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Stereocontrolled syntheses of O-glycans of core class 2 with a linear tetrameric lactosamine chain and with three lactosamine branches

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Abstract

Synthetic routes to O-glycans of core class 2 with a linearly extended tetralactosamine moiety and with three lactosamine branches are discussed. By a glycosyl fluoride-method, the mono- and the di-lactosaminyl units were attached to the core disaccharide (Galβ1 → 3GalN$_3$) derivatives in high stereoselectivity. © 1996 Elsevier Science Ltd.

Keywords: O-Glycan of core class 2; Poly-*N*-acetyllactosamine; Glycosyl fluoride

1. Introduction

In the biosynthesis of glycoprotein oligosaccharides, glycosylation with β6- and/or β3-GlcNAc transferases is often followed by that with β4-Gal transferases to furnish type 2 (*neolacto*) poly-*N*-acetyllactosaminoglycans. While these structures are common to the complex or hybrid type N-glycans, the presence of polylactosamines in a linearly extended or branched form has also been in evidence for core class 2, core class 4, and I antigenic O-glycan families. Among them, the linearly repeating lactosaminoglycans are of particular interest in connection with the alteration of glycoforms at such biological

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events as development, differentiation, and oncogenesis [1]. The polylactosamine backbone may be modified further by sialylation and fucosylation to a selectin ligand, sialyl Le^X [2]. Furthermore, it is noteworthy that mucin-like glycoproteins carrying polylactosamine oligosaccharides have been demonstrated on a variety of tumor-relevant cells [3].

As part of an attempt to synthesize the O-glycans of biological importance [4], we recently reported a synthesis of 6-*O*-dimeric lactosamine-bound GalNAc*α* → Ser (**1**) [5] by taking advantage of the stereocontrolled glycosylation with the *N*-phthaloylated lactosaminyl fluorides using Suzuki's promoter (Cp_2HfCl_2/AgOTf) [6], the efficiency of which was previously demonstrated for the synthesis of I-active polylactosamine type glycosphingolipids [7]. We describe herein the syntheses of two O-glycans of core class 2 possessing a linear tetrameric lactosamine chain **2** and a branched trimeric lactosamine substructure **3**. The tetralactosaminyl extension-structure present in the former has been identified in the disialylated oligosaccharides of O-glycan released from the *β*-subunit of equine chorionic gonadotropin [8], while the latter was found as a neutral component of oligosaccharides derived from the human milk secretory immunoglobulin A hinge region [9].

Galβ1→4GlcNAcβ1→3Galβ1→4GlcNAcβ1→6GalNAcα1→3Ser(Ac)

1

(Galβ1→4GlcNAcβ1→3)$_3$Galβ1→4GlcNAcβ1→6
GalNAcα1→3Ser
Galβ1→3

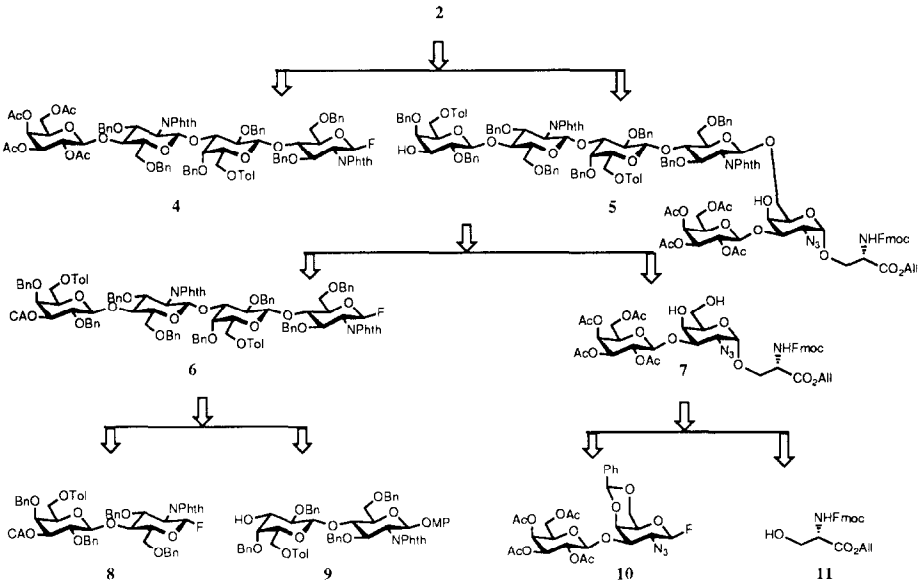
2

Galβ1→4GlcNAcβ1 → 6
Galβ1→4GlcNAcβ1→6
GalNAc
Galβ1→3
Galβ1→4GlcNAcβ1→3

3

2. Results and discussion

Construction of the tetralactosaminyl chain of **2** was designed so as to couple essentially two dimeric lactosamine segments, because our earlier studies on **1** revealed that the glycosyl fluoride **4** corresponding to the nonreducing-end dimer was reactive



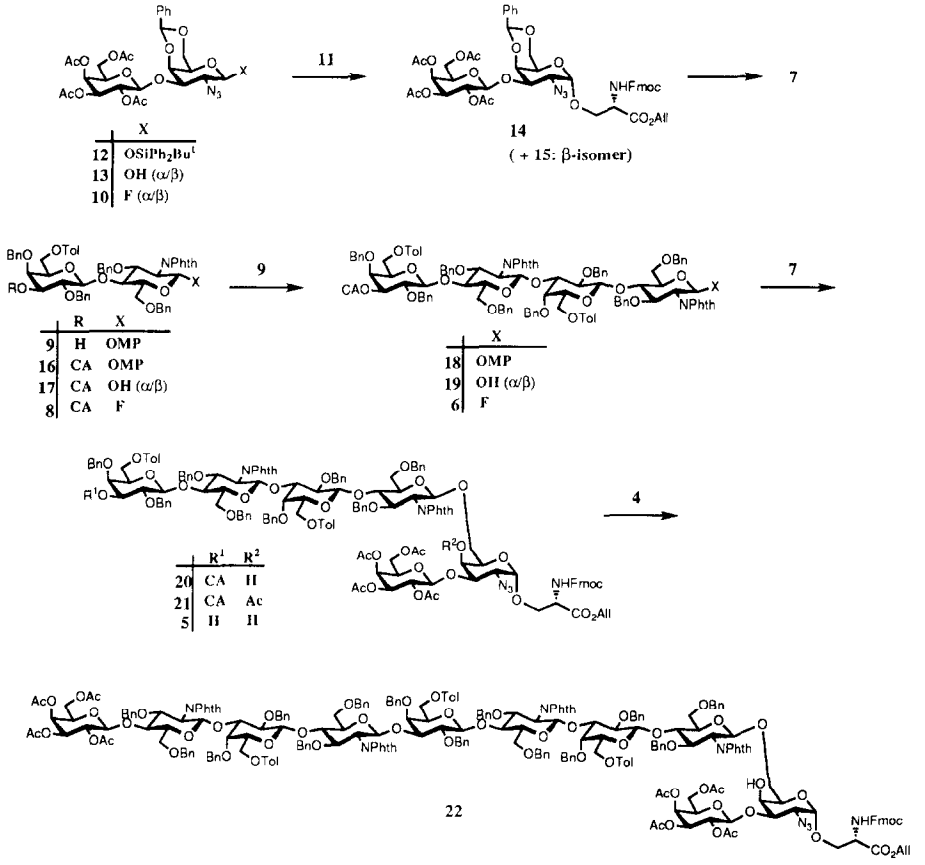
All = allyl, CA = chloroacetyl, Fmoc = 9-fluorenylmethoxycarbonyl, MP = 4-methoxyphenyl, Phth = phthaloyl, Tol = 4-methylbenzoyl (toluoyl)

Scheme 1.

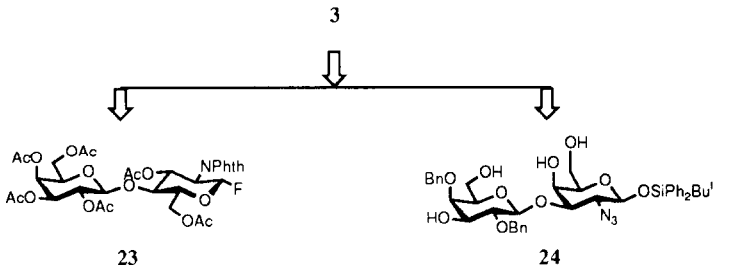
enough to elaborate a $\beta 1 \rightarrow 6$ linkage in good yield. In designing a convergent synthesis of the counterpart **5**, retrosynthetic analysis led us to the key intermediates **6** and **7**, which were further retrosynthesized into three disaccharide fragments **8–10** and a serine derivative **11** (Scheme 1).

Known disaccharide **12** [10] was converted into glycosyl fluoride **10** via hemiacetal **13** [(1) Bu_4NF, AcOH, THF [11], (2) Et_2NSF_3 (DAST), 1,2-dichloroethane [12], 72% in two steps]. The fluoride **10** ($\alpha:\beta = 1.4:1$) was condensed with Fmoc serine allyl ester **11** [13] in the presence of $Cp_2ZrCl_2/AgClO_4$ to afford a mixture of $\alpha:\beta$ glycosides **14** and **15** (**14**:**15** = 5.6:1) in 93% yield. Hydrolysis of benzylidene acetal of the α glycoside **14** with aqueous trifluoroacetic acid gave the key intermediate **7**. The tetrasaccharide donor **6** was synthesized as follows. The common intermediate **9** was readily obtainable as described previously [5]. The 4-methylbenzoyl (toluoyl) group at the 6-O position was intentionally introduced to facilitate assignment of the synthesized polylactosamine structures. Compound **9** was converted into a glycosyl fluoride **8** by chloroacetylation ($\rightarrow$ **16**), cleavage of 4-methoxyphenyl glycoside ($\rightarrow$ **17**), and fluorination in 82% yield (three steps). Glycosylation of **9** with **8** was promoted by $Cp_2HfCl_2/AgOTf$ to afford exclusively a tetrasaccharide **18**, which, by the same procedure for **9** to **8**, was converted into the fluoride **6** in 73% yield (two steps). Having the necessary synthons **6** and **7**, coupling was executed. When the reaction was performed with $Cp_2HfCl_2/AgOTf$ in 1,2-dichloroethane, consumption of **6** was too fast to produce the desired coupling product **20**, and the reaction resulted in a low conversion of acceptor **7**. On the other hand, in ethereal medium (3:1, ether–dichloromethane) the slower reaction afforded a

75% yield of the hexasaccharide **20**, though it was necessary to use three equivalents of glycosyl donor **6**. The regioselective formation of 1 → 6 linkage was confirmed after acetylation to **21** by ^{1}H NMR spectroscopy. In the spectrum of **21**, characteristic lower field shift of H-4 ($GalN_3$) signal was observed at δ 5.28 ppm. By treatment with thiourea in DMF, the chloroacetyl group was selectively removed from **20** to give a glycosyl acceptor **5** in 85% yield. With **5** and 2.5 equiv of **4**, formation of a linear tetralactosaminyl chain was realized under the same glycosylation conditions as those for preparation of **18**. Chromatography of the crude product by gel permeation gave the target compound **22** in 82% yield. The structure was revealed by its FAB mass spectrum as well as by its ^{1}H NMR spectrum, in which three separate signals for the 4-methylbenzoyl group appeared at δ 2.27, 2.29, and 2.37 ppm. The synthesized glycosyl serine derivative **22** would be a useful synthon for the synthesis of polylactosamine type glycooligopeptide molecules, although the selective transformations of an azide group and the *N*-phthalimide groups into the acetamido groups remains to be achieved. Further extension of the linear lactosaminyl chain would also be expected by repeated use of glycosyl donor **6** instead of **4** (Scheme 2).



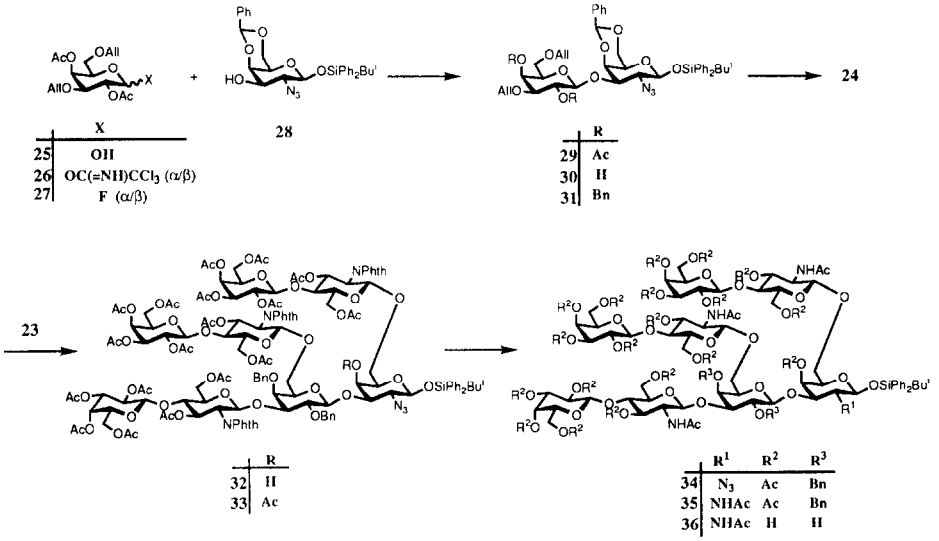
Scheme 2.



Scheme 3.

Synthesis of the octasaccharide **3** carrying three lactosamine branches was performed more concisely by a one-step glycosylation strategy with the lactosamine glycosyl donor **23** [7] and the tetraol acceptor **24** (Scheme 3).

The necessary acceptor **24** was synthesized as follows (Scheme 4): 2,4-Di-*O*-acetyl-3,6-di-*O*-allyl-α-D-galactopyranosyl trichloroacetimidate **26** and glycosyl fluoride **27** were readily prepared from the known hemiacetal **25** [14]. Glycosylation of **28** with **26** (1.5 equiv) was promoted by $BF_3 \cdot OEt_2$ in 1,2-dichloroethane to give disaccharide **29** in 75% yield, whereas the reaction using the fluoride **27** (1.2 equiv) as glycosyl donor resulted in only a moderate yield of **29**. Deacetylation and benzylation gave **31** (52%, two steps), which by treatment with the Ir-complex [15] and then by *p*-TsOH-catalyzed methanolysis afforded the key intermediate **24** in 80% yield. $Cp_2HfCl_2/AgOTf$-promoted glycosylation of **24** with 6 molar equivalents of fluoride **23** produced a mixture of glycosylation products, from which the desired octasaccharide **32** was isolated in 44% yield by gel-permeation and preparative thin-layer chromatography. Generation of some



Scheme 4.

byproducts might be ascribed to incompletion of tri-glycosylation. However, attempts to assign their structures were unsuccessful. In the 500 MHz ^{1}H NMR spectrum of **32**, the signals for eighteen acetyl groups were assigned at δ 1.88–2.15 ppm. The anomeric protons of the *N*-phthaloylglucosamine residues were observed as three doublets with the coupling constant of 8.3–8.8 Hz at δ 5.33, 5.49, and 5.57 ppm. Acetylation of **32** gave **33**, which showed a broad singlet signal characteristic of four H-4 protons of Gal and $GalN_3$ residues at δ 5.33 ppm. These data showed that the glycosylation reaction took place both stereo- and regio-selectively at the positions of Gal 3-O, 6-O, and $GalN_3$ 6-O. We next examined deprotective transformations of the trilactosaminoglycan. Dephthaloylation of **33** was performed with ethylenediamine in BuOH [16], and acetylation gave triacetamide **34** in 56% yield, which was treated with AcSH–pyridine to furnish tetraacetamide **35**. Hydrogenation of **35** with 20% $Pd(OH)_2/C$ in 1:1 THF–MeOH afforded a mixture of the desired diol and partly deacetylated compounds, thin-layer chromatography of which showed the presence of more than seven components. Finally, the mixture was deacetylated by heating (60 °C) with hydrazine hydrate in EtOH for 2 h to exclusively give the deprotected octasaccharide **36** as a stable *tert*-butyldiphenylsilyl glycoside. The ^{1}H NMR spectrum of the synthetic compound was in good agreement with that of the related natural sample [9]. Further investigations are underway to explore the condensation of the synthesized octasaccharide with Ser and Thr derivatives.

In summary, we have demonstrated the synthetic routes to two types of O-glycans of core class 2, which carries either a linear tetralactosamine chain or a trimeric lactosamine-branching structure. Both syntheses were carried out by stereocontrolled methods using the appropriately protected mono- and di-lactosaminyl fluorides as the key glycosyl donors.

3. Experimental

General.—Optical rotations were determined with a Jasco DIP-370 polarimeter for solutions in $CHCl_3$ at 23 ± 2 °C, unless noted otherwise. Column chromatography was performed on Silica Gel-60 (E. Merck 70–230 mesh or 230–400 mesh). TLC and HPTLC were performed on Silica Gel 60 F_{254} (E. Merck). ^{1}H and ^{13}C NMR spectra were recorded with either a JEOL GSX500 [^{1}H (500 MHz)] or EX270 [^{1}H (270 MHz), ^{13}C (68 MHz)] spectrometer. Chemical shifts are expressed in ppm downfield from the signal for internal Me_4Si for solutions in $CDCl_3$. FAB mass spectra were measured with a JEOL HX110 spectrometer. 3-Nitrobenzyl alcohol was use as the matrix, unless noted otherwise.

*2,3,4,6-Tetra-*O*-acetyl-β-*D*-galactopyranosyl-(1 → 3)-2-azido-4,6-*O*-benzylidene-2-deoxy-*D*-galactopyranose* (**13**).—To a solution of **12** (1.0 g, 1.2 mmol) in THF (50 mL) were added AcOH (0.53 mL, 9.3 mmol) and M Bu_4NF/THF solution (4.64 mL, 4.64 mmol) at 0 °C. The mixture was stirred at room temperature overnight, concentrated in vacuo to 1/3 volume, then diluted with 1:1 EtOAc–ether, washed with water, aq $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed on silica gel with 1:4 hexane–EtOAc to afford **13** (0.55 g, 77%): $[\alpha]_D$ +12° (*c* 2.6), R_f 0.34 (1:4 hexane–EtOAc). NMR data ^{1}H: δ 7.10–7.62 (m, 5 H, Ar),

5.54 [s, 1 H, PhC*H*(O)$_2$], 5.40 (d, *J* 3.3 Hz, H-4b), 5.02 and 5.00 (2 dd, *J* 3.3, 8.6 Hz, H-3b) 4.76 and 4.75 (2 d, *J* 7.9 and *J* 8.3 Hz, H-1b), 4.55 and 4.54 (d, *J* 7.6 and *J* 7.5 Hz, H-1a), 2.10, 2.08, 2.06, and 2.04 (4 s, 12 H, 4 Ac), ^{13}C: 102.3 (C-1a), 100.6 [Ph*C*H(O)$_2$], 96.6 (C-1b). Anal. Calcd for $C_{27}H_{33}N_3O_{14} \cdot 0.45CHCl_3$: C, 48.97; H, 4.98; N, 6.25. Found: C, 48.92; H, 5.00; N, 6.05.

2,3,4,6-Tetra-O-*acetyl*-β-D-*galactopyranosyl*-(*1* → *3*)-*2-azido-4,6*-O-*benzylidene-2-deoxy*-D-*galactopyranosyl fluoride* (**10**).—To a solution of **13** (480 mg, 0.77 mmol) in dry CH_2Cl_2 (10 mL) was added DAST (0.44 mL, 4.6 mmol) at 0 °C. The mixture was stirred at 0 °C for 1 h, then diluted with EtOAc, washed with aq $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by chromatography on silica gel with 1:1 toluene–EtOAc to give **10** (α-fluoride: 275 mg, β-fluoride: 195 mg, 93%). α-fluoride: $[\alpha]_D$ +47° (*c* 1.3), R_f 0.40 (1:2 hexane–EtOAc). ^{1}H NMR data: δ 7.42–7.60 (m, 5 H, Ar), 5.89 (dd, *J* 2.0, 53.0 Hz, H-1a), 5.58 [s, 1 H, PhC*H*(O)$_2$], 5.40 (d, 1 H, *J* 3.6 Hz, H-4b), 5.32 (dd, 1 H, *J* 7.9, 10.5 Hz, H-2b), 5.02 (dd, 1 H, *J* 3.6, 10.5 Hz, H-3b), 4.08 (d, 1 H, *J* 7.9 Hz, H-1b), 4.45 (d, 1 H, *J* 3.0 Hz, H-4a), 2.06, 2.05, 2.04, and 1.98 (4 s, 12 H, 4 Ac). Anal. Calcd for $C_{27}H_{32}FN_3O_{13} \cdot 0.3$toluene: C, 53.51; H, 5.31. Found: C, 53.65; H, 5.37. β-fluoride: $[\alpha]_D$ +26° (*c* 0.9), R_f 0.23 (1:2 hexane–EtOAc). ^{1}H NMR data: δ 7.40–7.60 (m, 5 H, Ar), 5.54 [s, 1 H, PhC*H*(O)$_2$], 5.41 (d, 1 H, *J* 3.3 Hz, H-4b), 5.28 (dd, 1 H, *J* 7.9, 10.3 Hz, H-2b), 5.08 (dd, 1 H, *J* 7.9, 52.5 Hz, H-1a), 5.06 (dd, 1 H, *J* 3.3, 10.3 Hz, H-3b), 4.80 (d, 1 H, *J* 7.9 Hz, H-1b), 2.07, 2.06, 2.04, and 2.03 (4 s, 12 H, 4 Ac). Anal. Calcd for $C_{27}H_{32}FN_3O_{13}$: C, 52.64; H, 5.19. Found: C, 52.44; H, 5.26.

N-(*9-Fluorenylmethoxycarbonyl*)-O-[*2,3,4,6-tetra*-O-*acetyl*-β-D-*galactopyranosyl*-(*1* → *3*)-*2-azido-4,6*-O-*benzylidene-2-deoxy*-α- (**14**) *and* β-D-*galactopyranosyl*]-L-*serine allyl ester* (**15**).—A mixture of **10** (α-fluoride: 256 mg, 0.41 mmol) and **11** (181 mg, 0.49 mmol) in dry CH_2Cl_2 (5 mL) was added at −25 °C (ice–MeOH–dry ice) to a mixture of $AgClO_4$ (254 mg, 1.23 mmol), Cp_2ZrCl_2 (179 mg, 0.61 mmol) and dried 4A molecular sieves powder (1 g). The mixture was stirred at −25 to 10 °C for 3 h, then neutralized with aq $NaHCO_3$, and filtered through Celite. The filtrate was washed with aq $NaHCO_3$, brine, and concentrated in vacuo. The residue was purified by gel permeation on Bio-Beads S-X8 with toluene, and then by chromatography on silica gel to afford **14** (317 mg, 79%) and **15** (57 mg, 14%). The reaction with the β-fluoride gave a similar result. **14**: $[\alpha]_D$ +82° (*c* 2.5), R_f 0.20 (1:1 toluene–EtOAc). NMR data ^{1}H: δ 7.20–7.70 (m, 13 H, Ar), 5.70–5.90 (m, 2 H, NH, C*H*=CH$_2$), 5.51 [s, 1 H, PhC*H*(O)$_2$], 5.36 (d, 1 H, *J* 3.3 Hz, H-4b), 5.37 (d, 1 H, *J* 17.4 Hz, CH=C*H*$_2$), 5.27 (dd, 1 H, *J* 7.9, 10.6 Hz, H-2b), 5.01 (dd, 1 H, *J* 10.6, 3.3 Hz, H-3b), 4.99 (d, 1 H, *J* 3.7 Hz, H-1a), 4.70 (d, 1 H, *J* 7.9 Hz, H-1b), 2.14, 2.04, 2.01, and 1.98 (4 s, 12 H, 4 Ac), ^{13}C: 102.3 (C-1b), 100.5 [Ph*C*H(O)$_2$], 100.0 (C-1a). Anal. Calcd for $C_{48}H_{52}N_4O_{18} \cdot 1.5H_2O$: C, 57.65; H, 5.50; N, 5.60. Found: C, 57.57; H, 5.49; N, 5.27. **15**: $[\alpha]_D$ +28° (*c* 0.7), R_f 0.10 (3:1 toluene–EtOAc). NMR data ^{1}H: δ 7.15–7.80 (m, 13 H, Ar), 5.80–6.00 (m, 2 H, NH, C*H*=CH$_2$), 5.55 [s, 1 H, PhC*H*(O)$_2$], 5.40 (d, 1 H, *J* 3.3 Hz, H-4b), 5.12 (dd, 1 H, *J* 3.3, 10.6 Hz, H-3b), 4.78 (d, 1 H, *J* 7.9 Hz, H-1b), 4.48 (d, *J* 8.0 Hz, H-1a), 2.16, 2.08, 2.06, and 1.99 (4 s, 12 H, 4 Ac), ^{13}C: δ 102.3 (C-1a), 102.2 (C-1b), 100.7 [Ph*C*H(O)$_2$]. Anal. Calcd for $C_{48}H_{52}N_4O_{18} \cdot 1.5H_2O$: C, 57.45; H, 5.50; N, 5.60. Found: C, 57.65; H, 5.28; N, 5.12.

N-(9-Fluorenylmethoxycarbonyl)-O-[2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl-(1 → 3)-2-azido-2-deoxy-α-D-galactopyranosyl]-L-serine allyl ester (**7**).—To an ice-cooled solution of **15** (145 mg, 0.15 mmol) in dry CH_2Cl_2 (0.1 mL) was added 90% aq trifluoroacetic acid (1 mL). The resultant was stirred at 0 °C for 2 h, then concentrated in vacuo. The residue was chromatographed on silica gel with 1:1 EtOAc–toluene to give **7** (112 mg, 85%), $[\alpha]_D$ +60° (*c* 1.0), R_f 0.40 (2:1 EtOAc–toluene). ^{1}H NMR data: δ 7.18–7.80 (m, 13 H, Ar), 5.80–6.00 (m, 2 H, NH, C*H*=CH_2), 5.40 (d, 1 H, *J* 3.3 Hz, H-4b), 5.02 (dd, 1 H, *J* 3.3, 10.6 Hz, H-3b), 4.89 (d, 1 H, *J* 3.3 Hz, H-1a), 4.68 (d, 1 H, *J* 7.9 Hz, H-1b), 2.16, 2.08, 2.02, and 2.00 (4 s, 12 H, 4 Ac). FAB MS: *m/z* 885 $(M + 1)^+$, 907 $(M + Na)^+$.

4-Methoxyphenzyl 2,4-di-O-benzyl-3-O-chloroacetyl-6-O-(4-methylbenzoyl)-β-D-galactopyranosyl-(1 → 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**16**).—A mixture of **9** (870 mg, 0.82 mmol), triethylamine (2.2 mL), chloroacetic anhydride (480 mg, 2.8 mmol), and 4,4-dimethylaminopyridine (10 mg) in dry CH_2Cl_2 (10 mL) was stirred at room temperature for 1 h, and diluted with EtOAc (150 mL). After washing with 0.1 N HCl, aq $NaHCO_3$, and brine, the organic layer was dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by chromatography on silica gel to afford **16** (905 mg, 97%), R_f 0.56 (3:2 hexane–EtOAc). ^{1}H NMR data: δ 6.80–8.00 (m, 29 H, Ar), 5.62 (d, 1 H, *J* 8.3 Hz, H-1a), 4.92 (d, 2 H, *J* 11.6 Hz, PhCH_2), 4.70 (d, 1 H, *J* 11.3 Hz, PhCH_2), 4.62 (d, 1 H, *J* 11.8 Hz, PhCH_2), 5.49 (d, 1 H, *J* 11.3 Hz, PhCH_2), 3.72 (s, 2 H, COCH_2Cl), 2.42 (s, 3 H, OCH_3), 2.45 (s, 3 H, $C_6H_4CH_3$).

2,4-Di-O-benzyl-3-O-chloroacetyl-6-O-(4-methylbenzoyl)-β-D-galactopyranosyl-(1 → 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl fluoride (**8**).—To an ice-cooled mixture of **16** (850 mg, 0.77 mmol) in 2:2:1 toluene–CH_3CN–H_2O (500 mL) was added ceric ammonium nitrate (CAN, 10 g, 18.2 mmol). The mixture was stirred at room temperature for 2 h. The separated aqueous layer was extracted with EtOAc. The combined organic layer was washed with aq $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed on silica gel to afford **17** (780 mg, 87%).

To a solution of **17** (660 mg, 0.64 mmol) in dichloroethane (15 mL) was added DAST (511 μL, 3.86 mmol) at −15 °C. This mixture was stirred at −15 to 0 °C for 50 min, then quenched by addition of MeOH (1 mL). After concentration in vacuo, the residue was extracted with EtOAc, washed with aq $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated in vacuo. Chromatography of the crude product on silica gel afforded **8** (648 mg, 98%), R_f 0.45 (3:2 hexane–EtOAc). ^{1}H NMR data: δ 7.80–8.00 (d, 4 H, *J* 8.3 Hz, Phth), 6.80–7.60 (m, 25 H, Ar), 5.85 (dd, 1 H, *J* 7.6, 54 Hz, H-1a), 3.62 (s, 2 H, COCH_2Cl), 2.45 (s, 3 H, $C_6H_4CH_3$).

4-Methoxyphenyl 2,4-di-O-benzyl-3-O-chloroacetyl-6-O-(4-methylbenzoyl)-β-D-galactopyranosyl-(1 → 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 3)-2,4-di-O-benzyl-6-O-(4-methylbenzoyl)-β-D-galactopyranosyl-(1 → 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**18**).—A mixture of Cp_2HfCl_2 (48 mg, 0.13 mmol), AgOTf (65 mg, 0.25 mmol), and dried 4A molecular sieves powder (1.3 g) in dichloroethane (5 mL) was stirred at room temperature for 15 min, then cooled to −23 °C in a CCl_4–dry-ice bath. To this mixture was added a mixture of **8** (100 mg,

0.10 mmol) and **9** (86 mg, 0.08 mmol) in dichloroethane (5 mL). Stirring was continued at −23 °C for 3 h before aq $NaHCO_3$ (1 mL) was added to quench the reaction. The mixture was filtered through Celite, the filtrate was diluted with EtOAc, washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by chromatography on Bio-Beads S-X3 with toluene, and then on a short column of silica gel to afford **18** (135 mg, 81%), $[\alpha]_D$ +28° (*c* 1.2), R_f 0.24 (3:2 hexane–EtOAc). NMR data ^{1}H: δ 6.80–8.00 (m, Ar), 5.42 (d, 1 H, *J* 8.3 Hz, H-1a), 5.02 (d, 1 H, *J* 11.7 Hz, PhCH_2), 4.87 (d, 1 H, *J* 11.7 Hz, PhCH_2), 3.66 (s, 2 H, COCH_2Cl), 2.39 and 2.37 (2 s, 6 H, $C_6H_4CH_3$), ^{13}C: δ 103.0 (C-1b and C-1d), 99.9 (C-1c), 97.5 (C-1a). Anal. Calcd for $C_{121}H_{115}ClN_2O_{27}$: C, 70.40; H, 5.57; N, 1.35. Found: C, 70.74; H, 5.69; N, 1.36.

2,4-Di-O-benzyl-3-O-chloroacetyl-6-O-(4-methylbenzoyl)-β-D-galactopyranosyl-(1 → 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 3)-2,4-di-O-benzyl-6-O-(4-methylbenzoyl)-β-D-galactopyranosyl-(1 → 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl fluoride (**6**).—A mixture of **18** (280 mg, 0.14 mmol) and CAN (1.48 g, 2.71 mmol) in 2:2:1 toluene–CH_3CN–H_2O (75 mL) was stirred at room temperature for 2 h. The separated aqueous layer was extracted with EtOAc. The combined organic layer was washed with aq $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed on silica gel with 2:1 hexane–EtOAc to give **19** (190 mg). The solution of **19** (0.5 mmol) in dichloroethane (10 mL) was stirred with DAST (77 μL, 0.58 mmol) at 0 °C for 1 h. MeOH was added to quench the reaction. In the same manner as described for **8**, extractive workup and chromatography on silica gel gave **6** (190 mg, 73%), $[\alpha]_D$ +30° (*c* 1.4), R_f 0.50 (1:1 hexane–EtOAc). ^{1}H NMR data: δ 6.70–7.90 (m, Ar), 5.70 (dd, 1 H, *J* 8.0, 54 Hz, H-1a), 5.38 (d, 1 H, *J* 8.6 Hz, H-1c), 3.49 (s, 2 H, COCH_2Cl), 2.37 and 2.39 (2 s, 6 H, 2 $C_6H_4CH_3$).

N-(9-Fluorenylmethoxycarbonyl)-O-[2,4-di-O-benzyl-3-O-chloroacetyl-6-O-(4-methylbenzoyl)-β-D-galactopyranosyl-(1 → 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 3)-2,4-di-O-benzyl-6-O-(4-methylbenzoyl)-β-D-galactopyranosyl-(1 → 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl-(1 → 6)-[2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl-(1 → 3)]-2-azido-2-deoxy-α-D-galactopyranosyl]-L-serine allyl ester (**20**).—To a stirred mixture of **7** (12 mg, 14 μmol), Cp_2HfCl_2 (58 mg, 150 μmol), AgOTf (79 mg, 300 μmol), and dried 4A molecular sieves powder (1.2 g) in dry ether (2 mL), was added a solution of **6** (82 mg, 42 μmol) in a mixture of dry ether (1 mL) and CH_2Cl_2 (1 mL) at −23 °C. The resulting mixture was stirred at −23 °C to room temperature overnight. Aq $NaHCO_3$ was added to the reaction mixture, and the mixture was stirred for 5 min before being diluted with EtOAc and filtered though Celite. The filtrate was washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed on Bio-Beads S-X2 with toluene to give **20** (29 mg, 75%), $[\alpha]_D$ +43° (*c* 1.3), R_f 0.36 (1:1 hexane–EtOAc). ^{1}H NMR data: δ 6.75–7.95 (m, Ar), 5.84–5.90 (m, 1 H, C*H*=CH_2), 5.80 (d, 1 H, *J* 8.8 Hz, NH), 5.38 (d, 2 H, *J* 8.3 Hz, H-1b′ and H-1d′), 5.32 (d, 1 H, *J* 2.7 Hz, H-4b), 3.67 (s, 2 H, COCH_2Cl), 2.37 and 2.35 (2 s, 6 H, 2 $C_6H_4CH_3$), 2.05, 2.04, 2.01, and 1.97 (4 s, 12 H, 4 Ac). FABMS: *m/z* 2823 $(M + 1)^+$.

Acetylated derivative **21**.—^{1}H NMR data: δ 6.80–7.95 (m, Ar), 5.90 (m, 1 H,

C*H*=CH_2), 5.32 (d, 1 H, *J* 3.0 Hz, H-4b), 5.28 (d, 1 H, *J* 3.0 Hz, H-4a), 2.05, 2.04, 2.03, 2.01, and 1.98 (5 s, 15 H, 5 Ac).

N-*(9-Fluorenylmethoxycarbonyl)-*O-*{2,4-di-*O-*benzyl-6-*O-*(4-methylbenzoyl)-β-*D-*galactopyranosyl-(1 → 4)-3,6-di-*O-*benzyl-2-deoxy-2-phthalimido-β-*D-*glucopyranosyl-(1 → 3)-2,4-di-*O-*benzyl-6-*O-*(4-methylbenzoyl)-β-*D-*galactopyranosyl-(1 → 4)-3,6-di-*O-*benzyl-2-deoxy-2-phthalimido-β-*D-*glucopyranosyl-(1 → 6)-[2,3,4,6-tetra-*O-*acetyl-β-*D-*galactopyranosyl-(1 → 3)]-2-azido-2-deoxy-α-*D-*galactopyranosyl}-*L-*serine allyl ester* (**5**).—A mixture of **20** (25 mg, 9 μmol) and thiourea (3.5 mg, 46 μmol) in dry DMF (2 mL) was stirred at 90 °C under argon for 3 h, then concentrated in vacuo. The residue was purified by gel permeation on Sephadex LH-20 with 1:1 $CHCl_3$–MeOH and by chromatography on silica gel to afford **5** (20.7 mg, 85%), $[\alpha]_D$ +42° (*c* 1.1), R_f 0.69 (1:1 toluene–EtOAc). ^{1}H NMR data: δ 6.70–7.80 (m, Ar), 5.70–6.00 (m, 2 H, NH and C*H*=CH_2), 5.40 (d, 2 H, *J* 8.2 Hz, 2 GlcNPhth H-1), 5.32 (d, 1 H, *J* 3.0 Hz, H-4b), 5.02 (d, 1 H, *J* 11.6 Hz, PhCH_2), 2.36 (s, 6 H, 2 $C_6H_4CH_3$), 2.10, 2.05, 1.98, and 1.95 (4 s, 12 H, 4 Ac). FABMS: *m/z* 2749 $(M + 1)^+$.

N-*(9-Fluorenylmethoxycarbonyl)-*O-*{2,3,4,6-tetra-*O-*acetyl-β-*D-*galactopyranosyl-(1 → 4)-3,6-di-*O-*benzyl-2-deoxy-2-phthalimido-β-*D-*glucopyranosyl-(1 → 3)-2,4-di-*O-*benzyl-6-*O-*(4-methylbenzoyl)-β-*D-*galactopyranosyl-(1 → 4)-3,6-di-*O-*benzyl-2-deoxy-2-phthalimido-β-*D-*glucopyranosyl-(1 → 3)-2,4-di-*O-*benzyl-6-*O-*(4-methylbenzoyl)-β-*D-*galactopyranosyl-(1 → 4)-3,6-di-*O-*benzyl-2-deoxy-2-phthalimido-β-*D-*glucopyranosyl-(1 → 3)-2,4-di-*O-*benzyl-6-*O-*(4-methylbenzoyl)-β-*D-*galactopyranosyl-(1 → 4)-3,6-di-*O-*benzyl-2-deoxy-2-phthalimido-β-*D-*glucopyranosyl-(1 → 6)-[2,3,4,6-tetra-*O-*acetyl-β-*D-*galactopyranosyl-(1 → 3)]-2-azido-2-deoxy-α-*D-*galactopyranosyl}-*L-*serine allyl ester* (**22**).—To a stirred mixture of **5** (15 mg, 5 μmol), Cp_2HfCl_2 (10.3 mg, 27 μmol), AgOTf (13.8 mg, 54 μmol), and dried 4A molecular sieves powder (200 mg) in anhydrous ether (3 mL), was added a solution of **4** (20 mg, 12 μmol) in 1:1 ether–CH_2Cl_2 (2 mL) at −23 °C. The mixture was stirred at −23 °C for 3 h, then an additional amount (20 mg) of **4** in 1:1 ether–CH_2Cl_2 (2 mL) was added, and the resultant mixture was stirred further at −23 °C to room temperature overnight. The reaction was quenched by addition of aq $NaHCO_3$ before filtration through Celite. The filtrate was diluted with EtOAc, washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed on Bio-Beads S-X1 with toluene to afford **22** (20 mg, 82% based on consumed acceptor), $[\alpha]_D$ +11° (*c* 1), R_f 0.25 (2:1 toluene–EtOAc). NMR data ^{1}H: δ 6.75–7.95 (m, Ar), 5.95 (m, 1 H, C*H*=CH_2), 5.80 (d, 1 H, *J* 10.0 Hz, NH), 5.40, 5.21, 5.18, and 5.14 (4 d, 4 H, *J* 8.2 Hz, 4 GlcNPhth H-1), 2.37, 2.29, and 2.27 (3 s, 9 H, 3 $C_6H_4CH_3$), 2.17, 2.09, 2.06, 2.04, 2.01, 1.98, 1.97, and 1.93 (8 s, 24 H, 8 Ac), ^{13}C: δ 103.0, 101.5, 100.3, 100.2, 99.9, 98.5. FABMS: *m/z* 4521 $(M + Na)^+$.

*2,4-Di-*O-*acetyl-3,6-di-*O-*allyl-α and β-*D-*galactopyranosyl trichloroacetimidate* (**26**).—A mixture of **25** (80 mg, 0.23 mmol), trichloroacetonitrile (160 μL, 16 mmol) and Cs_2CO_3 (20 mg, 65 μmol) in dry CH_2Cl_2 (5 mL) was stirred at 0 °C for 30 min, then the insoluble solid was filtered off, and the filtrate was concentrated in vacuo. The crude product was chromatographed on silica gel with 2:1 hexane–EtOAc to give α-**26** (56 mg, 51%) and β-**26** (37 mg, 34%). For the coupling reaction with **28**, the α:β mixture was used.

α-trichloroacetimidate: $[\alpha]_D$ +104° (*c* 1.4), R_f 0.40 (2:1 hexane–EtOAc). NMR data ^{1}H: δ 8.60 (s, 1 H, NH), 6.56 (d, 1 H, *J* 3.3 Hz, H-1), 5.79–5.88 (m, 2 H, C*H*=CH$_2$), 5.63 (brd, 1 H, *J* 3.0 Hz, H-4), 5.22–5.30 (m, 3 H, H-2 and 2 CH=C*H*$_2$), 4.28 (brt, 1 H, *J* 6.6 Hz, H-5), 4.18 (m, 1 H, C*H*$_2$CH=CH$_2$), 3.97–4.03 (m, 3 H, C*H*$_2$CH=CH$_2$ and H-3), 3.92 (m, 1 H, C*H*$_2$CH=CH$_2$), 3.54 (dd, 1 H, *J* 5.8, 9.8 Hz, H-6), 3.45 (dd, 1 H, *J* 6.8, 9.8 Hz, H-6), 2.15 and 2.04 (2 s, 6 H, 2 Ac), ^{13}C: δ 20.6 and 20.7 (2*C*H$_3$CO), 67.0 (C-4), 67.7 (C-6), 68.9 (C-2), 70.4 (C-3), 70.6 (C-5), 72.3 and 72.5 (*C*H$_2$CH=CH$_2$), 94.1 (C-1), 117.3 and 117.7 (CH=*C*H$_2$), 134.1 (*C*H=CH$_2$), 160.9 (*C*=NH), 170.0 and 170.2 (*C*O). FABMS: *m/z* 327 [M − O(C=NH)CCl$_3$]$^+$, 488 (M + 1)$^+$, 510 (M + Na)$^+$.

β-trichloroacetimidate: $[\alpha]_D$ +52° (*c* 0.3), R_f 0.26 (2:1 hexane–EtOAc). NMR data ^{1}H: δ 8.66 (s, 1 H, NH), 5.75–5.88 (m, 2 H, C*H*=CH$_2$), 5.78 (d, 1 H, *J* 8.3 Hz, H-1), 5.55 (brd, 1 H, *J* 3.2 Hz, H-4), 5.38 (dd, 1 H, *J* 8.3, 9.8 Hz, H-2), 5.38 (dd, 2 H, *J* 1.5, 17.3 Hz, CH=C*H*$_2$), 5.26 (m, 2 H, CH=C*H*$_2$), 4.16 (m, 1 H, C*H*$_2$CH=CH$_2$), 4.02 (m, 1 H, C*H*$_2$CH=CH$_2$), 3.91–3.96 (m, 3 H, 2 C*H*$_2$CH=CH$_2$ and H-5), 3.59–3.63 (m, 2 H, H-3 and H-6), 3.51 (dd, 1 H, *J* 7.1, 9.8 Hz, H-6), 2.17 and 2.04 (2 s, 6 H, 2 Ac), ^{13}C: δ 20.8 and 20.9 (*C*H$_3$CO), 66.1 (C-4), 67.4 (C-6), 69.4 (C-2), 70.5 and 72.5 (*C*H$_2$CH=CH$_2$), 73.5 (C-5), 76.5 (C-3), 96.4 (C-1), 117.5 and 117.8 (CH=*C*H$_2$), 134.0 and 134.1 (*C*H=CH$_2$), 161.4 (*C*=NH), 169.1 and 170.2 (*C*O). FABMS: *m/z* 327 [M − O(C=NH)CCl$_3$]$^+$, 488 (M + 1)$^+$.

*2,4-Di-*O*-acetyl-3,6-di-*O*-allyl-α and β-*D*-galactopyranosyl fluoride* (**27**).—Compound **25** was converted into **27** (82%, α:β = 1:1) according to the procedure described for **10**. The α:β mixture was used for the next reaction. α-fluoride: $[\alpha]_D$ +91° (*c* 1.3), R_f 0.41 (2:1 hexane–EtOAc). ^{1}H NMR data: δ 5.78–5.93 (m, 2 H, C*H*=CH$_2$), 5.78 (dd, 1 H, *J* 2.6, 53.8 Hz, H-1), 5.59 (dd, *J* 1.0, 3.3 Hz, H-4), 5.31 (m, 1 H, CH=C*H*$_2$), 5.17–5.26 (m, 3 H, CH=C*H*$_2$), 5.09 (ddd, 1 H, *J* 2.6, 10.2, 24.7 Hz, H-2), 4.25 (brt, 1 H, *J* 5.8 Hz, H-5), 4.16 (m, 1 H, C*H*$_2$CH=CH$_2$), 3.93–4.06 (m, 3 H, C*H*$_2$CH=CH$_2$), 3.89 (dd, 1 H, *J* 3.3, 10.2 Hz, H-3), 3.54 (dd, 1 H, *J* 5.9, 9.9 Hz, H-6), 3.46 (dd, 1 H, *J* 5.9, 9.9 Hz, H-6), 2.14 and 2.13 (2 s, 6 H, 2 Ac). FABMS: *m/z* 327 (M − F)$^+$, 368 (M + Na)$^+$.

β-fluoride: $[\alpha]_D$ +42° (*c* 1.4), R_f 0.31 (2:1 hexane–EtOAc). ^{1}H NMR data: δ 5.73–5.91 (m, 2 H, C*H*=CH$_2$), 5.48 (brs, 1 H, H-4), 5.19 (dd, 1 H, *J* 7.3, 54.4 Hz, H-1), 5.15–5.30 (m, 5 H, H-2 and 4 CH=C*H*$_2$), 4.14 (m, 1 H, C*H*$_2$CH=CH$_2$), 3.83–4.05 (m, 4 H, 3 C*H*$_2$CH=CH$_2$ and H-5), 3.61 (dd, 1 H, *J* 6.3, 9.6 Hz, H-6), 3.49–3.57 (m, 2 H, H-3 and H-6), 2.16 and 2.12 (2 s, 6 H, 2 Ac). FABMS: *m/z* 327 (M − F)$^+$, 347 (M + 1)$^+$.

tert-*Butyldiphenylsilyl 2,4-di-*O*-acetyl-3,6-di-*O*-allyl-β-*D*-galactopyranosyl-(1 → 3)-2-azido-4,6-*O*-benzylidene-2-deoxy-β-*D*-galactopyranoside* (**29**).—(a) To a stirred mixture of **26** (520 mg, 1.06 mmol), **28** (380 mg, 0.72 mmol), and dried 4A molecular sieves powder (1.2 g) in dichloroethane (15 mL), was added $BF_3 \cdot OEt_2$ (38 μL, 0.30 mmol) at −15 °C. The resulting mixture was stirred at −15 °C for 2 h before aq $NaHCO_3$ was added to quench the reaction. The resultant was filtered through Celite. The filtrate was washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed on silica gel with 2:1 hexane–EtOAc to afford **29** (460 mg, 75%).

(b) To a stirred mixture of AgOTf (3.70 g, 14.4 mmol), $SnCl_2$ (2.74 g, 14.4 mmol) and dried 4A molecular sieves powder (9 g) in dichloroethane (10 mL) was added a mixture of **27** (2.5 g, 7.2 mmol) and **28** (3.2 g, 6.0 mmol) in dichloroethane (10 mL) at −20 °C. Stirring was continued at −20 °C to room temperature overnight. The reaction was quenched with aq $NaHCO_3$, diluted with ethyl acetate, and filtered through Celite. The filtrate was washed with water and brine, dried (Na_2SO_4), and concentrated in vacuo. Purification of the residue on silica gel afforded **29** (2.77 g, 54%), $[\alpha]_D$ +50° (*c* 0.7), R_f 0.25 (2:1 hexane–EtOAc). NMR data ^{1}H: 7.20–7.80 (m, 15 H, Ar), 5.80 (m, 2 H, 2 C*H*=CH_2), 5.46 [s, 1 H, PhC*H*(O)$_2$], 5.40 (d, 1 H, *J* 2.9 Hz, H-4b), 5.22 (d, 2 H, *J* 17.5 Hz, CH=CH_2), 5.15 (d, 2 H, *J* 11.2 Hz, CH=CH_2), 4.65 (d, 2 H, *J* 7.91 Hz, H-1a and H-1b), 2.12 and 2.09 (2 s, 6 H, 2 Ac), 1.12 (s, 9 H, ^{t}Bu), ^{13}C: δ 102.0 (C-1b), 100.3 [Ph*C*H(O)$_2$], 97.0 (C-1a). Anal. Calcd for $C_{45}H_{55}N_3O_{12}Si$: C, 63.06; H, 6.46; N, 4.89. Found: C, 63.07; H, 6.53; N, 4.62.

tert-*Butyldiphenylsilyl 3,6-di*-O-*allyl*-β-D-*galactopyranosyl*-(*1* → *3*)-*2-azido-4,6*-O-*benzylidene-2-deoxy*-β-D-*galactopyranoside* (**30**).—To an ice-cooled solution of **29** (100 mg, 1.2 mmol) in THF (2.5 mL) were added 1.25 N aq LiOH (0.37 mL, 0.46 mmol) and then 31% H_2O_2 (0.7 mL). The mixture was stirred at 0 °C for 1 h and then diluted with EtOAc, washed with cold water and brine, dried (Na_2SO_4), and concentrated in vacuo. Chromatography of the residue on silica gel with 1:1 toluene–EtOAc afforded **30** (60 mg, 67%), $[\alpha]_D$ +10° (*c* 2.7), R_f 0.58 (1:1 toluene–EtOAc). NMR data ^{1}H: δ 7.20–7.80 (m, 15 H, Ar), 5.80–6.00 (m, 2 H, 2 C*H*=CH_2), 5.45 [s, 1 H, PhC*H*(O)$_2$], 5.35 (dd, 2 H, *J* 1.2, 17,1 Hz, 2 CH=CH_2), 5.26 (dd, 1 H, *J* 1.2, 10.4 Hz, CH=CH_2), 4.44 (d, 2 H, *J* 7.6 Hz, H-1a and H-1b), 2.80 and 2.54 (2 s, 2 H, 2 OH), 1.14 (s, 9 H, ^{t}Bu), ^{13}C: δ 104.7 (C-1b), 100.9 [Ph*C*H(O)$_2$], 97.0 (C-1a). Anal. Calcd for $C_{41}H_{51}N_3O_{10}Si \cdot 0.5H_2O$: C, 62.90; H, 6.70; N, 5.36. Found: C, 62.90; H, 6.64; N, 4.96.

tert-*Butyldiphenylsilyl 3,6-di*-O-*allyl-4,6-di*-O-*benzyl*-β-D-*galactopyranosyl*-(*1* → *3*)-*2-azido-4,6*-O-*benzylidene-2-deoxy*-β-D-*galactopyranoside* (**31**).—A mixture of 60% NaH (23 mg, 0.58 mmol, washed with hexane), **30** (100 mg, 0.13 mmol) in dry THF (1 mL), and benzyl bromide (62 μL, 0.52 mmol) was stirred at 55 °C for 3 h. After cooling, the reaction mixture was quenched with MeOH, diluted with ether, washed with water and brine, dried (Na_2SO_4), and concentrated in vacuo. Chromatography of the residue on silica gel afforded **31** (69 mg, 77%), $[\alpha]_D$ +16° (*c* 0.5), R_f 0.39 (2:1 hexane–EtOAc). ^{1}H NMR data: δ 7.20–7.80 (m, 25 H, Ar), 5.72–6.00 (m, 2 H, 2 C*H*=CH_2), 5.45 [s, 1 H, PhC*H*(O)$_2$], 1.12 (s, 9 H, ^{t}Bu). Anal. Calcd for $C_{55}H_{64}N_3O_{10}Si$: C, 69.16; H, 6.75; N, 4.40. Found: C, 69.12; H, 6.67; N, 4.30.

tert-*Butyldiphenylsilyl 4,6-di*-O-*benzyl*-β-D-*galactopyranosyl*-(*1* → *3*)-*2-azido-4,6*-O-*benzylidene-2-deoxy*-β-D-*galactopyranoside* (**24**).—A degassed suspension of [Ir(COD)(PMePh$_2$)$_2$]PF_6 (8 mg) in dry THF (3.5 mL) was stirred in an atmosphere of H_2 until the mixture became colourless. The solution was degassed again and added under Ar to a stirred solution of **31** (230 mg, 0.24 mmol) in dry THF (3.5 mL). The resultant mixture was stirred at room temperature for 30 min. To this reaction mixture were added MeOH (3 mL) and *p*-TsOH monohydrate (10 mg). Stirring was continued for 1 h at room temperature. The reaction was quenched by addition of Et_3N (1 mL) before concentration. The residue was chromatographed on silica gel with 1:1 toluene–

EtOAc to afford **24** (150 mg, 80%), $[\alpha]_D$ +33° (*c* 0.8), R_f 0.43 (1:2 hexane–EtOAc). ^{1}H NMR data: δ 7.20–7.80 (m, 20 H, Ar), 5.12 (d, 1 H, *J* 11.3 Hz, PhCH_2), 4.89 (d, 1 H, *J* 11.3 Hz, PhCH_2), 4.71 (d, 1 H, *J* 11.5 Hz, PhCH_2), 4.63 (d, 1 H, *J* 11.5 Hz, PhCH_2), 4.50 (d, 2 H, *J* 7.6 Hz, H-1a and H-1b), 1.12 (s, 9 H, ^{t}Bu). Anal. Calcd for $C_{42}H_{51}N_3O_{10}Si$: C, 64.18; H, 6.54; N, 5.35. Found: C, 64.14; H, 6.52; N, 5.05.

tert-*Butyldiphenylsilyl 2,3,4,6-tetra*-O-*acetyl*-β-D-*galactopyranosyl-(1 → 4)-3,6-di*-O-*acetyl-2-deoxy-2-phthalimido*-β-D-*glucopyranosyl-(1 → 6)-[2,3,4,6-tetra*-O-*acetyl*-β-D-*galactopyranosyl-(1 → 4)-3,6-di*-O-*acetyl-2-deoxy-2-phthalimido*-β-D-*glucopyranosyl-(1 → 3)]-2,4-di*-O-*benzyl*-β-D-*galactopyranosyl-(1 → 3)-[2,3,4,6-tetra*-O-*acetyl*-β-D-*galactopyranosyl-(1 → 4)-3,6-di*-O-*acetyl-2-deoxy-2-phthalimido*-β-D-*glucopyranosyl-(1 → 6)]-2-azido-2-deoxy*-β-D-*galactopyranoside* (**32**).—A mixture of Cp_2HfCl_2 (317 mg, 0.83 mmol), AgOTf (430 mg, 1.67 mmol), and 4A molecular sieves powder (1 g) in CH_2Cl_2 (2 mL) was stirred at room temperature for 15 min, then cooled to −23 °C on a CCl_4–dry-ice bath. A solution of **24** (84 mg, 0.11 mmol) in CH_2Cl_2 (1 mL) and that of **23** (460 mg, 0.63 mmol) in CH_2Cl_2 (1 mL) were added successively to the above mixture. The resultant mixture was stirred at −23 °C to room temperature overnight. The mixture was quenched with aq NaHCO3, diluted with EtOAc, and filtered through Celite. The filtrate was washed with brine, dried(Na_2SO_4), and concentrated in vacuo. The residue was purified by chromatography on Bio-Beads S-X3 and then by preparative TLC to afford **32** (136 mg, 44%), $[\alpha]_D$ +0.6° (*c* 0.9), R_f 0.69 (4:1 EtOAc–hexane). ^{1}H NMR data: δ 7.10–7.90 (m, Ar), 5.60–5.75 (m, 3 H, 3 GlcNPhth H-3), 5.57, 5.49, and 5.33 (d, 1 H, *J* 8.8 Hz, 3 GalNPhth H-1), 5.33 (d, 3 H, *J* 2.4 Hz, 3 Gal H-4), 4.72 (d, 1 H, *J* 10.7 Hz, PhCH_2), 2.15, 2.14, 2.13, 2.10, 2.08, 2.06, 2.04, 2.03, 2.02, 1.99, 1.98, and 1.97 (12 s, 54 H, 18 Ac), 0.92 (s, 9 H, ^{t}Bu). Anal. Calcd for $C_{138}H_{156}N_6O_{61}Si$: C, 57.09; H, 5.43; N, 2.89. Found C 57.26; H, 5.40; N, 2.71.

Acetylated derivative **33**.—^{1}H NMR data: δ 6.90–7.90 (m, Ar), 5.71 (dd, 1 H, *J* 8.3, 10.2 Hz, Gal H-3), 5.62 and 5.57 (2 dd, 2 H, *J* 8.3, 10.7 Hz, 2 Gal H-3), 5.37 (d, 1 H, *J* 8.3 Hz, Gal H-1), 5.40 and 5.30 (2 d, 2 H, *J* 8.8 Hz, 2 Gal H-1), 5.33 (brs, 4 H, 3 Gal and $GalN_3$ H-4), 1.75–2.18 (19 s, 57 H, 19 Ac), 0.92 (s, 9 H, ^{t}Bu).

tert-*Butyldiphenylsilyl 2,3,4,6-tetra*-O-*acetyl*-β-D-*galactopyranosyl-(1 → 4)-2-acetamido-3,6-di*-O-*acetyl-2-deoxy*-β-D-*glucopyranosyl-(1 → 6)-[2,3,4,6-tetra*-O-*acetyl*-β-D-*galactopyranosyl-(1 → 4)-2-acetamido-3,6-di*-O-*acetyl-2-deoxy*-β-D-*glucopyranosyl-(1 → 3)]-2,4-di*-O-*benzyl*-β-D-*galactopyranosyl-(1 → 3)-[2,3,4,6-tetra*-O-*acetyl*-β-D-*galactopyranosyl-(1 → 4)-2-acetamido-3,6-di*-O-*acetyl-2-deoxy*-β-D-*glucopyranosyl-(1 → 6)]-4*-O-*acetyl-2-azido-2-deoxy*-β-D-*galactopyranoside* (**34**).—A mixture of **32** (96 mg, 33 μmol) and ethylenediamine (8 mL) in BuOH (30 mL) was heated at 90 °C under Ar for 28 h and concentrated in vacuo. The volatile material was removed by coevaporation with toluene in vacuo. The residue was dissolved in pyridine (2 mL) and stirred with Ac_2O (2 mL) at room temperature for 18 h. The reaction mixture was concentrated in vacuo. The residue was passed through Sephadex LH-20, then purified by preparative TLC to give **34** (50 mg, 56%), $[\alpha]_D$ −8.5° (*c* 1.3), R_f 0.70 (10:1 $CHCl_3$–MeOH). ^{1}H NMR data: δ 7.20–7.80 (m, 20 H, Ar), 5.35 (s, 4 H, 3 Gal and $GalN_3$ H-4), 1.90–2.10 (22 s, 66 H, 22 Ac), 1.06 (s, 9 H, ^{t}Bu). Anal. Calcd for $C_{122}H_{158}N_6O_{59}Si \cdot H_2O$: C, 54.27; H, 5.97; N, 3.11. Found: C, 54.13; H, 5.87; N, 3.00. FABMS: *m/z* 2680 $(M + 1)^+$, 2702 $(M + Na)^+$, 2623 $(M - OAc)^+$.

tert-*Butyldiphenylsilyl 2,3,4,6-tetra*-O-*acetyl*-β-D-*galactopyranosyl*-(*1 → 4*)-*2-acetamido-3,6-di*-O-*acetyl-2-deoxy*-β-D-*glucopyranosyl*-(*1 → 6*)-[*2,3,4,6-tetra*-O-*acetyl*-β-D-*galactopyranosyl*-(*1 → 4*)-*2-acetamido-3,6-di*-O-*acetyl-2-deoxy*-β-D-*glucopyranosyl*-(*1 → 3*)]-*2,4-di*-O-*benzyl*-β-D-*galactopyranosyl*-(*1 → 3*)-[*2,3,4,6-tetra*-O-*acetyl*-β-D-*galactopyranosyl*-(*1 → 4*)-*2-acetamido-3,6-di*-O-*acetyl-2-deoxy*-β-D-*glucopyranosyl*-(*1 → 6*)]-*2-acetamido-4*-O-*acetyl-2-deoxy*-β-D-*galactopyranoside* (**35**).—To an ice-cooled solution of **34** (60 mg, 22 μmol) in pyridine (2 mL) was added freshly distilled thioacetic acid (4.5 mL, 63 mmol). The resultant was stirred at 0 °C–room temperature overnight. The reaction mixture was diluted with $CHCl_3$, washed with 0.15 N HCl, aq $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed on silica gel with $CHCl_3$, then with 15:1 $CHCl_3$–MeOH. The product was further purified by preparative TLC to give **35** (35 mg, 58%), $[\alpha]_D$ −15° (*c* 0.9). ^{1}H NMR data: δ 7.22–7.80 (m, 20 H, Ar), 6.44 (d, 1 H, *J* 9.3 Hz, NH), 5.98 (d, 1 H, *J* 9.2 Hz, NH), 2.16–1.98 (m, 24 Ac), 0.98 (s, 9 H, ^{t}Bu). FABMS: 2697 $(M + 1)^+$, 2720 $(M + Na)^+$.

tert-*Butyldiphenylsilyl* β-D-*galactopyranosyl*-(*1 → 4*)-*2-acetamido-2-deoxy*-β-D-*glucopyranosyl*-(*1 → 6*)-[β-D-*galactopyranosyl*-(*1 → 4*)-*2-acetamido-2-deoxy*-β-D-*glucopyranosyl*-(*1 → 3*)]-β-D-*galactopyranosyl*-(*1 → 3*)-[β-D-*galactopyranosyl*-(*1 → 4*)-*2-acetamido-2-deoxy*-β-D-*glucopyranosyl*-(*1 → 6*)]-*2-acetamido-2-deoxy*-β-D-*galactopyranoside* (**36**).—A mixture of **35** (20 mg, 7 μmol), and 20% $Pd(OH)_2/C$ (25 mg) in 3:5 THF–MeOH (4 mL), was stirred in an atmosphere of H_2 at room temperature for 4 days and filtered. The filtrate was concentrated in vacuo to give a mixture of the debenzylated products (19 mg), the minor components of which comprised some acetyl-migrated and/or partly deacetylated derivatives. The heterogeneous mixture of the debenzylated compounds (7 mg) was dissolved in MeOH (1 mL) and heated with hydrazine hydrate (1 mL) at 60 °C for 2 h. After concentration of the mixture in vacuo, the residue was purified by chromatography on Sephadex LH-20 with MeOH to quantitatively afford **36**, R_f 0.52 (1:1:1 BuOH–EtOH–H_2O). ^{1}H NMR data (CD_3OD): δ 7.72–7.40 (m, 10 H, Ar), 4.78 (d, 1 H, *J* 8.4 Hz, GlcNAc H-1), 4.65 (d, 1 H, *J* 8.0 Hz, GlcNAc H-1), 4.55 (d, 1 H, *J* 8.4 Hz, GlcNAc H-1), 4.47 (d, 3 H, *J* 7.6 Hz, 3 Gal H-1), 4.46 and 4.44 (2 d, 2 H, *J* 7.7 Hz, Gal and GalNAc H-1), 2.07, 2.05, 2.04, 2.01 (4 s, 12 H, 4 Ac), 1.05 (s, 9 H, ^{t}Bu). FABMS (glycerol as matrix): 1718 $(M + 1)^+$.

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