then treated [16,17] with DAST to form the cyclic carbonate **22** with concomitant inversion of configuration at C-4. Protecting group manipulation of **22** gave aglycone **18** in 48% yield.

The analogous 2-acetamido-2-deoxy-D-galactopyranoside **27** bearing the nine-carbon tether [6] was synthesized from galactosamine hydrochloride via triacetate **23** [19] and the imidate **24**. Reaction of methyl 9-hydroxynonanoate with the imidate gave the acetylated glycoside **25** and subsequently the triol **26** after transesterification in methanol. Treatment of **26** with benzaldehyde and formic acid gave the benzylidene acetal **27** (Scheme 3).



Scheme 3. *Reagents*: (*i*) Cl_3CCN–CH_2Cl_2–NaH; (*ii*) $HO(CH_2)_8CO_2CH_3$–4 Å MS–TMSOTf–CH_2Cl_2; (*iii*) $NaOCH_3$–CH_3OH; $PhCHO$–HCO_2H.

In order to maximize the yield of disaccharide **5** with the β-D-*arabino* configuration, a glycosyl donor **30** possessing a nonparticipating C-2 benzyloxy group was selected. Glycosyl donor **30** was prepared from methyl 3,6-dideoxy-α-D-*arabino*-hexopyranoside (**2**) [7]. Benzylation with sodium hydride and benzyl bromide gave the dibenzyl derivative **28,** and acid hydrolysis [20] afforded the reducing sugar **29**. This was subsequently converted to the glycosyl chloride **30** using oxalyl chloride and DMF [7,20]. Since **30** was relatively unstable, it was prepared from **29** immediately prior to use in glycosylation reactions and was not characterized.



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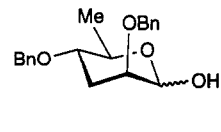

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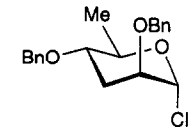

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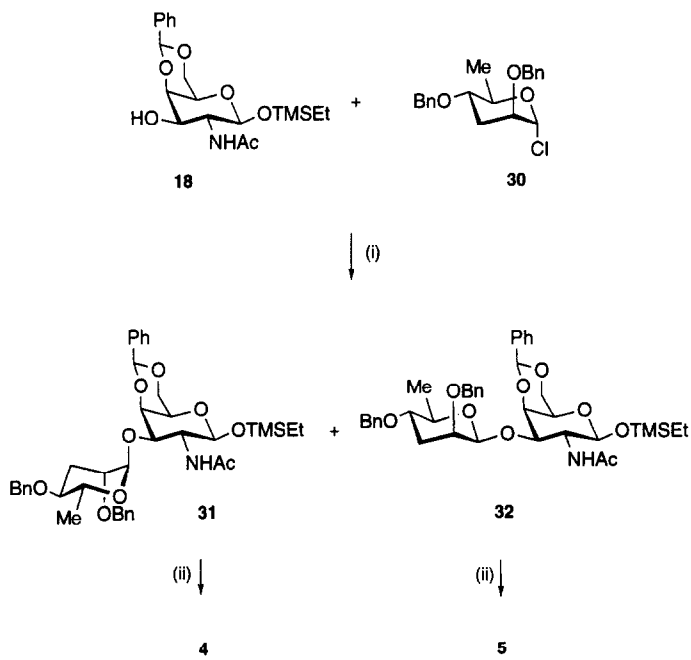
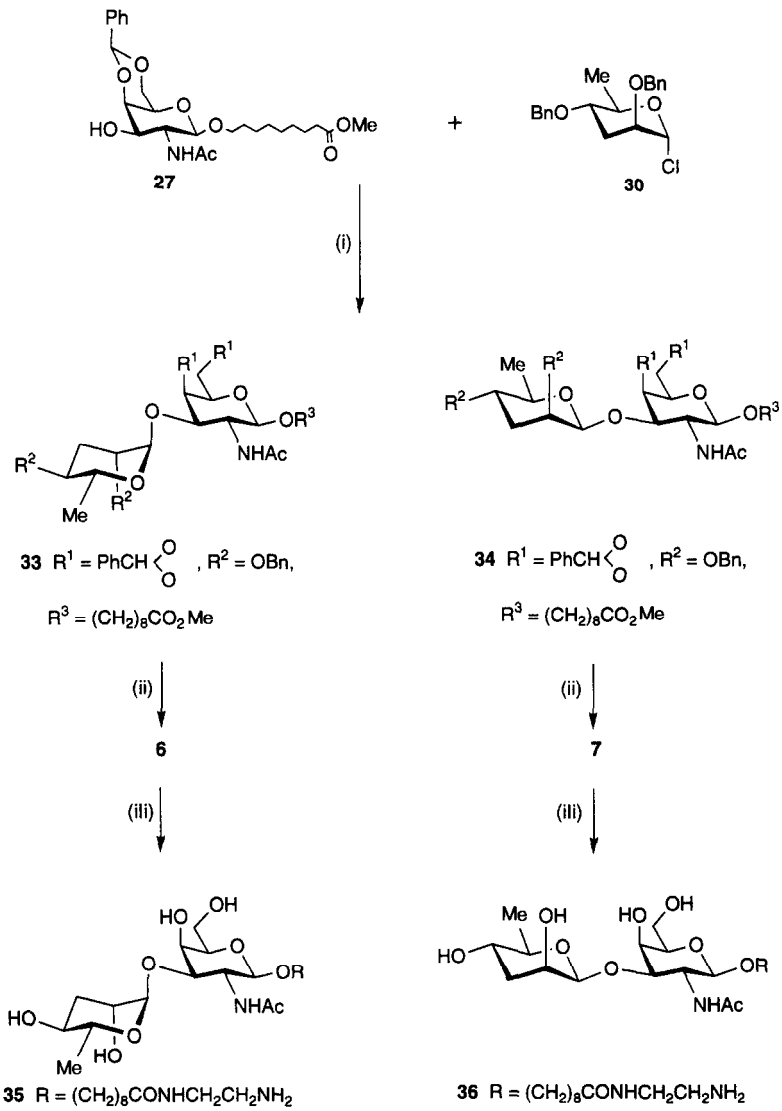
This reactive dideoxyglycosyl donor was used with an insoluble silver catalyst of the type suggested by Paulsen and Lockhoff, silver silicate on alumina [21], or the modification introduced by Garegg and Ossowski, silver zeolite [22], to maximize the yield of 1,2-*cis*-glycoside.

Glycosylation of the selectively protected alcohol **18** with the glycosyl donor **30** in dichloromethane using silver zeolite [22] as catalyst, initiation of the reaction at −78 °C,



Scheme 4. *Reagents and conditions*: (*i*) Silver zeolite–CH_2Cl_2, −78 → 20 °C, H_2–Pd–HOAc.



Scheme 5. *Reagents and conditions*: (*i*) Silver zeolite–CH_2Cl_2, $-78 \rightarrow 20$ °C, H_2–Pd–HOAc.

and subsequent overnight warming to room temperature (Scheme 4) gave the α and β disaccharides **31** and **32**, in yields of 20% and 14%. The related tether-linked disaccharides **33** and **34** were obtained in higher yields of 49% and 24% by reaction of **30** with **27** under similar conditions (Scheme 5). The analogous glycosylation procedure using silver silicate on alumina [21] gave no glycosylation products. A single hydrogenation step in acetic acid with 10% palladium-on-charcoal afforded the target disaccharide glycosides **4** and **5** in high yield from **31** and **32**. The nine-carbon tether glycosides **33** and **34** were deprotected in a similar fashion to give **6** and **7**, and finally the methyl ester

Table 1
^{1}H Chemical shifts [a] for D_2O solutions of compounds **2–5** recorded at 500 MHz

Hexose	Me α-D-Tyv	Me β-D-Tyv	TMSEt α-D-Tyv-(1 → 3)-β-D-GalNAc	TMSEt β-D-Tyv-(1 → 3)-β-D-GalNAc
	2	**3**	**4**	**5**
Tyv				
H-1	4.54	4.55	4.77	4.68
H-2	3.92	3.98	3.97	3.89
H-3	2.04, 1.76	2.17, 1.68	2.03, 1.74	2.17, 1.65
H-4	3.60	3.57	3.60	3.55
H-5	3.66	3.48	3.59	3.44
H-6	1.27	1.29	1.26	1.27
GalNAc				
H-1			4.59	4.53
H-2			3.95	3.99
H-3			3.81	3.85
H-4			4.15	4.11
H-5			3.65	3.68
H-6a			3.82	3.76
H-6b			3.77	4.06

[a] First-order chemical shifts for 10-mM solutions in D_2O are referenced to 0.1% acetone.

moieties of the tether were converted to amides **35** and **36** by reaction with 1,2-diaminoethane. The amides have been converted to neoglycoconjugates [39], by application of the diethyl squarate coupling method [23].

The anomeric configuration of the two glycosides **2** and **3** was confirmed by the ^{1}H NMR chemical shifts of the H-1, H-3, and H-5 resonances (Table 1), as well as by ^{13}C NMR assignments via two-dimensional HMQC experiments [24]. The heteronuclear C-1–H-1 one-bond coupling constants [25] (methyl glycoside **2** $^1J_{H\text{-}1,C\text{-}1} = 166.8$ Hz; **3** $^1J_{H\text{-}1,C\text{-}1} = 156.9$ Hz) (Table 2) unambiguously confirmed the assignments determined by ^{1}H NMR experiments.

The anomeric configuration of the tyvelose linkage in each deprotected disaccharide was assigned on the basis of the H-5′ proton chemical shifts (Table 1) and confirmed by the anomeric C–H coupling constants [25] $^1J_{H\text{-}1',C\text{-}1'}$ (Table 2) obtained from gradient HMQC experiments (**4** $^1J_{H\text{-}1',C\text{-}1'} = 169.1$ Hz; **5** $^1J_{H\text{-}1',C\text{-}1'} = 159.1$ Hz). The proton chemical shifts for the monosaccharide glycosides and disaccharide glycosides in D_2O are unexceptional. The chemical shift of the anomeric proton of the dideoxyhexose residue varies over a 0.2 ppm range for both α and β glycosides **2–5**, and, therefore, chemical shifts are not diagnostic of anomeric configuration. However, the chemical shift of the dideoxyhexose H-5 resonance in β glycosides **3** and **5** showed the expected deshielding [26] of ~0.15 ppm. The ^{13}C NMR chemical shifts (Table 2) of the dideoxyhexose anomeric carbon atom in the disaccharides **4** and **5** are seen to be diagnostic of anomeric configuration and exhibit typical glycosylation shifts, with the most pronounced effect for C-1 of the α anomer [27,28]. In agreement with published data, glycosylation shifts at C-2, C-3, and C-4 may be seen to correlate with the stereochemistry of substituents around the glycosidic linkage [27,28]. Thus the glyco-

Table 2
^{13}C Chemical shifts [a] for D_2O solutions of compounds **2–5** recorded at 125 MHz

Hexose	Me α-D-Tyv	Me β-D-Tyv	TMSEt α-D-Tyv-(1 → 3)-β-D-GalNAc	TMSET β-D-Tyv-(1 → 3)-β-D-GalNAc
	2	**3**	**4**	**5**
Tyv				
C-1	100.3 (170.0 Hz) [b]	102.8 (160.0 Hz) [b]	95.7 (169.1 Hz) [b]	103.3 (159.1 Hz) [b]
C-2	68.0	67.7	68.3	68.2
C-3	34.2	37.1	33.9	36.9
C-4	67.6	67.8	67.3	67.5
C-5	70.3	76.7	71.0	76.8
C-6	17.4	17.7	17.5	17.8
GalNAc				
C-1			101.2 (161.7 Hz)	101.2 (161.2 Hz)
C-2			51.5	52.0
C-3			75.9	80.2
C-4			64.5	68.7
C-5			75.6	75.4
C-6			61.7	61.7

[a] Chemical shifts for 10-mM solutions in D_2O were determined from ^1H-detected HMQC experiments with an accuracy of ±0.15 ppm.
[b] Heteronuclear one-bond coupling constants were measured directly from HMQC spectra with an accuracy of ±0.4 Hz.

sylation shift ~ 8 ppm at C-3 is largest for the β-linked disaccharide, while the α-linked disaccharide exhibits a large upfield shift ~ 4 ppm at C-4 [28]. These chemical shift characteristics also correlate with preferred conformations about the glycosidic linkage [27,28]. As expected, the disaccharides **6** and **7** exhibited ^1H and ^{13}C NMR chemical shifts very close to those seen for **4** and **5**.

3. Discussion

The detection of rare and unusual sugar components in N- and O-linked glycans by the analytical methods currently employed [29–31] poses difficulties for their structural analysis. Generally *exo* or *endo* glycosidases are unavailable to characterize the anomeric configuration of rare monosaccharides, and the minute quantities of available antigen often preclude the use of NMR spectroscopy as an analytical tool [32]. The determination of anomeric configuration by one-dimensional ^1H NMR methods is particularly difficult for hexoses with the *manno* configuration (for tyvelose the *arabino* configuration). The magnitude of the three-bond coupling constant $^3J_{1,2}$ is notoriously inconclusive, and the chemical shift of H-1 is also unreliable, unless both anomers are available [26]. Deshielding of the H-3 and H-5 resonances in the case of the α anomer is a more reliable assignment tool [26], if these resonances can be identified. Assignment of anomeric configuration via the C-1, H-1 heteronuclear coupling constant is unambiguous [25], but time and material requirements are demanding, even for the proton-de-

tected HMQC experiment [24]. Chemical techniques to determine anomeric configuration such as chromium trioxide oxidation do not solve the problem reliably, especially for 3,6-dideoxyhexoses. Glycosidic linkages with the equatorial orientation (generally β anomers) are oxidized to 5-hexulosonates, and this technique has been proposed as an analytical tool [33]; however, the same paper showed only a very small difference in the rates of oxidation for the α and β anomers of methyl 3,6-dideoxy-D-*xylo*-hexopyranoside.

The glycosides described here have been used in immunochemical assays to infer the anomeric configuration of tyvelose in the *Trichinella spiralis* antigen. Initial immunochemical inhibition data suggests that the β-tyvelose epitopes are more active than the corresponding α glycosides. Confirmation of these conclusions with neoglycoconjugates prepared from **35** and **36** will be reported elsewhere, and, if validated, the *Trichinella* antigens would be the first instance of a naturally occurring β-linked 3,6-dideoxyhexoside.

4. Experimental

General methods.—Melting points were determined on glass plates using a Fisher–Johns melting point apparatus and are uncorrected. Optical rotations were measured at room temperature using a Perkin–Elmer model 241 polarimeter. High-resolution HRFABMS and FABMS were run in a Cleland matrix (dithioerythritol–dithiothreitol). TLC was performed on Silica Gel 60 F_{254} (E. Merck) precoated glass plates and visualized by charring with H_2SO_4 and flash chromatography (FC) used Silica Gel 60 (230–400 mesh ASTM) (Merck). Anhydrous dichloromethane was obtained from refluxing with calcium hydride, and pyridine was dried over potassium hydroxide and distilled from calcium hydride. MeOH and EtOH were dried with magnesium [34]. DMF was distilled under vacuum and stored over activated 4 Å molecular sieves. Dry ether was from Aldrich (Milwaukee, WI).

NMR measurements.—All spectra whose data are reported in Tables 1 and 2 were recorded on a Varian Unity 500 spectrometer operating at 500 and 125.7 MHz, respectively, while the ^1H data of synthetic intermediates were acquired on a Bruker AM 360 console. Samples were 6–8 mM and 30–34 mM in concentration for ^1H and ^{13}C, respectively. All data in Tables 1 and 2 were recorded under temperature-controlled conditions at 30.0 ± 0.1 °C. Chemical shifts for $CDCl_3$ solutions were referenced to residual $CHCl_3$ at 7.24 ppm and relative to 0.1% external acetone at 2.225 ppm for solutions in D_2O. Reported coupling constants are first order. Carbon-13 chemical shifts in $CDCl_3$ were referenced to the solvent resonance, δ_C 77.0 ppm, and for solutions in D_2O relative to 1.0% acetone, δ_C 31.07 ppm. All two-dimensional spectra were recorded at 500 MHz as $4K \times 512$ (zero-filled to $4K \times 1K$) data sets, the homonuclear correlations with the aid of gradients (GCOSY, 3 scans per t_1 increment) [35] while the HMQCs were acquired proton-coupled, 8 scans per t_1-increment, without gradients but with a BIRD sequence (delay 0.5 s) and delays based on a 150 Hz coupling constant [24]. Spectral widths were 2500 Hz in F2 and F1 (homonuclear) and 2500 Hz/12 kHz in the HMQC experiments.

Preparation of methyl 2,3-anhydro-4,6-O-benzylidene-β-D-mannopyranoside (**9**) and *methyl 2,3-anhydro-4,6-O-benzylidene-β-D-allopyranoside* (**10**).—A solution of methyl 4,6-*O*-benzylidene-β-D-glucopyranoside [20] (**6**) (6.4 g, 22.7 mmol) in dry DMF (150 mL) was treated with sodium hydride (80%, 1.53 g, 51 mmol) and stirred at room temperature for 30 min. *N*-Tosyl imidazole (6.05 g, 27.3 mmol) was then added, and the solution was stirred for a further hour before being poured into water with stirring. The aqueous mixture was then extracted with CH_2Cl_2 (1 × 1500 mL), and the organic phase was in turn washed with water and dried (Na_2SO_4). Concentration in vacuo gave a yellow solid purified by FC (10:1 pentane–EtOAc) to give two white solids R_f 0.10 (1.40 g, 23.3%) and 0.20 (1.47 g, 24.5%), identified as **9** and **10**, respectively.

Data for the *manno* epoxide **9**: mp 183–186 °C, lit. 182 °C [12]; $[\alpha]_D$ −31.2° (*c* 0.78, $CHCl_3$), lit. −31.4° [12]; ^{1}H NMR (360 MHz, $CDCl_3$): δ 3.25 (d, 1 H, *J* 3.7 Hz, H-2 or 3), 3.33 (dt, 1 H, $J_{4,5} = J_{5,6a} = 9.6$, $J_{5,6b}$ 4.7 Hz, H-5), 3.49 (d, 1 H, *J* 3.7 Hz, H-2 or 3), 3.59 (s, 3 H, CH_3O), 3.74 (d, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 3.79 (m, 1 H, H-6ax), 4.27 (dd, 1 H, $^2J_{6eq,6ax}$ 10.4, $J_{5,6eq}$ 4.6 Hz, H-6eq), 4.94 (s, 1 H, H-1), 5.55 (s, 1 H, PhCHO$_2$), 7.32–7.50 (m, 5 H, Ph).

Data for the *allo* epoxide **10**: mp 132–136 °C, lit 138 °C [12,13]; $[\alpha]_D$ −15.9° (*c* 0.8, $CHCl_3$), lit. −15.6° [12,13]; ^{1}H NMR (360 MHz, $CDCl_3$): δ 3.33, 3.52 (2 × m, 2 H, H-2,3), 3.52 (s, 3 H, CH_3O), 3.63 (m, 2 H, H-4,5), 4.08 (m, 1 H, H-6ax), 4.24 (m, 1 H, H-6eq), 4.89 (s, 1 H, H-1), 5.56 (s, 1 H, PhCHO$_2$), 7.32–7.52 (m, 5 H, Ph).

Preparation of methyl 3-deoxy-4,6-O-benzylidene-β-D-arabino-hexopyranoside (**11**). —A solution of **9** (500 mg, 1.89 mmol) in dry ether (25 mL) was refluxed with lithium aluminum hydride (250 mg, 6.59 mmol) for 6 h and then cooled to room temperature, and solid sodium sulfate decahydrate was added slowly down the condenser. The mixture was filtered, and the filter cake was extracted twice with warm ether. The combined organic fractions were then concentrated in vacuo to give a colorless syrup that was purified by FC (5:1 toluene–EtOAc 5:1), R_f 0.21, to give a white amorphous solid (405 mg, 81%): mp 168–172 °C, lit. 172–174 °C [9]; $[\alpha]_D$ −66.2° (*c* 0.48, $CHCl_3$), lit. −75° [9]; ^{1}H NMR (360 Hz, $CDCl_3$): δ 1.77 (m, 1 H, H-3ax), 2.38 (m, 1 H, H-3eq), 3.44 (m, 1 H, H-5), 3.56 (s, 3 H, CH_3O), 3.82 (t, 1 H, $^2J_{6ax,6eq} \approx J_{5,6ax} \approx 10.4$ Hz, H-6ax), 3.99 (m, 2 H, H-2,4), 4.29 (dd, 1 H, $J_{6eq,6ax}$ 10.5, $J_{5,6eq}$ 5.0 Hz, H-6eq), 4.49 (s, 1 H, H-1), 5.55 (s, 1 H, PhCHO$_2$), 7.27–7.49 (m, 5 H, Ph). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.13; H, 6.83. Found: C, 63.10; H, 6.81.

Preparation of methyl 4,6-O-benzylidene-2-deoxy-β-D-ribo-hexopyranoside (**12**).—A solution of **10** (168 mg, 0.64 mmol) in dry ether (10 mL) was refluxed with lithium aluminum hydride (85 mg, 2.24 mmol) for 6 h and then cooled to room temperature, and solid sodium sulfate decahydrate was added slowly down the condenser. The mixture was filtered, and the filter cake extracted twice with warm ether. The combined organic fractions were then concentrated in vacuo to give a colorless syrup that was purified by FC (5:1 toluene–EtOAc), R_f 0.24, to give a colorless syrup (152 mg, 89%). This crystallized on standing at 0 °C for 1 week; mp 87–91 °C, lit. 96–97 °C [36]; $[\alpha]_D$ −29.4° (*c* 1.03, $CHCl_3$), lit. −34° [36]; ^{1}H NMR (360 MHz, $CDCl_3$): δ 1.75 (ddd, 1 H, $^2J_{2ax,2eq}$ 14.2, $J_{1,2ax}$ 9.7, $J_{2ax,3}$ 3.0 Hz, H-2ax), 2.17 (ddd, 1 H, $^2J_{2eq,2ax}$ 14.2, $J_{2ex,3}$ 3.12 Hz, H-2eq), 3.50 (s, 3 H, CH_3O), 3.61 (dd, 1 H, $J_{4,5}$ 9.5, $J_{3,4}$ 2.7 Hz, H-4), 3.78 (t, 1 H, $^2J_{6ax,6eq} = J_{5,6ax} = 10.3$ Hz, H-6ax), 4.00 (dt, 1 H, $J_{5,6ax} = J_{4,5} = 10.0$, $J_{5,6eq}$ 5.0

Hz, H-5), 4.27 (q, 1 H, H-3), 4.35 (dd, 1 H, $^2J_{6eq,6ax}$ 10.3, $J_{6eq,5}$ 5.0 Hz, H-6eq), 4.85 (dd, 1 H, $J_{1,2ax}$ 9.7, $J_{1,2eq}$ 2.3 Hz, H-1), 7.32–7.49 (m, 5 H, Ph).

*Preparation of methyl 4-O-benzoyl-6-bromo-3,6-dideoxy-β-*D-arabino-*hexopyranoside* (**13**).—A solution of **11** (100 mg, 0.376 mmol) in dry carbon tetrachloride (10 mL) was heated to reflux with NBS (74 mg, 0.416 mmol) and barium carbonate (297 mg, 1.505 mmol) until the color of the solution changed to orange and back to colorless. The suspension was filtered, the filtercake washed with CH_2Cl_2, the combined filtrates were washed with sodium bicarbonate solution, dried (Na_2SO_4) and evaporated in vacuo to give a yellow syrup. This was purified by FC (5:1 toluene–EtOAc), R_f 0.27, to give a colorless syrup (110 mg, 85%); $[\alpha]_D$ −15.6° (*c* 0.66, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$): δ 1.86 (dddd, 1 H, $^2J_{3ax,3eq}$ 13.7, $J_{3ax,4}$ 9.1, $J_{3ax,2}$ 3.5, $J_{3ax,OH}$ 1.1 Hz, H-3ax), 2.22 (dd, 1 H, $J_{OH,2}$ 4.7, $J_{OH,3ax}$ 1.1 Hz, 2-O*H*), 2.40 (ddd, 1 H, $^2J_{3eq,3ax}$ 13.7, $J_{2,3eq}$ 5.7, $J_{3eq,4}$ 4.5 Hz, H-3eq), 3.52 (dd, 1 H, $^2J_{6a,6b}$ 10.9, $J_{5,6a}$ 7.6 Hz, H-6a), 3.59 (s, 4 H, dd, $^2J_{6b,6a}$ 10.9, $J_{5,6b}$ 4.4 Hz, CH_3O, H-6b), 3.90 (dt, 1 H, $J_{4,5} = J_{5,6a} = 7.5$, $J_{5,6b}$ 4.4 Hz, H-5), 3.99 (m, 1 H, H-2), 4.58 (d, 1 H, $J_{1,2}$ 1.9 Hz, H-1), 5.33 (ddd, 1 H, $J_{4,5}$ 7.4 Hz, H-4), 7.41–8.05 (m, 5 H, Ph). Anal. Calcd for $C_{14}H_{17}BrO_5$: C, 48.70; H, 4.96. Found: C, 48.49; H, 4.65.

*Preparation of methyl 4-O-benzoyl-3,6-dideoxy-β-*D-arabino-*hexopyranoside* (**14**).—A solution of **13** (102 mg, 0.296 mmol) in MeOH (10 mL) and Et_3N (0.2 mL) with palladium-on-charcoal (10%, 30 mg) was hydrogenated until complete by TLC (3:1 toluene–EtOAc). The solution was then filtered through Celite, and the catalyst was washed with MeOH. The combined filtrates were then concentrated in vacuo to give a syrup that was immediately purified by FC (3:1 toluene–EtOAc), R_f 0.24, to give a colorless syrup (73 mg, 93%): $[\alpha]_D$ −38.5° (*c* 1.12, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$): δ 1.33 (d, 3 H, $J_{6,5}$ 6.4 Hz, H-6), 1.76 (ddd, 1 H, $^2J_{3ax,3eq}$ 13.4, $J_{3ax,4}$ 9.8, $J_{2,3ax}$ 3.3 Hz, H-3ax), 2.25 (d, 1 H, *J* 3.2 Hz, 2-O*H*), 2.45 (dt, 1 H, $J_{2,3eq} = J_{3eq,4} = 4.7$ Hz, H-3eq), 3.55 (s, 3 H, CH_3O), 3.74 (dq, 1 H, $J_{4,5}$ 8.0, $J_{5,6}$ 6.4 Hz, H-5), 3.96 (m, 1 H, H-2), 4.51 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1), 5.11 (ddd, 1 H, H-4), 7.40–8.00 (m, 5 H, Ph). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.13; H, 6.95. Found: C, 63.27; H, 6.95.

*Preparation of methyl 3,6-dideoxy β-*D-arabino-*hexopyranoside* (**3**).—A solution of **14** (70 mg, 0.26 mmol) in MeOH (10 mL) with NaOMe (cat.) was stirred at room temperature overnight and was then neutralized by the addition of Amberlite IR-120 (H^+) resin. After 5 min the resin was removed by filtration and washed with MeOH. The combined filtrate was then concentrated in vacuo to give a pale yellow syrup that was purified by FC (85:10:5 EtOAc–MeOH–water). The white amorphous solid (37 mg, 88%) had R_f 0.34, (250:10:5, EtOAc–MeOH–water): mp 93–95 °C; $[\alpha]_D$ −82.0° (*c* 0.2, $CHCl_3$), lit. −72° (MeOH) [9]; ^{1}H NMR (360 MHz, $CDCl_3$): δ 1.34 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6), 1.54 (ddd, 1 H, $^2J_{3ax,3eq}$ 13.8, $J_{2,3ax}$ 3.0, $J_{3ax,4}$ 10.9 Hz, H-3ax), 2.28 (dt, 1 H, $J_{2,3eq} \approx J_{3eq,4} \approx 4.0$ Hz, H-3eq), 3.32 (dq, 1 H, $J_{4,5}$ 8.8 Hz, H-5), 3.52 (s, 3 H, CH_3O), 3.67 (m, 1 H, H-4), 3.89 (m, 1 H, H-2), 4.37 (d, 1 H, $J_{1,2}$ 1.2 Hz, H-1). Anal. Calcd for $C_7H_{14}O_4$: C, 51.83; H, 8.72. Found: C, 51.88; H, 8.85.

*Preparation of methyl 3,6-dideoxy-α-*D-arabino-*hexopyranoside* (**2**) and *methyl 3,6-dideoxy-β-*D-arabino-*hexopyranoside* (**3**).—A solution of methyl 4-*O*-benzoyl-3,6-dideoxy-α-D-*arabino*-hexopyranoside [15] (2.0 g, 7.52 mmol) in MeOH (50 mL) was stirred at room temperature with NaOMe (cat.) overnight before neutralizing by stirring with

Amberlite IR-120 (H^+) resin for 2 h. The mixture was filtered, and the resin was washed with MeOH, and the combined filtrates concentrated in vacuo to give a syrup. This was purified by FC (85:10:5 EtOAc–MeOH–water) to give colorless syrups, identified as methyl 3,6-dideoxy-α-D-*arabino*-hexopyranoside (**2**) (1.035 g, 85%) and methyl 3,6-dideoxy-β-D-*arabino*-hexopyranoside (**3**) (77 mg, 6.3%). Data for (**2**); ^{1}H NMR (360 MHz, $CDCl_3$): δ 1.29 (d, 3 H, $J_{5,6}$ 5.8 Hz, H-6), 1.79 (ddd, 1 H, $^2J_{3ax,3eq}$ 13.1, $J_{3ax,4}$ 10.9, $J_{2,3ax}$ 3.0 Hz, H-3ax), 2.06 (dt, 1 H, $J_{3eq,4} = J_{2,3eq} = 3.5$ Hz, H-3eq), 3.37 (s, 3 H, CH_3O), 3.57 (m, 2 H, H-4,5), 3.85 (m, 1 H, H-2), 4.46 (s, 1 H, H-1).

*Preparation of methyl 2,4-di-*O*-benzyl-3,6-dideoxy-α-*d-arabino-*hexopyranoside* (**28**). —A suspension of sodium hydride (80%, 438 mg, 14.6 mmol) in dry DMF (30 mL) was stirred with **2** [7] (947 mg, 5.84 mmol) at room temperature for 1 h, and benzyl bromide (1.75 mL, 14.7 mmol) was subsequently added at 0 °C. The solution was allowed to warm to room temperature and was stirred for a further 3 h, at the end of which time it was poured into water and extracted into CH_2Cl_2. The organic layer was washed with sodium bicarbonate, dried (Na_2SO_4) and evaporated in vacuo to give a syrup purified by FC (10:1 pentane–EtOAc): R_f 0.44, to give an oil (1.16 g, 58%); ^{1}H NMR (360 MHz, $CDCl_3$): δ 1.30 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6), 1.70 (ddd, 1 H, $^2J_{3ax,3eq}$ 13.6, $J_{3ax,4}$ 11.0, $J_{2,3ax}$ 3.1 Hz, H-3ax), 2.20 (m, 1 H, H-3eq), 2.25 (s, 3 H, CH_3O), 3.43 (ddd, 1 H, $J_{3eq,4} = J_{4,5} = 9.4$, 4.4 Hz, H-4), 3.57 (m, 1 H, H-2), 3.70 (dq, 1 H, $J_{5,6}$ 6.2 Hz, H-5), 4.43–4.58 (m, 5 H, $PhCH_2$, H-1), 7.22–7.37 (m, 10 H, Ph).

*Preparation of 2,4-di-*O*-benzyl-3,6-dideoxy-*D-arabino-*hexopyranoside* (**29**).—A solution of **28** (1.16 g, 3.39 mmol) in 80% aq CH_3COOH (32 mL) and M hydrochloric acid (8 mL) was warmed to 85 °C and stirred for 2 h. The mixture was then concentrated in vacuo and coevaporated with toluene twice to give a yellow syrup that was purified by flash chromatography (3:1 pentane–EtOAc), giving a colorless syrup (0.98 g, 88%): R_f (2:1 pentane–EtOAc), 0.50. Pyranose **29** was converted to glycosyl chloride **30** immediately prior to use (see compounds **31** and **32**).

Data for α anomer: ^{1}H NMR (360 MHz, $CDCl_3$): δ 1.28 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6), 1.79 (ddd, 1 H, $^2J_{3ax,3eq}$ 13.7, $J_{2,3ax} = J_{3ax,4} = 10.9$, 3.1 Hz, H-3ax), 2.20 (dt, 1 H, $J_{2,3eq} = J_{3eq,4} = 3.6$ Hz, H-3eq), 3.46 (m, 1 H, H-4), 3.61 (m, 1 H, H-2), 3.95 (1 H, $J_{4,5}$ 9.1 Hz, H-5), 4.50 (m, 4 H, $PhCH_2$), 7.22–7.39 (m, 10 H, Ph).

Data for β anomer: ^{1}H NMR (360 MHz, $CDCl_3$): δ 1.33 (d, 3 H, $J_{6,5}$ 6.1 Hz, H-6), 1.41 (ddd, 1 H, $^2J_{3ax,3eq}$ 13.9, $J_{2,3ax} = J_{3ax,4} = 11.0$, 2.7 Hz, H-3ax), 2.40 (ddd, 1 H, $J_{2,3e}$ 3.6 Hz, H-3eq), 3.33 (ddd, 1 H, $J_{4,5}$ 9.1, $J_{3eq,4}$ 4.3 Hz, H-4), 3.46 (m, 2 H, H-2,5), 4.50 (m, 4 H, $PhCH_2$), 7.22–7.39 (m, 10 H, Ph). Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.13; H, 7.38. Found: C,72.98; H, 7.55.

*Preparation of 2-(trimethylsilyl)ethyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-*D-*galactopyranoside* (**17**).—A solution of **15** [15] (609 mg, 1.14 mmol) in MeOH (7.3 mL) was stirred with NaOMe (cat.) at room temperature for 4 h and was then neutralized by the addition of Amberlite IR-120 (H^+) resin. The resin was filtered off, and the solution was concentrated in vacuo to give a white solid **16** (454 mg, 99%). The solid was dissolved in dry acetonitrile (7.7 mL), and α,α-dimethoxytoluene (0.34 mL, 2.27 mmol) and *p*-toluenesulfonic acid (16 mg, 0.68 mmol) were added. The mixture was stirred at room temperature with monitoring by TLC (3:2 pentane–EtOAc). After 15 min Et_3N (0.15 mL) was added, and the solution was concentrated in vacuo to give **17**,

which was purified by FC (3:1 pentane–EtOAc). The appropriate fractions were evaporated to a syrup (R_f 361 mg, 65%): $[\alpha]_D$ +18.8° (*c* 1.0, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$): δ −0.15 [s, 9 H, $(CH_3)_3Si$], 0.68, −0.90 (m, 2 H, OCH_2CH_2TMS), 2.49 (d, 1 H, J_{3OH} 11.2 Hz, OH-3), 3.50 (dt, 1 H, *J* 9.8, 6.8 Hz, OCH_2CH_2TMS), 3.64 (m, 1 H, H-5), 3.99 (ddd, 1 H, ^2J 9.6, ^3J 10.6, 5.2 Hz, OCH_2CH_2TMS), 4.13 (dd, 1 H, $^2J_{6a,6b}$ 12.5, $J_{5,6a}$ 1.8 Hz, H-6a), 4.27 (dd, 1 H, *J* 3.6, $J_{4,5}$ 1.0 Hz, H-4), 4.35–4.53 (m, 3 H, H-2,3,6b), 5.26 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 5.60 (s, 1 H, $PhCHO_2$), 7.37–7.85 (m, 5 H, Ph). Anal. Calcd for $C_{26}H_{31}NO_7Si$: C, 62.76; H, 6.28; N, 2.81. Found: C, 62.43; H, 6.42; N, 2.78.

Preparation of 2-(trimethylsilyl)ethyl 2-acetamido-4,6-O-benzylidene-2-deoxy-β-D-galactopyranoside (**18**).—*Method A*. A solution of **17** (200 mg, 0.40 mmol) in butanol (30 mL) was heated with ethylenediamine (6 mL) at 90 °C for 24 h, and the mixture was then evaporated in vacuo to give a pale yellow syrup. This was coevaporated twice with toluene to give a solid that was then dissolved in 10:1 pyridine–acetic anhydride (11 mL) and stirred at room temperature overnight. Evaporation in vacuo gave a syrup that was purified by FC (1:2 pentane–EtOAc) to give a white foam that was dissolved in MeOH (30 mL) and treated with a catalytic amount of NaOMe at room temperature overnight. This solution was neutralized with Amberlite IR-120 (H^+) resin and evaporated to give a white foam in quantitative yield: $[\alpha]_D$ −30.0° (*c* 0.46, $CHCl_3$); ^{1}H (360 MHz, $CDCl_3$): δ 0.01 [s, 9 H, $(CH_3)_3Si$], 0.97 (m, 2 H, OCH_2CH_2TMS), 2.02 (s, 3 H, CH_3CO), 2.48 (m, 1 H, H-5), 3.54 (dt, 1 H, ^2J 10.1, *J* 10.1, 6.8 Hz, OCH_2CH_2TMS), 3.69 (ddd, 1 H, $J_{2,3}$ 10.5, $J_{1,2}$ 8.3, $J_{2,NH}$ 6.0 Hz, H-2), 4.05 (m, 3 H, OCH_2CH_2TMS, H-3,6a), 4.19 (m, 1 H, H-4), 4.36 (dd, 1 H, $^2J_{6a,6b}$ 12.4, $J_{5,6b}$ 1.4 Hz, H-6b), 4.67 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 5.56 (s, 1 H, $PhCHO_2$), 5.61 (m, 1 H, NH), 7.32–7.53 (m, 5 H, Ph). Anal. Calcd for $C_{20}H_{31}NO_6Si$: C, 58.64; H, 7.64; N, 3.42. Found: C, 58.29; H, 7.73; N, 3.31.

Method B. A solution of **22** (4.00 g, 7.61 mmol) in MeOH (60 mL) and CH_2Cl_2 (20 mL) was stirred with a catalytic amount of NaOMe at room temperature until the de-esterification was complete as judged by TLC (3:1 pentane–EtOAc). The solution was then neutralized by the addition of Amberlite IR-120 (H^+) resin, the resin was filtered off, and the filtrate was concentrated in vacuo. The syrup obtained was dissolved in butanol (300 mL) containing ethylenediamine (100 mL), and the mixture was heated at 90 °C for 24 h. Concentration and coevaporation with toluene gave a sticky solid that was dissolved in pyridine (200 mL) and acetic anhydride (60 mL) and was stirred at room temperature overnight. Evaporation in vacuo gave a sticky solid which was purified by FC (1:1 pentane–EtOAc), R_f 0.10, to give a solid (3.00 g, 82%). The solid was dissolved in MeOH (100 mL), transesterified with NaOMe, and stirred at room temperature until complete by TLC (2:1 pentane–EtOAc), and was then neutralized with Amberlite IR-120 (H^+) resin. Evaporation of this solution gave a solid that was dissolved in CH_3COOH (75 mL) with 10% palladium-on-charcoal (600 mg), and the mixture was hydrogenated until the reaction was complete by TLC (9:1 EtOAc–MeOH), R_f 0.11. The reaction mixture was filtered through Celite and concentrated in vacuo to give a syrup, which was dissolved in formic acid (25 mL) and benzaldehyde (25 mL) and stirred at room temperature until the acetalation was complete by TLC (9:1 EtOAc–MeOH), R_f 0.55. The mixture was poured into water and CH_2Cl_2 and was

extracted with CH_2Cl_2. The organic phase was then washed with sodium bicarbonate solution, dried (Na_2SO_4), evaporated to a syrup and purified by FC (99:1 EtOAc–MeOH) to give a white solid (1.50 g, 48%).

Preparation of 2-(trimethylsilyl)ethyl 4,6-O-benzylidene-2-deoxy-3-O-(phenylcarbamoyl)-2-phthalimido-β-D-glucopyranoside (**20**).—A solution of **19** [15] (25.9 g, 52.1 mmol), phenyl isocyanate (8.2 mL, 75.5 mmol), pyridine (6 mL), and DMAP (75 mg, 6.1 mmol) in 1,2-dichloroethane (225 mL) was stirred at 50 °C overnight. The mixture was then concentrated in vacuo and the syrup thus formed was purified by FC (4:1 pentane–EtOAc), R_f 0.45, to give a foam in quantitative yield: $[\alpha]_D$ −15.2° (*c* 1.22, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$): δ −0.13 [s, 9 H, $(CH_3)_3Si$], 0.79 (m, 2 H, OCH_2CH_2TMS), 3.53 (dt, 1 H, ^2J 10.0, *J* 10.0, 6.8 Hz, OCH_2CH_2TMS), 3.76 (m, 2 H, H-4,5), 3.84 (m, 1 H, H-6ax), 3.93 (m, 1 H, OCH_2CH_2TMS), 4.32 (dd, 1 H, $J_{2,3}$ 10.4 Hz, H-2), 4.43 (dd, 1 H, $^2J_{6ax,6eq}$ 10.3, $J_{5,6eq}$ 4.2 Hz, H-6eq), 5.49 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 5.54 (s, 1 H, $PhCHO_2$), 5.83 (dd, 1 H, $J_{3,4}$ 9.1 Hz, H-3), 6.52 (s, 1 H, NH), 6.90–7.92 (m, 15 H, Ph). Anal. Calcd for $C_{33}H_{36}N_2O_8Si$: C, 64.26; H, 5.90; N, 4.54. Found: C, 64.29; H, 5.98; N, 4.70.

Preparation of 2-(trimethylsilyl)ethyl 6-O-benzyl-2-deoxy-3-O-(phenylcarbamoyl)-2-phthalimido-β-D-glucopyranoside (**21**).—To a cooled (0 °C) suspension of **20** (2.0 g, 3.24 mmol) in dry THF (55 mL) with sodium cyanoborohydride (1.83 g, 29.2 mmol), powdered 3 Å molecular sieves (1.6 g) and methyl orange (10 mg) was added hydrogen chloride in ether until strongly acidic. The reaction was monitored by TLC (3:1 pentane–EtOAc) until complete, and EtOAc and sodium bicarbonate solution were then added. The mixture was filtered through Celite and washed with sodium bicarbonate and water, and the organic phase was dried (Na_2SO_4). Concentration in vacuo and purification by flash chromatography (4:1 pentane–EtOAc), R_f 0.20, gave a syrup (1.59 g, 79%): $[\alpha]_D$ +12.8° (*c* 0.89, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$): δ −0.15 [s, 9 H, $(CH_3)_3Si$], 0.79 (m, 2 H, OCH_2CH_2TMS), 3.51 (dt, 1 H, ^2J 9.8, *J* 9.8, 6.8 Hz, OCH_2CH_2TMS), 3.78 (m, 4 H, H-4,5,6), 3.94 (ddd, 1 H, *J* 10.2, 5.6 Hz, OCH_2CH_2TMS), 4.26 (dd, 1 H, $J_{2,3}$ 10.8 Hz, H-2), 4.61 (d, 1 H, ^2J 12.0 Hz, $PhCH_aH_b$), 4.64 (d, 1 H, $PhCH_aH_b$), 5.35 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 5.56 (dd, 1 H, $J_{3,4}$ 8.5 Hz, H-3), 6.51 (s, 1 H, NH), 6.92–7.82 (m, 15 H, Ph). Anal. Calcd for $C_{33}H_{38}N_2O_8Si$: C, 64.05; H, 6.20; N, 4.53. Found: C, 64.05; H, 6.11; N, 4.79.

Preparation of 2-(trimethylsilyl)ethyl 6-O-benzyl-3,4-O-carbonyl-2-deoxy-2-phthalimido-β-D-galactopyranoside (**22**).—A solution of **21** (7.40 g, 12.0 mmol) and DAST (2.8 mL, 21.2 mmol) in dry THF (187 mL) was stirred at 50 °C overnight, then cooled to 0 °C, and M hydrochloric acid (106 mL) was added. This was then warmed to room temperature, diluted with EtOAc and washed with sodium bicarbonate solution, before drying (Na_2SO_4) and concentrating in vacuo to give a syrup purified by FC (4:1 pentane–EtOAc), R_f 0.20, giving a yellow foam (4.1 g, 65%): $[\alpha]_D$ −1.1° (*c* 0.93, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$): δ −0.15 [s, 9 H, $(CH_3)_3Si$], 0.77 (m, 2 H, OCH_2CH_2TMS), 3.47 (dt, 1 H, ^2J 9.6, *J* 9.6, 6.7 Hz, OCH_2CH_2TMS), 3.84 (d, 2 H, $J_{6,5}$ 6.6 Hz, H-6), 3.91 (dt, 1 H, *J* 9.7, 5.9 Hz, OCH_2CH_2TMS), 4.14 (dt, 1 H, $J_{5,6}$ 6.7 Hz, H-5), 4.33 (t, 1 H, $J_{2,3}$ 8.2 Hz, H-2), 4.59 (d, 1 H, ^2J 13.1 Hz, $PhCH_aH_b$), 4.61 (d, 1 H, $PhCH_aH_b$), 4.86 (dd, 1 H, $J_{4,5}$ 2.1 Hz, H-4), 5.00 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 5.30

(dd, 1 H, $J_{3,4}$ 6.8 Hz, H-3), 7.27–7.89 (m, 10 H, Ph). Anal. Calcd for $C_{27}H_{31}NO_8Si$: C, 61.69; H, 5.96; N, 2.67. Found: C, 62.13; H, 6.10; N, 2.90.

*Preparation of 2-(trimethylsilyl)ethyl 2-acetamido-3-*O*-(2,4-di-*O*-benzyl-3,6-dideoxy-α-*D*-arabino-hexopyranosyl)-4,6-*O*-benzylidene-2-deoxy-β-*D*-galactopyranoside* (**31**) and *2-(trimethylsilyl)ethyl 2-acetamido-3-*O*-(2,4-di-*O*-benzyl-3,6-dideoxy-β-*D*-arabino-hexopyranosyl)-4,6-*O*-benzylidene-2-deoxy-β-*D*-galactopyranoside* (**32**).—A solution of **29** (97.5 mg, 0.297 mmol) in dry CH_2Cl_2 (2 mL) with oxalyl chloride (78 μL, 0.898 mmol) was treated with DMF (20 μL). After stirring for 5 h the solution was diluted with (1:1 pentane–CH_2Cl_2) and was filtered through glass wool and concentrated under high vacuum for 30 min. The oil **30** obtained was dissolved in dry CH_2Cl_2 (2 mL) and was added to a solution of **18** (65.2 mg, 0.159 mmol) in CH_2Cl_2 with silver zeolite (250 mg) in the dark at −78 °C. The mixture was stirred and allowed to warm to room temperature overnight. The mixture was diluted with CH_2Cl_2, filtered, concentrated and then chromatographed by FC (3:2 pentane–EtOAc) to give two compounds, **31** (23.5 mg, 20.5%), R_f 0.18, and **32** (16.4 mg, 14.3%), R_f 0.12.

Data for **31**: $[\alpha]_D$ +78.8° (*c* 0.78, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$): δ −0.02 [s, 9 H, $(CH_3)_3Si$], 0.93 (m, 2 H, OCH_2CH_2TMS), 1.27 (d, 3 H, $J_{5',6'}$ 6.2 Hz, H-6'), 1.68 (ddd, 1 H, $^2J_{3'ax,3'eq}$ 13.3, $J_{2',3'ax} = J_{3'ax,4'} = 10.8$, 3.2 Hz, H-3'ax), 1.93 (s, 3 H, CH_3CO), 2.17 (dt, 1 H, $J_{2',3'eq} = J_{3'eq,4'} = 4.0$ Hz, H-3'eq), 3.37 (m, 1 H, H-2), 3.42 (m, 1 H, OCH_2CH_2TMS), 3.49 (s, 1 H, H-5), 3.55 (m, 2 H, H-2', 4'), 3.64 (dq, 1 H, $J_{4',5'}$ 9.2 Hz, H-5'), 4.00 (ddd, 1 H, ^2J 9.6, *J* 11.3, 5.0 Hz, OCH_2CH_2TMS), 4.04 (dd, 1 H, $^2J_{6a,6b}$ 12.4, $J_{5,6a}$ 1.7 Hz, H-6a), 4.26 (d, 1 H, $J_{3,4}$ 3.7 Hz, H-4), 4.32 (d, 1 H, H-6b), 4.45 (d, 1 H, ^2J 12.0 Hz, $PhCH_aH_b$), 4.47 (s, 2 H, $PhCH_2$), 4.55 (d, 1 H, ^2J 12.0 Hz, $PhCH_aH_b$), 4.63 (dd, 1 H, $J_{2,3}$ 11.0 Hz, H-3), 4.87 (s, 1 H, H-1'), 5.19 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1), 5.46 (s, 1 H, $PhCHO_2$), 5.55 (m, 1 H, NH), 7.15-7.46 (m, 15 H, Ph). HRFABMS: Calcd for $C_{40}H_{53}NNaO_9Si$ $[M + Na]^+$: *m/z* 742.3387. Found: *m/z* 742.3367 ± 0.0020.

Data for **32**: $[\alpha]_D$ +20.0° (*c* 0.33, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$): δ −0.01 [s, 9 H, $(CH_3)_3Si$], 0.92 (m, 2 H, OCH_2CH_2TMS), 1.33 (d, 3 H, $J_{5',6'}$ 5.8 Hz, H-6'), 1.41 (m, 1 H, H-3'ax), 1.81 (s, 3 H, CH_3CO), 2.30 (dt, 1 H, $^2J_{3'eq,3'ax}$ 13.3, $J_{2',3'eq} = J_{3'eq,4'} \approx 3.8$ Hz, H-3'eq), 3.47 (m, 5 H, OCH_2CH_2TMS, 2, 4', 5, 5'), 3.60 (m, 1 H, H-2'), 3.99 (ddd, 1 H, ^2J 9.6, *J* 11.3, 5.2 Hz, OCH_2CH_2TMS), 4.04 (dd, 1 H, $^2J_{6a,6b}$ 12.2, $J_{5,6a}$ 1.7 Hz, H-6a), 4.29 (d, 1 H, H-6b), 4.32 (d, 1 H, $J_{3,4}$ 3.4 Hz, H-4), 4.43, 4.53 (2 × d, 2 H, ^2J 11.4 Hz, $PhCH_2$), 4.59 (s, 1 H, H-1'), 4.63 (dd, 1 H, $J_{2,3}$ 11.0 Hz, H-3), 4.67, 4.71 (2 × d, 2 H, ^2J 12.9 Hz, $PhCH_2$), 5.08 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1), 5.47 (m, 1 H, NH), 5.55 (s, 1 H, $PhCHO_2$), 7.21–7.53 (m, 15 H, Ph). HRFABMS: Calcd for $C_{40}H_{53}NNaO_9Si$ $[M + Na]^+$: *m/z* 742.3387. Found: *m/z* 742.3374 ± 0.0014.

*Preparation of 2-(trimethylsilyl)ethyl 2-acetamido-2-deoxy-3-*O*-(3,6-dideoxy-α-*D*-arabino-hexopyranosyl)-β-*D*-galactopyranoside* (**4**).—A solution of **31** (58.3 mg, 81 μmol) in CH_3COOH (3 mL) with 10% palladium-on-charcoal (45 mg) was hydrogenated at room temperature for 6 h, filtered through Celite, and the catalyst washed with more CH_3COOH. The combined filtrates were concentrated in vacuo and purified by FC (85:10:5 EtOAc–MeOH–water) to give a glass that was further purified by filtration through Bio Gel P-2 (10% EtOH in water) to give on lyophilization a white solid (32.8 mg, 93%): $[\alpha]_D$ +49.1° (*c* 0.2 in H_2O); ^{1}H NMR (360 MHz, $CDCl_3$): δ

0.01 [s, 9 H, $(CH_3)_3Si$], 0.88 and 1.00 (2 × m, 2 H, OCH_2CH_2TMS), 1.26 (d, 3 H, $J_{5',6'}$ 5.6 Hz, H-6'), 1.74 (ddd, 1 H, $^2J_{3'ax,3'eq}$ 14.2, $J_{2',3'ax} = J_{3'ax,4'} = 11.4$, 3.1 Hz, H-3'ax), 2.03 (m, 4 H, H-3'eq, CH_3CO), 3.58 (m, 2 H, H-4', 5'), 3.64 (dd, 1 H, $J_{5,6}$ 4.6, 7.6 Hz, H-5), 3.71 (m, 1 H, OCH_2CH_2TMS), 3.78 (m, 3 H, H-3,6), 3.95 (m, 2 H, H-2,2'), 4.07 (dd, 1 H, J 4.9, 10.4 Hz, OCH_2CH_2TMS), 4.14 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-4), 4.59 (d, 1 H, $J_{1,2}$ 8.6 Hz, H-1), 4.76 (s, 1 H, H-1'). HRFABMS: Calcd for $C_{19}H_{37}NNaO_9Si$ $[M + Na]^+$: m/z 474.2135. Found: m/z 474.2128 ± 0.0008.

*Preparation of 2-(trimethylsilyl)ethyl 2-acetamido-2-deoxy-3-*O*-(3,6-dideoxy-β-*D*-arabino-hexopyranosyl)-β-*D*-galactopyranoside* (**5**).—A solution of **32** (27.3 mg, 38 μmol) in CH_3COOH (2 mL) with 10% palladium-on-charcoal (30 mg) was hydrogenated at room temperature for 6 h, filtered through Celite, and the catalyst was washed with more CH_3COOH. The combined filtrates were concentrated in vacuo and purified by FC (85:10:5 EtOAc–MeOH–water) to give a glass that was further purified by filtration through Bio Gel P-2 (10% EtOH in water) to give on lyophilization a white solid (15.3 mg, 92%): $[\alpha]_D$ −23.2° (*c* 0.19, H_2O); ^1H NMR (360 MHz, $CDCl_3$): δ 0.01 [s, 9 H, $(CH_3)_3Si$], 0.87, 0.99 (2 × m, 2 H, OCH_2CH_2TMS), 1.65 (ddd, 1 H, $^2J_{3'ax,3'eq}$ 14.2, $J_{2',3'ax} = J_{3'ax,4'} = 11.6$, 3.0 Hz, H-3'ax), 2.17 (ddd, 1 H, $J_{2',3'eq} = J_{3'eq,4'}$ = 4.6, 3.4 Hz, H-3'eq), 3.44 (dq, 1 H, $J_{4',5'}$ 9.5 Hz, H-5'), 3.55 (ddd, 1 H, $J_{4',3'eq}$ 4.7 Hz, H-4'), 3.68 (m, 1 H, H-5), 3.72 (m, 1 H, OCH_2CH_2TMS), 3.78 (m, 2 H, H-6), 3.85 (dd, 1 H, $J_{3,4}$ 3.2 Hz, H-3), 3.89 (t, 1 H, H-2'), 3.99 (dd, 1 H, $J_{2,3}$ 10.8 Hz, H-2), 4.06 (dd, 1 H, J 10.4, 4.9 Hz, OCH_2CH_2TMS), 4.15 (d, 1 H, H-4), 4.53 (d, 1 H, $J_{1,2}$ 8.6 Hz, H-1), 4.68 (s, 1 H, H-1'). HRFABMS: Calcd for $C_{19}H_{37}NNaO_9Si$ $[M + Na]^+$: m/z 474.2135. Found: m/z 474.2124 ± 0.0011.

*Preparation of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-*D*-galactopyranose* (**23**) [19]. —A solution of D-galactosamine hydrochloride (1.5 g, 6.94 mmol) in anhydrous pyridine (12 mL) and acetic anhydride (12 mL) was stirred overnight at room temperature, concentrated, co-evaporated with toluene, and dried under high vacuum to give a yellow solid. The crude product was purified by FC (1:1 pentane–acetone), to give 2-Acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α/β-D-galactopyranose as a white solid (1.20 g, 55%) [37]. A solution of the peracetates (1.44 g, 3.70 mmol) and hydrazine acetate (0.4 g, 4.43 mmol) in anhydrous DMF (20 mL) was stirred for 40 min at room temperature [38], then the mixture was concentrated to a dryness and dried at high vacuum to give a yellow solid. Flash chromatography (1:1 pentane–acetone) and solvent removal gave the title compound as a solid (1.02 g, 80%).

Data for α anomer: ^1H NMR (360 MHz, $CDCl_3$): δ 1.92–2.12 (12 H, CH_3CO), 4.03 (m, 2 H, H-6), 4.20 (m, 1 H, H-5), 4.68 (ddd, 1 H, $J_{2,3}$ 11.5 Hz, H-2), 5.28 (dd, 1 H, $J_{3,4}$ 3.2 Hz, H-3), 5.37 (d, 1 H, H-4), 5.51 (d, 1 H, $J_{NH,2}$ 9.2 Hz, N-*H*), 6.18 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1).

Data for β anomer: ^1H NMR (360 MHz, $CDCl_3$): δ 1.91–1.98 (12 H, CH_3CO), 4.01 (m, 3 H, H-5,6a), 4.38 (m, 1 H, H-6b), 4.43 (m, 1 H, H-2), 5.20 (m, 1 H, H-3), 5.16 (m, 1 H, H-4), 5.30 (d, 1 H, $J_{NH,2}$ 2.4 Hz, N-*H*), 6.19 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1). Anal. Calcd for $C_{14}H_{21}NO_9$: C, 48.41; H, 6.09; N, 4.03. Found: C, 48.42; H, 6.18; N, 3.89.

*Preparation of methyl 9-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-galactopyranosyloxy)nonanoate* (**25**).—Compound **23** (1.25 g, 3.60 mmol), trichloroacetonitrile (0.8 mL, 7.78 mmol) and 4 Å molecular sieves (2.0 g) in anhydrous dichloromethane

(10 mL) were stirred for 15 min at room temperature, and sodium hydride (80%, 10 mg) was added to the stirred mixture. After 1.5 h at room temperature [TLC (1:1 pentane:acetone)] revealed a major new spot. The mixture was filtered through Celite and concentrated to give the α-imidate as a crude yellow solid **24**. The crude imidate was used directly in the next step.

^{1}H NMR for **24**: (360 MHz, $CDCl_3$): δ 1.93–2.16 (12 H, CH_3CO), 4.05 (dd, 1 H, $J_{5,6a}$ 6.6, $J_{6a,6b}$ 11.4 Hz, H-6a), 4.15 (dd, 1 H, $J_{5,6b}$ 6.6, $J_{6a,6b}$ 11.4 Hz, H-6b), 4.23 (dd, 1 H, H-5), 4.79 (ddd, 1 H, $J_{2,3}$ 11.5 Hz, H-2), 5.26 (dd, 1 H, $J_{3,4}$ 3.3 Hz, H-3), 5.46 (d, 1 H, H-4), 5.48 (d, 1 H, $J_{NH,2}$ 9.1 Hz, N-*H*), 6.38 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 8.76 (s, 1 H, =N-*H*). The imidate **24**, methyl 9-hydroxynonanoate (677 mg, 3.6 mmol) [14], 4 Å molecular sieves (2.0 g) and anhydrous dichloromethane (15 mL) were stirred for 15 min at room temperature, then the promoter TMSOTf (30 μL) was added. The reaction was complete after 15 min at room temperature [TLC (2:1 toluene–acetone)]. The mixture was filtered through Celite, concentrated, and the residue was purified by FC (2:1 toluene–acetone) to give a white solid **25** (1.23 g, 66%), $[\alpha]_D^{20}$ −15.3° (*c* 0.78, $CHCl_3$).

^{1}H NMR (360 MHz, $CDCl_3$): δ 1.27–1.56 [m, 12 H, -$(CH_2)_6$-], 1.93–2.12 (12 H, CH_3CO), 2.28 (t, 2 H, -CH_2-CO), 3.42 (m, 1 H, O-CH_2-), 3.63 (s, 3 H, CH_3-O), 3.87 (m, 3 H, H-6a,2, O-CH_2-), 4.11 (m, 2 H, H-5,6_b), 4.70 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 5.30 (dd, 1 H, $J_{2,3}$ 11.1 Hz, H-3), 5.33 (d, 1 H, $J_{3,4}$ 3.3 Hz, H-4), 5.50 (d, 1 H, $J_{NH,2}$ 8.5 Hz, N-*H*). Anal. Calcd for $C_{24}H_{39}NO_{11}$: C, 55.70; H, 7.60; N, 2.71. Found: C, 55.74; H, 7.56; N, 2.70.

*Preparation of methyl 9-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-*D*-galactopyranosyloxy)nonanoate* (**27**).—Glycoside **25** (910 mg, 1.76 mmol) dissolved in MeOH (20 mL) was deacetylated by addition of sodium methylate (10 mg, cat.). The reaction mixture was stirred for 1.5 h at room temperature, dry-ice was added, and the mixture was concentrated to a white solid **26**. The crude solid was dissolved in benzaldehyde (5 mL) and formic acid (5 mL) and stirred for 2.5 h at room temperature. The mixture was then co-evaporated with toluene (8 mL), concentrated, and the residue was purified by FC (2:1 toluene–acetone) to give compound **27** as a white solid (696 mg 83%): mp 169–171 °C, $[\alpha]_D^{20}$ −8.2° (*c* 0.9, $CHCl_3$) ^{1}H NMR (360 MHz, $CDCl_3$): δ 1.27–1.58 [m, 12 H, -$(CH_2)_6$-], 2.01 (s, 3 H, CH_3CO), 2.27 (t, 2 H, -CH_2-CO), 3.45 (m, 2 H, H-5, O-CH_2-), 3.65 (s, 3 H, CH_3-O), 3.69 (ddd, 1 H, $J_{2,3}$ 10.2 Hz, H-2), 3.90 (m, 1 H, O-CH_2-), 4.08 (dd, 1 H, $J_{6a,6b}$ 12.4 Hz, H-6a), 4.09 (m, 1 H, H-3), 4.18 (d, 1 H, $J_{3,4}$ 3.7 Hz, H-4), 4.31 (dd, 1 H, $J_{5,6b}$ 1.4 Hz, H-6b), 4.67 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 5.54 (d, 1 H, $J_{NH,2}$ 5.9 Hz, N-*H*), 5.69 (s, 1 H, PhC*H*O_2), 7.35–7.50 (m, 5 H, Ph*H*). Anal. Calcd for $C_{25}H_{37}NO_8$: C, 62.61; H, 7.78; N, 2.92. Found: C, 62.49; H, 7.86; N 2.85.

*Preparation of methyl 9-(2-acetamido-3-*O*-(2,4-di-*O*-benzyl-3,6-dideoxy-α-*D*-arabino-hexopyranosyl)-4,6-*O*-benzylidene-2-deoxy-β-*D*-galactopyranosyloxy)nonanoate* (**33**) and *methyl 9-(2-acetamido-3-*O*-(2,4-di-*O*-benzyl-3,6-dideoxy-β-*D*-arabino-hexopyranosyl)-4,6-*O*-benzylidene-2-deoxy-β-*D*-galactopyranosyloxy)nonanoate* (**34**).—The dibenzyl tyvelose **29** (500 mg, 1.52 mmol) in dry dichloromethane (10 mL) was reacted with oxalyl chloride (0.4 mL, mmol) and a catalytic amount of DMF (0.2 mL). After stirring for 5 h under argon, the solution was diluted with pentane (10 mL) and then filtered

through cotton and concentrated under high vacuum for 30 min. Glycosyl chloride **30**, obtained as an oil, was dissolved in anhydrous dichloromethane (8 mL) and cooled to −78 °C. The solution was slowly added by cannula to a mixture of **27** (650 mg, 1.36 mmol), silver zeolite [27] (1.5 g) and 4 Å molecular sieves (2.0 g) in dichloromethane (8 mL) that had been previously stirred for 50 min at −78 °C. The mixture was kept in the dark at −78 °C and after 40 min the mixture was allowed to warm slowly to room temperature and stir for 24 h. The mixture was applied directly to a column of silica gel and eluted (1:1 toluene–EtOAc) to give two compounds, **33**, (525 mg, 49%), $[\alpha]_D^{20}$ 74.4° (*c* 0.5, $CHCl_3$) and **34** (257 mg, 24%), $[\alpha]_D^{20}$ +19.5° (*c* 1.0, $CHCl_3$), as well as an unresolved mixture of both compounds (75 mg).

Data for **33**: ^{1}H NMR (360 MHz, $CDCl_3$): δ 1.24 (d, 3 H, $J_{5,6}$ 6.1 Hz, H-6′), 1.25 [m, 8 H, -(CH_2)$_4$-], 1.56 [m, 4 H, -(CH_2)$_2$-], 1.68 (ddd, 1 H, $^2J_{3'ax,3'eq}$ 13.5, $J_{3'ax,4'}$ 10.5 Hz, H-3′ax), 1.92 (s, 3 H, CH_3CO), 2.25 (t, 2 H, CH_2-CO-), 2.50 (m, 1 H, H-3′eq), 3.38–3.50 (m, 4 H, H-2,2′,5, -CH_2-O-), 3.57 (m, 1 H, H-4′), 3.63 (s, 3 H, CH_3-O-), 3.64 (m, 1 H, H-5′), 3.88 (m, 1 H, -CH_2-O-), 4.04 (dd, 1 H, $J_{6a,6b}$ 12.1 Hz, H-6a), 4.25 (d, 1 H, H-4), 4.31 (d, 1 H, H-6b), 4.42–4.57 (m, 4 H, PhCH_2), 4.60 (dd, 1 H, $J_{2,3}$ 10.9, $J_{3,4}$ 3.6 Hz, H-3), 4.86 (s, 1 H, H-1′), 5.15 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 5.45 (s, 1 H, PhCHO_2), 5.58 (d, 1 H, $J_{NH,2}$ 7.3 Hz, N*H*), 7.15–7.46 (m, 15 H, Ph*H*). Anal. Calcd for $C_{45}H_{59}NO_{11}$: C, 68.44; H 7.48; N, 1.77. Found: C, 68.27; H, 7.62; N, 1.76.

Data for **34**: ^{1}H NMR (360 MHz, $CDCl_3$): δ 1.28 [m, 8 H, -(CH_2)$_4$-], 1.33 (d, 3 H, $J_{5',6'}$ 5.7 Hz, H-6′), 1.40 (dt, 1 H, $^2J_{3'eq,3'ax}$ 10.2, $J_{3'eq,4'} = J_{2',3'eq}$ = 3.0 Hz, H-3′ax), 1.82 (s, 3 H, CH_3CO), 2.27 (t, 2 H, CH_2-CO), 2.30 (m, 1 H, H-3′eq), 3.40–3.54 (m, 5 H, H-2,4,5,5′, CH_2-O), 3.61 (m, 1 H, H-2′), 3.63 (s, 3 H, CH_3-O), 3.88 (m, 1 H, CH_2O), 4.03 (dd, 1 H, $J_{6a,6b}$ 12.3, $J_{5,6a}$ 1.4 Hz, H-6a), 4.28 (d, 1 H, $J_{5,6b}$ 1.2 Hz, H-6b), 4.31 (d, 1 H, $J_{3,4}$ 3.4 Hz, H-4), 4.43, 4.53 (2 × d, 2 H, ^2J 11.5 Hz, PhCH_2), 4.59 (s, 1 H, H-1′), 4.62 (dd, 1 H, $J_{2,3}$ 8.3, $J_{3,4}$ 3.4 Hz, H-3), 4.63, 4.73 (2 × d, 2 H, ^2J 12.8 Hz, PhCH_2), 5.06 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 5.55 (m, 2 H, N*H*, PhCHO_2), 7.15–7.55 (15H, m, Ph*H*). Anal. Calcd for $C_{45}H_{59}NO_{11}$: C, 68.44; H, 7.48; N, 1.77. Found: C, 68.30; H, 7.63; N 1.77.

*Preparation of methyl 9-(2-acetamido-3-*O*-(3,6-dideoxy-α-*D*-arabino-hexopyranosyl)-2-deoxy-β-*D*-galactopyranosyloxy)nonanoate* (**6**).—A solution of **33** (448 mg, 567 mmol) in CH_3COOH (5 mL) with 10% palladium-on-charcoal (300 mg) was hydrogenated at room temperature for 12 h. The mixture was filtered through Celite, and the residue was washed with CH_3COOH. The combined filtrates were concentrated in vacuo and purified on Iatrobeads (3:1 EtOAc–MeOH) to give a white solid (290 mg, 98%): $[\alpha]_D^{20}$ 7.0° (*c* 1.0, CH_3OH); ^{1}H NMR (500 MHz, D_2O): δ 1.27 (d, 3 H, $J_{5',6'}$ 6.2 Hz, H-6′), 1.31 [m, 8 H, -(CH_2)$_4$-], 1.53–1.62 [m, 4 H, -(CH_2)$_2$-], 1.74 (ddd, 1 H, $^2J_{3'ax,3'eq}$ 10.8, $J_{3'ax,4'}$ 8.8, $J_{3'ax,2'}$ 2.9 Hz, H-3′ax), 2.03 (m, 1 H, H-3′eq), 2.04 (s, 3 H, CH_3-CO), 2.39 (t, 2 H, -CH_2-CO-), 3.54 (s, 3 H, CH_3-O), 3.58 (m, 1 H, H-5′), 3.60 (m, 1 H, H-4′), 3.62 (m, 1 H, -CH_2-O-), 3.65 (m, 1 H, H-5), 3.79 (m, 2 H, H-6), 3.83 (m, 1 H, H-3), 3.92 (m, 2 H, H-2, -CH_2-O), 3.96 (m, 1 H, H-2′), 4.14 (d, 1 H, $J_{3,4}$ 3.5 Hz, H-4), 4.56 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 4.77 (s, 1 H, H-1′); ^{13}C NMR (125 MHz, D_2O): δ 102.6 (C-1, $^1J_{C1,H1}$ 161.8 Hz), 96.3 (C-1′, $^1J_{C1',H1'}$ 167.8 Hz), 75.8 (C-3), 71.2 (C-5′), 75.7 (C-5), 71.2 (*C*H_2-O), 67.4 (C-4′), 68.5 (C-2′), 64.7 (C-4), 62.0 (C-6), 53.0 (*C*H_3-O), 51.8 (C-2), 34.6 (*C*H_2-CO), 34.0 (C-3′), 23.0–30.0 [(-*C*H_2)$_7$-, *C*H_3-CO], 17.6 (C-6′).

FABMS: *m/z* 544 $[M + Na]^+$, 522 $[M + 1]^+$. Anal. Calcd for $C_{24}H_{43}NO_{11}$: C, 55.28; H, 8.25; N, 2.69. Found: C, 55.18; H, 8.56; N, 2.72.

*Preparation of methyl 9-(2-acetamido-3-*O*-(3,6-dideoxy-β-*D*-*arabino*-hexopyranosyl)-2-deoxy-β-*D*-galactopyranosyloxy)nonanoate* (**7**).—A solution of **34** (207 mg, 262 mmol) in CH_3COOH (8 mL) was hydrogenated at room temperature for 12 h with 10% palladium-on-charcoal (189 mg). The reaction mixture was filtered through Celite, and the residue was washed with CH_3COOH. The combined filtrates were concentrated in vacuo and purified on Iatrobeads (3:1 EtOAc–MeOH) to give a white solid (132 mg, 96%): $[\alpha]_D^{20}$ −23.5° (*c* 0.5, CH_3OH); ^{1}H NMR (500 MHz, D_2O): δ 1.28 (d, 3 H, $J_{5',6'}$ 6.1 Hz, H-6′), 1.30 [m, 8 H, -$(CH_2)_4$-], 1.54–1.60 [m, 4 H, -$(CH_2)_2$-], 1.63 (ddd, 1 H, $^2J_{3'ax,3'eq}$ 13.7, $J_{3'ax,4'}$ 11.5, $J_{2',3'ax}$ 3.8 Hz, H-3′ax), 2.02 (s, 3 H, CH_3-CO), 2.13 (ddd, 1 H, $J_{2',3'eq}$ 3.6, $J_{3'eq,4'}$ 4.5 Hz, H-3′eq), 2.39 (t, 2 H, -CH_2-CO-), 3.44 (dq, 1 H, H-5′), 3.53 (ddd, 1 H, $J_{4',5'}$ 9.4 Hz, H-4′), 3.61 (m, 1 H, -CH_2-O-), 3.68 (m, 1 H, H-5), 3.69 (s, 3 H, CH_3-O), 3.78 (m, 2 H, H-6), 3.87 (dd, 1 H, $J_{3,4}$ 3.0 Hz, H-3), 3.90 (m, 2 H, H-2′, -CH_2-O), 3.98 (dd, 1 H, $J_{2,3}$ 10.9 Hz, H-2), 4.12 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-4), 4.51 (d, 1 H, $J_{1,2}$ 8.5 Hz, H-1), 4.69 (s, 1 H, H-1′); ^{13}C NMR (125 MHz, D_2O): δ 103.5 (C-1′, $^1J_{C1',H1'}$ 159.8 Hz), 102.2 (C-1, $^1J_{C1,H1}$ 160.6 Hz), 80.2 (C-3), 76.9 (C-5′), 75.8 (C-5), 71.4 (CH_2-O), 69.1 (C-4), 68.5 (C-2′), 67.5 (C-4), 61.8 (C-6), 52.8 (CH_3-O), 52.4 (C-2), 37.4 (C-3′), 23.0–29.3 [-$(CH_2)_7$-, CH_3-CO], 19.0 (C-6′). FABMS: *m/z* 544 $[M + Na]^+$, 522 $[M + 1]^+$. Anal. Calcd for $C_{24}H_{43}NO_{11}$: C: 55.28; H, 8.25; N, 2.69. Found: C, 55.23; H, 8.56; N, 2.60.

*Preparation of methyl 9-(2-acetamido-3-*O*-(3,6-dideoxy-α-*D*-*arabino*-hexopyranosyl)-2-deoxy-β-*D*-galactopyranosyloxy) N-2-aminoethyl nonanamide* (**35**).—Compound **6** (130 mg) in ethylenediamine (5 mL) was stirred for 48 h at 70 °C [TLC (1:1 EtOAc–MeOH)]. Water (5 mL) was added, and the mixture was loaded on a C_{18} Sep-Pak cartridge previously washed with MeOH (10 mL) and then water (10 mL). The cartridge was washed with water (10 mL), and the product was eluted with MeOH. The MeOH solution was concentrated to dryness and water (10 mL) was added. After filtration through a 0.2 μm millifilter, the water solution was lyophilized to give a white solid (132 mg, 96%): $[\alpha]_D^{20}$ 28.0° (*c* 1.2, H_2O); ^{1}H NMR (500 MHz, D_2O): δ 1.27 (d, 3 H, $J_{6',5'}$ 6.2 Hz, H-6′), 1.31 [m, 8 H, -$(CH_2)_4$-], 1.57 [m, 4 H, -$(CH_2)_2$-], 1.74 (ddd, 1 H, $^2J_{3'ax,3'eq}$ 8.8, $J_{3'ax,4'}$ 11.1, $J_{2',3'ax}$ 2.8 Hz, H-3′ax), 2.03 (m, 1 H, H-3′eq), 2.04 (s, 3 H, CH_3-O), 2.26 (t, 2 H, CH_2-CO), 2.89 (t, 2 H, CH_2-N), 3.35 (t, 2 H, CH_2-N), 3.57–3.67 (m, 4 H, H-5′,4′, -CH_2-O-, H-5), 3.74–3.85 (m, 3 H, H-6,3), 3.89–3.97 (m, 3 H, H-2, -CH_2-O, H-2′), 4.14 (d, 1 H, $J_{3,4}$ 2.9 Hz, H-4), 4.55 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 4.77 (s, 1 H, H-1′). FABMS: *m/z* 572 $[M + Na]^+$, 550 $[M + 1]^+$. Anal. Calcd for $C_{25}H_{47}N_3O_{10} \cdot 2.5H_2O$: C, 50.50; H, 8.75; N, 7.07. Found: C, 50.37; H, 9.04; N, 6.89

*Preparation of methyl 9-(2-acetamido-3-*O*-(3,6-dideoxy-β-*D*-*arabino*-hexopyranosyl)-2-deoxy-β-*D*-galactopyranosyloxy) N-2-aminoethyl nonanamide* (**36**).—Compound **7** (15 mg) in ethylenediamine (2 mL) was stirred for 48 h at 70 °C [TLC (1:1 EtOAc–MeOH)]. Water (3 mL) was added, and the mixture was loaded on a C_{18} Sep-Pak cartridge that had been previously washed with MeOH (5 mL) and then water (5 mL). The cartridge was washed with water (10 mL), and the product was eluted with MeOH. The MeOH solution was concentrated to a dryness, and then water (10 mL) was added. After filtration through a 0.2 μm millifilter, the water solution was lyophilized to give a white

solid (15 mg, 98%): $[\alpha]_D^{20}$ −20.0° (*c* 0.5, H_2O); ^1H NMR (500 MHz, D_2O): δ 1.27 (d, 3 H, $J_{5',6'}$ 6.1 Hz, H-6′), 1.30 [m, 8 H, -$(CH_2)_4$-], 1.54–1.60 [m, 4 H, -$(CH_2)_2$-], 1.65 (ddd, 1 H, $^2J_{3'ax,3'eq}$ 13.7, $J_{2',3'ax}$ 3.8 Hz, H-3′ax), 2.02 (s, 3 H, CH_3-CO), 2.17 (ddd, 1 H, $J_{2',3'eq}$ 3.6, $J_{3'eq,4'}$ 4.5 Hz, H-3′eq), 2.25 (t, 2 H, CH_2-CO), 2.80 (t, 2 H, CH_2-N), 3.29 (t, 2 H, CH_2-N), 3.44 (dq, 1 H, $J_{4',5'}$ 9.4 Hz, H-5′), 3.55 (ddd, 1 H, $J_{3'ax,4'}$ 11.5 Hz, H-4′), 3.60 (m, 1 H, -CH_2-O-), 3.68 (m, 1 H, H-5), 3.78 (m, 2 H, H-6), 3.86 (dd, 1 H, $J_{2,3}$ 10.8 Hz, H-3), 3.90 (m, 2 H, H-2′, -CH_2-O, H-2′), 3.98 (dd, 1 H, $J_{2,3}$ 10.8 Hz, H-2), 4.11 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-4), 4.50 (d, 1 H, $J_{1,2}$ 8.5 Hz, H-1), 4.69 (s, 1 H, H-1′). FABMS: *m/z* 572 $[M + Na]^+$, 550 $[M + 1]^+$. Anal. Calcd for $C_{25}H_{47}N_3O_{10} \cdot 1.5H_2O$: C, 52.08; H, 8.68; N, 7.29. Found: C, 52.00; H, 8.50; N, 7.19.

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