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Linear Synthesis of the Tumor-Associated Carbohydrate Antigens Globo-H, SSEA-3, and Gb3

Folkert Bosse, Lisa A. Marcaurelle, and Peter H. Seeberger*

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

seeberg@mit.edu

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The tumor-associated carbohydrate antigens Globo-H, SSEA-3, and Gb3 were synthesized in a linear fashion using glycosyl phosphate monosaccharide building blocks. All of the building blocks were prepared from readily available common precursors. The difficult α-(1→4-*cis*)-galactosidic linkage was installed using a galactosyl phosphate donor with high selectivity. Introduction of the *β*-galactosamine unit required the screening a variety of amine protecting groups to ensure good donor reactivity and protecting group compatibility. An *N*-trichloroacetyl-protected galactosamine donor performed best for the installation of the *β*-glycosidic linkage. Conversion of the trichloroacetyl group to the *N*-acetyl group was achieved under mild conditions, fully compatible with the presence of multiple glycosidic bonds. This synthetic strategy is expected to be amenable to the synthesis of the globo-series of tumor antigens on solid-support.

Introduction

Altered glycosylation is a universal feature of cancer cells, and certain carbohydrate structures are markers of many tumors.[1,2] Like normal cells during embryonic development, tumor cells adhere to a variety of cell types, invade tissues, and undergo activation and rapid growth. Since changes in cellular glycosylation profiles are common during embryogenesis, it is not surprising that altered glycosylation is also characteristic of malignant transformation and tumor activation. A variety of changes occur in malignant cells, such as the loss of expression or excessive expression of certain structures, the persistence of incomplete or truncated structures, and the appearance of novel structures.[3] Carbohydrates are displayed on the surface of both normal and tumor cells in the context of membrane glycosphingolipids (GSLs) and glycoproteins. The carbohydrate epitopes of GSLs have been analyzed following extraction from whole cells and have been extensively studied for the treatment of cancer by both passive and active immunotherapy.[1,2]

One major class of GSLs is the globo-series of tumor antigens. Some prominent members of this family include Globo-H, Gb5, and Gb3 (Figure 1). Globo-H was first isolated and identified as an antigen on breast cancer cells[4,5] and is also expressed in prostate[6] and ovarian cancer.[7] A synthetic Globo-H construct is currently being evaluated and has shown very promising results as an antitumor vaccine in clinical trials.[8−10] Gb5 is abundant in testicular cancer[11−13] and is present during embryonic development.[14] In recognition of this latter property, the pentasaccharide moiety of Gb5 is often referred to as the stage specific embryonic antigen-3 (SSEA-3). Finally, Gb3 is highly enriched in ovarian cancer and Burkitt's B-cell lymphoma.[15]

Due to their importance as tumor markers and potential anticancer vaccines, several members of the globo-series of GSLs have been targets of total syntheses. Globo-H was first synthesized by Danishefsky and coworkers using the glycal assembly approach.[16,17] Further

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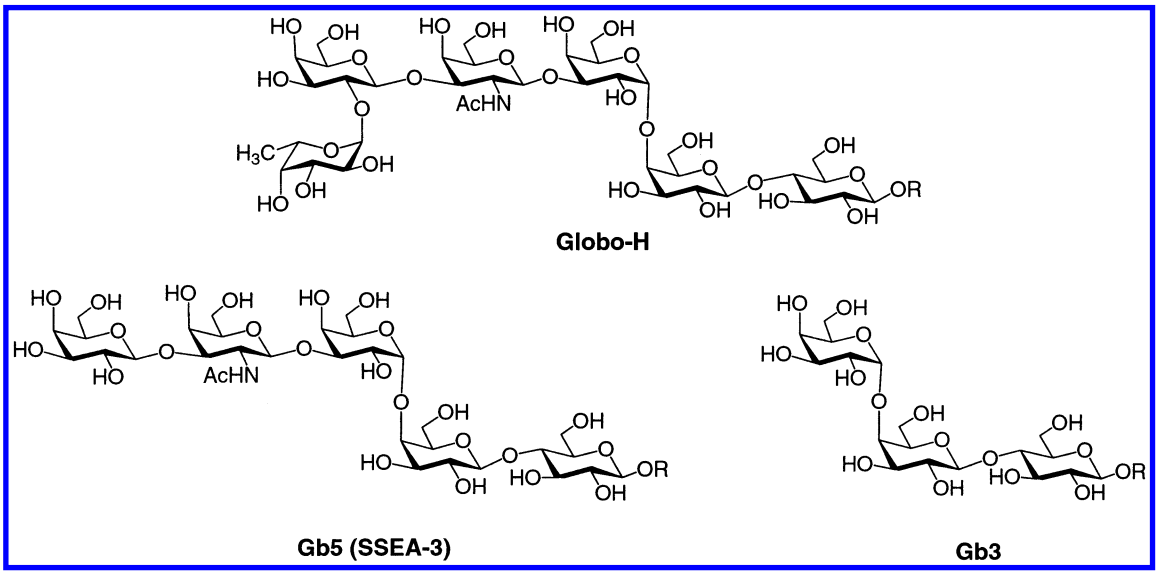

FIGURE 1. Globo-series of tumor-associated antigens (R = ceramide).

syntheses used trichloroacetimidate building blocks[18] and a two-directional glycosylation strategy.[19] Most recently, Wong and co-workers prepared Globo-H via a one-pot strategy using the computer program OptiMer to aid in synthesis planning.[20] The pentasaccharide SSEA-3 has been synthesized by Ogawa,[21] Danishefsky,[22] and Magnusson,[23] while the assembly of Gb3 has been reported by several groups.[24]

In this paper, we describe a solution-phase synthesis of the tumor antigens Globo-H, SSEA-3, and Gb3. A strictly linear strategy for the assembly of these oligosaccharides was investigated in anticipation of automating the synthesis on solid support.[25] Given their compatibility with solid-phase oligosaccharide chemistry, glycosyl phosphates were employed as donors in our solution-phase studies.[26,27] Glycosyl phosphates can be readily prepared from glycals using a one-pot procedure,[27] as well as from glycosyl trichloroacetimidates.[28] The use of glycosyl phosphate building blocks enabled the successful installation of the difficult α-galactosidic linkage, as well as the *β*-galactosamine moiety, in good yield with high stereoselectivity. The strategy described here is expected to be amenable to the preparation of the target tumor antigens on solid-support.

Results and Discussion

In keeping with our goal of automating solution-phase protocols on solid-support, six glycosyl donors were selected as building blocks for a sequential assembly of the Globo-H hexasaccharide **1** (Scheme 1). SSEA-3 and Gb3 became accessible by deprotection of the corresponding synthetic intermediates. This linear strategy differs markedly from previous routes, which had been striving for highest convergence. Acetyl and levulinoyl esters were chosen as temporary hydroxyl protecting groups, given their ease of removal[29] and compatibility with solid-phase synthesis.[25,30] The *n*-pentenyl group was selected for protection of the reducing end sugar in order to mimic the linker used during automated solid-phase synthesis.[25,31] In addition, the *n*-pentenyl glycoside can serve as a leaving group in a late-stage glycosylation[32] or as a handle for bioconjugation.[33]

Synthesis of the Lactose Disaccharide. The construction of the target oligosaccharides began with the preparation of the reducing end lactose disaccharide. Two monosaccharide building blocks had to be synthesized. Glucosyl phosphate **2** (Scheme 2) and galactosyl phosphate **3** were prepared using a one-pot procedure starting from 3,6-di-*O*-benzyl glucal **8**[29] and 3,6-di-*O*-benzyl galactal **10**,[34] respectively. It should be emphasized that while treatment of galactal **9** with benzyl bromide and sodium hydride at 0 °C[34] produced **10** in low yield (20%),

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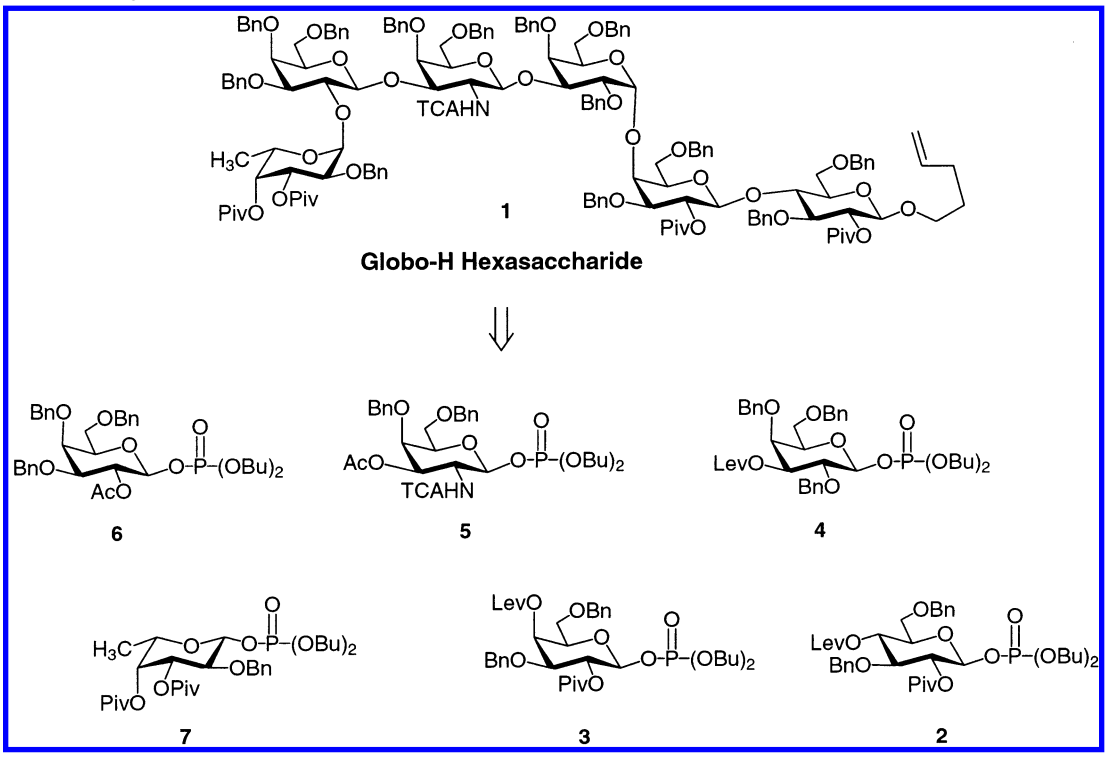
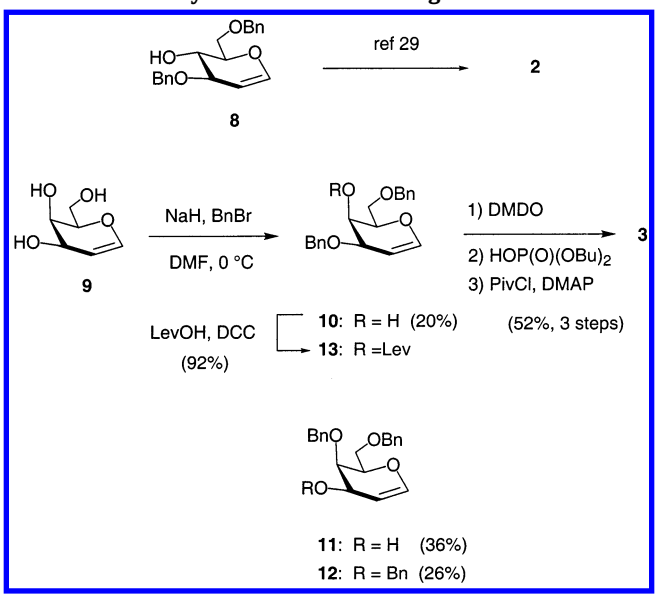
SCHEME 1. Retrosynthesis of the Protected Globo-H Hexasaccharide



SCHEME 2. Synthesis of Building Blocks 2 and 3



two other important intermediates, 4,6-di-*O*-benzyl galactal **11** (36%) and tri-*O*-benzyl galactal **12** (26%), were also generated in this reaction and were easily separated by column chromatography. Therefore, this procedure served as a starting point for the preparation of all four galactosyl building blocks (**3**−**6**) used in this synthesis. Protection of galactal **10** as the levulinate ester **13** (92%), followed by subsequent conversion to the glycosyl phosphate and esterification, produced **3** in 52% yield.

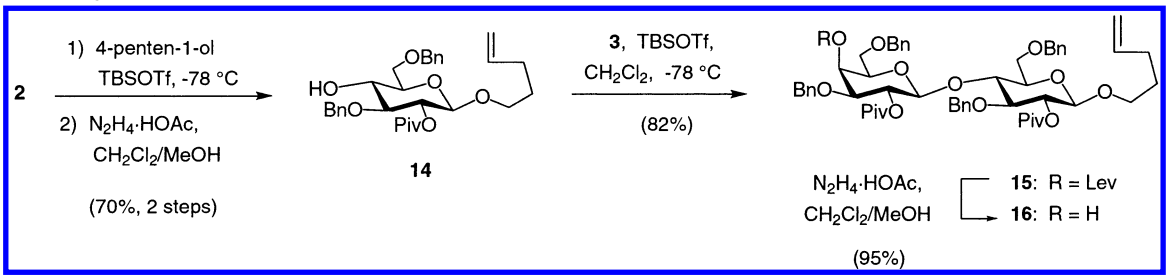
The assembly of the lactose disaccharide commenced with the installation of the *n*-pentenyl glycoside, followed by removal of the levulinoyl ester as described previously (Scheme 3).[29] Union of phosphate **3** with pentenyl glycoside **14** afforded lactose disaccharide **15** (82%), which upon deprotection with hydrazine yielded 95% of acceptor **16**.

Installation of the α-Galactosidic Linkage. A major challenge in the synthesis of the globo-series of tumor antigens is the installation of the α-(1→4-*cis*)-galactosidic linkage of the reducing end trisaccharide. While α-galactosidic linkages have been formed using a variety of glycosylating agents, the stereochemical outcome of this coupling is difficult to predict and is highly dependent on the glycosyl acceptor. High selectivity for all glycosylation reactions is mandatory, since this strategy is being developed for use on solid-support and cannot take advantage of the purification of reaction intermediates. To install the difficult α-linkage, we chose to explore the use of glycosyl phosphate **4**, given its compatibility with solid-phase oligosaccharide synthesis.

Since the presence of a benzyl ether at C2 was required to favor α-selectivity, donor **4** could not be synthesized directly from a glycal using the standard one-pot procedure[27,35] but was generated from a glycosyl trichloroacetimidate.[28] Hence, 4,6-di-*O*-benzyl galactal **11** was protected as the *p*-methoxybenzyl (PMB) ether **17**[17] (97%) and then converted to the allyl glycoside **18** (α:β = 1:5, 79%) by epoxidation with DMDO and solvolysis with allyl alcohol (Scheme 4). Installation of the C2 benzyl group **19** (71%), followed by exchange of the PMB ether for a levulinoyl ester, furnished **20** in 93% yield. Palladium-mediated cleavage of the allyl glycoside afforded the intermediate lactol, which was immediately converted to trichloroacetimidate **21** (76%, two steps) by reaction with trichloroacetonitrile and DBU. Transformation of the α-trichloroacetimidate (**21**) to the β-phosphate (**4**) was achieved in 90% yield upon exposure to dibutyl phos-

(35) Treatment of the intermediate glycosyl phosphate with sodium hydride and benzyl bromide leads to migration of the phosphate to yield the C2 phosphoryl benzyl glycoside.

SCHEME 3. Synthesis of the Lactose Disaccharide



SCHEME 4. Synthesis of the C2 Benzyl-Protected Galactose Donor

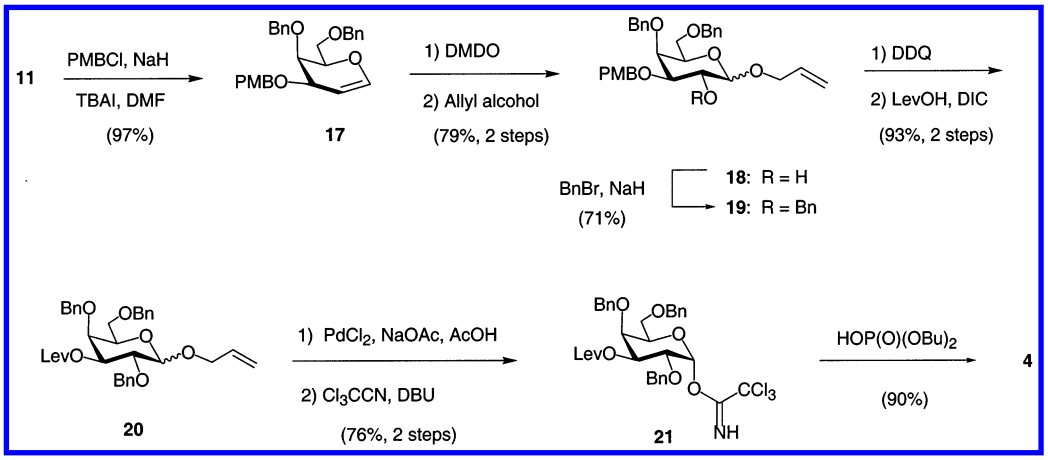
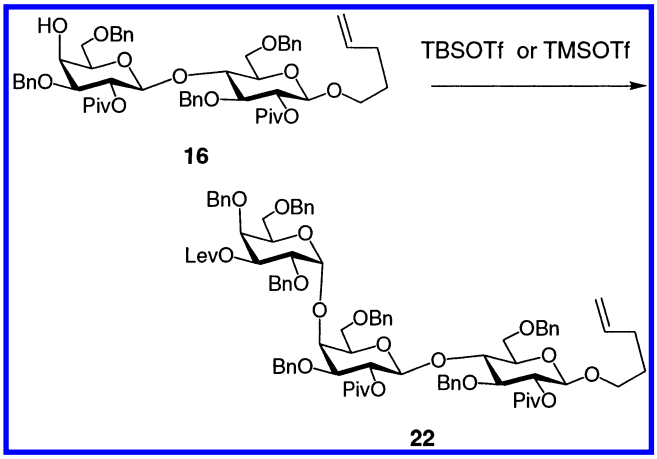


TABLE 1. Coupling Conditions Used To Generate the Gb3 Trisaccharide

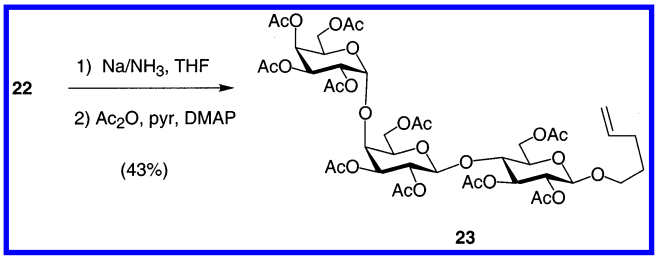


donor	solvent	temp (°C)	α:β selectivity	yield (%)
4	CH_2Cl_2	−78	11:1	58
4	CH_2Cl_2/THF	−20	1:1	80
4	CH_2Cl_2/THF	−78	20:1	61
4	CH_2Cl_2/Et_2O	−78	20:1	79
21	CH_2Cl_2	0	α only	54

phate. It should be noted that attempts to generate the glycosyl phosphate directly from the lactol led to the formation of 1,1 coupled disaccharides.

Synthesis of the Gb3 Trisaccharide. With the desired glycosyl phosphate in hand, conditions for glycosylation of the hindered lactose acceptor **16** were explored (Table 1). Initial reaction conditions employing TBSOTf as a promoter in dichloromethane at −78 °C led to the formation of target trisaccharide **22** in 58% yield but with only moderate α-selectivity (α:β = 11:1). Both

SCHEME 5. Deprotection of the Gb3 Trisaccharide

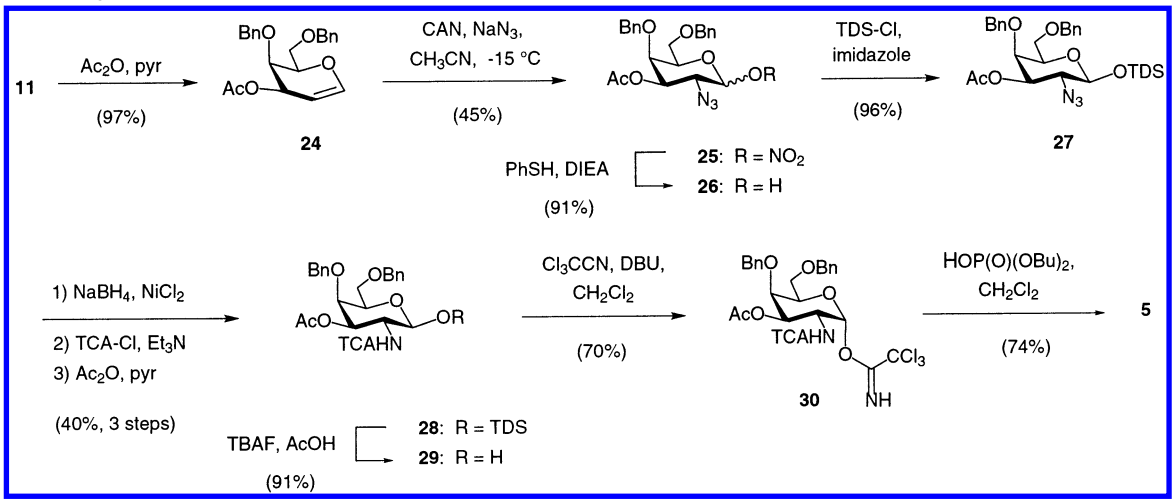


the yield and stereoselectivity of the reaction improved when a mixture of ether/dichloromethane was used (79%, α:β = 20:1). Reaction temperature proved crucial for achieving high α-selectivity. When the reaction was carried out at −20 °C, a 1:1 mixture of α- and β-anomers was obtained. The intermediate trichloroacetimidate **21** also proved to be a suitable glycosylating agent for the preparation of trisaccharide **22**. Reaction of **21** with disaccharide **16** at 0 °C in dichloromethane yielded α-linked trisaccharide **22** in 54% yield.

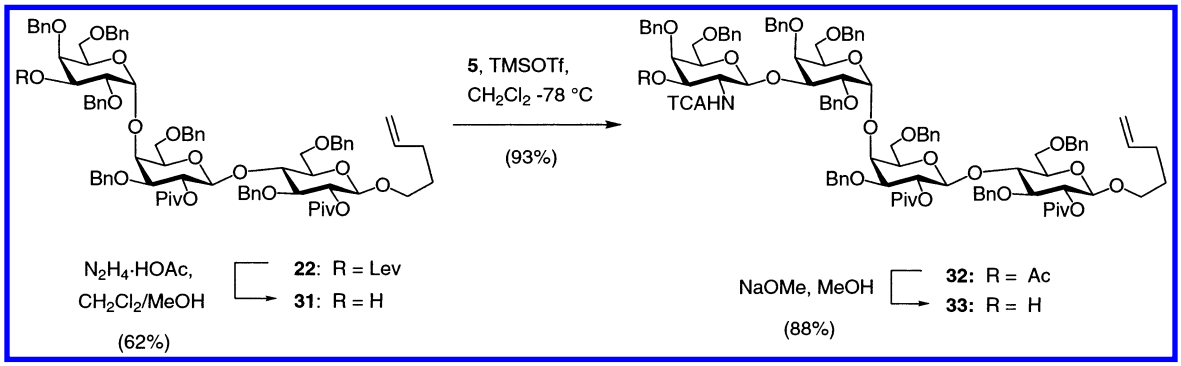
Removal of all ester and benzyl ether protecting groups of trisaccharide **22** was accomplished by a dissolving-metal reduction (Scheme 5). Subsequent treatment with acetic anhydride in pyridine furnished the peracetylated Gb3 trisaccharide **23** in 43%.

Synthesis of the Galactosamine Building Block. Having installed the challenging α-galactosidic linkage, we turned our attention to the synthesis of a suitable glycosylating agent for the introduction of the galactosamine unit. An important consideration in designing the galactosamine building block was the selection of an amine protecting group. A number of strategies for masking the C2 amino group were investigated, including protection as the *N*-carbamate (Troc and Cbz), *N*-tri-

SCHEME 6. Synthesis of *N*-TCA-Protected Galactosamine Donor 5



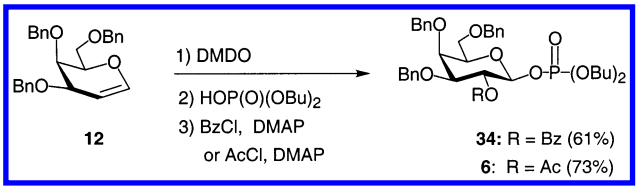
SCHEME 7. Installation of *N*-TCA-Protected Galactosamine



chloroacetamide, *N*-phthalimide, and azide. Glycosyl phosphate **5** bearing a C2 *N*-trichloroacetamide performed best. The *N*-trichloroacetyl (TCA) group has been reported to ensure high β-selectivity in glycosylation reactions, can be converted directly into the corresponding *N*-acetyl group under mild conditions that are fully compatible with sensitive glycosidic bonds, and has been used in the synthesis of several complex oligosaccharides.[36–39]

The synthesis of the required galactosamine donor commenced with 4,6-di-*O*-benzyl galactal **11**, which was protected as the C3 acetate **24**[40] and then subjected to an azidonitration reaction (Scheme 6). The resulting product (**25**) was hydrolyzed by exposure to thiophenol in the presence of diisopropylethylamine (DIEA), and lactol **26** was protected as the anomeric silyl ether (**27**) using thexyldimethylsilyl (TDS) chloride (96%). Reduction of the azido group with sodium borohydride in ethanol afforded the C2 amine, which was then treated with trichloroacetyl (TCA) chloride in the presence of triethylamine. Due to partial de-*O*-acetylation during the reaction with sodium borohydride, the crude mixture was reacetylated with acetic anhydride in pyridine to procure *N*-TCA protected **28** in 40% yield. Removal of the anomeric TDS group under the agency of TBAF (91%) followed by reaction of lactol **29** with trichloroacetonitrile in the presence of DBU afforded trichloroacetimidate **30** in 70% yield. Conversion of **30** into glycosyl phosphate **5** was accomplished in good yield (74%) by reaction with dibutyl phosphate.

SCHEME 8. Synthesis of C2 Ester-Protected Galactose Donors 6 and 34



Reaction of trisaccharide **22** with hydrazine acetate provided acceptor **31** in 62% yield (Scheme 7). Glycosylation of **31** with **5** at −78 °C in the presence of TMSOTf proceeded in excellent yield (93%) to afford exclusively the desired β-linked product **32**. In comparison, attempts to glycosylate **31** with trichloroacetimidate donor **30** using a catalytic amount of TMSOTf resulted only in acceptor decomposition. Deacetylation of tetrasaccharide **32** with sodium methoxide provided acceptor **33** in 88% yield.

Synthesis of the SSEA-3 Pentasaccharide. Elaboration of tetrasaccharide **33** to the SSEA-3 precursor required the introduction of a galactose unit at the C3 position of the terminal galactosamine residue. To achieve

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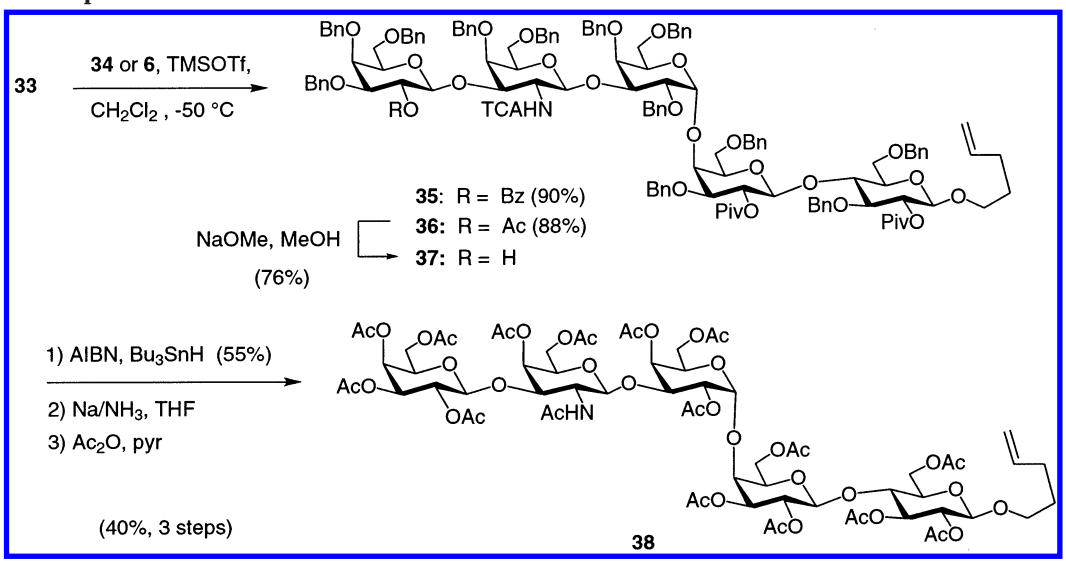
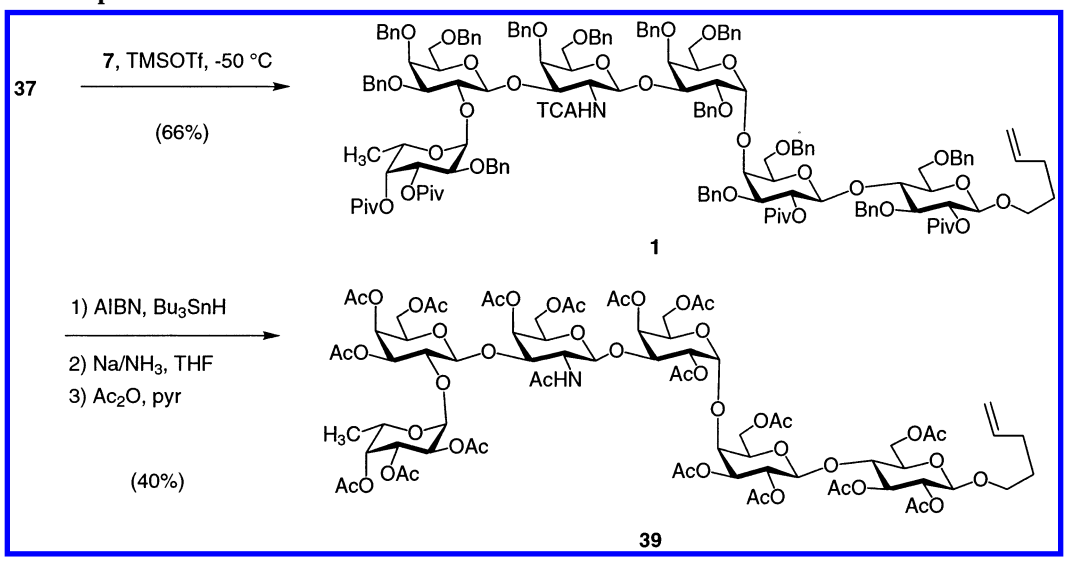
SCHEME 9. Completion of the SSEA-3 Pentasaccharide



SCHEME 10. Completion of the Globo-H Hexasaccharide



high β-selectivity in the glycosylation reaction, we investigated the use of a galactose building block bearing a C2 ester. Initially, a benzoate group was chosen as a means of protection for the C2 hydroxyl group. Building block **34**[27] was synthesized in one-pot starting from tri-*O*-benzyl galactal **12** (Scheme 8). While the union of phosphate **34** with tetrasaccharide **33** proceeded smoothly (90% yield) (Scheme 9), subsequent deprotection of the C2 benzoyl ester (**35**) proved problematic. Complete removal of the benzoate could not be achieved without concomitant loss of the pivaloyl esters. Replacement of the C2 benzoyl group of donor **34** with an acetate (**6**) enabled the successful synthesis of the target pentasaccharide. Glycosylation of tetrasaccharide **33** with phosphate donor **6** under the agency of TMSOTf provided pentasaccharide **36** in good yield (88%). Deacetylation of **36** with sodium methoxide cleanly afforded compound **37** (76%).

Following conversion of the *N*-TCA group to the corresponding *N*-acetamide with tributylstannane and AIBN, the protected pentasaccharide was converted to peracetylated SSEA-3 **38** (40%) by a dissolving-metal reduction and reaction with acetic anhydride. It is important to note that prior conversion of the *N*-TCA-group to the *N*-acetamide was crucial for the success of this reaction sequence. Subjection of *N*-TCA-protected pentasaccharide **37** to dissolving-metal reduction led to cleavage of the β-galactosamine linkage, producing trisaccharide **23** after peracetylation.

Completion of the Globo-H Hexasaccharide. Fucosyl phosphate **7** had performed well previously for the installation of α-(1→2-*cis*) glycosidic linkages[29] and was employed for the completion of the target hexasaccharide. Glycosylation of pentasaccharide **37** with fucosyl phosphate **7** provided protected Globo-H hexasaccharide **1** in 66% yield with complete α-selectivity (Scheme 10). Deprotection of **1** via dissolving-metal reduction as above provided peracetylated Globo-H **39** in 40% yield. NMR and mass spectral analysis of **39** was in accordance with previously reported data.[33]

Conclusions

In summary, the synthesis of three members of the globo-series of tumor antigens was accomplished in a

linear fashion using six glycosyl phosphate building blocks. In the context of these syntheses, methods for the installation of α-galactosidic and *β*-galactosamine linkages using glycosyl phosphates were developed. The strategy devised for this solution-phase synthesis is currently being applied to the synthesis of the globo-series of tumor antigens on solid-support in a fully automated fashion.

Experimental Section

General Methods. All chemicals were reagent grade and used as supplied, unless otherwise noted. Dichloromethane (CH_2Cl_2), tetrahydrofuran (THF), diethyl ether (Et_2O), and toluene were purified by a JT Baker Cycle-Trainer Solvent Delivery System. Analytical thin-layer chromatography was performed on silica gel 60 F_{254} plates (0.25 mm). Compounds were visualized by dipping the plates in a cerium sulfate-ammonium molybdate solution followed by heating. Flash chromatography was performed using forced flow of the indicated solvent on Silicylce silica (230−400 mesh). NMR spectra (^{1}H at 400 MHz, ^{13}C at 100 MHz) were recorded in $CDCl_3$ as the solvent and chemical shifts are reported in parts per million (δ) relative to $CHCl_3$ as an internal reference. ^{31}P spectra (120 MHz) are reported in δ relative to H_3PO_4 (0.0 ppm) as an external reference. Optical rotations were measured at 24 °C.

3,6-Di-*O*-benzyl-4-*O*-levulinoyl-D-galactal 13. Galactal **10**[34] (3.94 g, 10.7 mmol) was dissolved in CH_2Cl_2 (80 mL) and cooled to 0 °C. DCC (3.53 g, 17.1 mmol), DMAP (131 mg, 1.07 mmol), and levulinic acid (1.5 mL, 15.0 mmol) were added, and the mixture was stirred for 14 h at room temperature. The mixture was filtered, washed twice with water, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (3:1 hexane/EtOAc) to afford 4.20 g (92%) of **13** as a pale yellow oil. $[\alpha]_D$: +1.13 (c = 1.6, CH_2Cl_2). IR (thin film): 2920, 1738, 1717, 1362, 1155, 1099 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28−7.18 (m, 10 H), 6.32 (dd, J = 6.3, 1.8 Hz, 1 H), 5.56−5.52 (m, 1 H), 4.68−4.65 (m, 1 H), 4.57 (d, J = 11.8 Hz, 1 H), 4.50 (d, J = 11.7 Hz, 1 H), 4.45 (d, J = 11.7 Hz, 1 H), 4.39 (d, J = 11.8 Hz, 1 H), 4.17−4.15 (m, 1 H), 4.12−4.08 (m, 1 H), 3.60 (dd, J = 9.8, 6.2 Hz, 1 H), 3.50 (dd, J = 9.8, 6.3 Hz, 1 H), 2.67−2.53 (m, 4 H), 2.07 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.55, 172.47, 144.65, 138.18, 137.86, 128.62, 128.57, 128.26, 128.01, 127.87, 101.35, 74.56, 73.87, 71.15, 69.63, 68.61, 63.57, 38.17, 30.00, 28.29. ESI-MS: m/z (M + Na)$^+$ calcd 447.1778, obsd 447.1752.

Dibutyl 3,6-Di-*O*-benzyl-4-*O*-levulinoyl-2-*O*-pivaloyl-*β*-D-galactopyranoside Phosphate 3. Galactal **13** (0.831 g, 2.55 mmol) was dissolved in CH_2Cl_2 (15 mL) and cooled to 0 °C. DMDO (0.08 M in acetone, 45 mL, 3.6 mmol) was added and the reaction was stirred for 20 min. The solvent was evaporated at 0 °C and the residue dissolved in CH_2Cl_2 (40 mL) and cooled to −78 °C. A solution of dibutyl phosphate (0.56 mL, 2.8 mmol) in CH_2Cl_2 (10 mL) was added dropwise. After stirring for 10 min, the mixture was warmed to 0 °C, and DMAP (1.24 g, 10.2 mmol) and pivaloyl chloride (0.63 mL, 5.10 mmol) were added. After stirring for 14 h the solvent was removed in vacuo, and the residue was purified by flash chromatography (1:1 hexane/EtOAc), yielding 980 mg (52%) of **3** as a colorless oil. $[\alpha]_D$: +25.2 (c = 1.28, CH_2Cl_2). IR (thin film): 2928, 1740, 1494, 1277, 1050 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.23 (m, 10 H), 5.67−5.66 (m, 1 H), 5.23−5.21 (m, 2 H), 4.69 (d, J = 11.4 Hz, 1 H), 4.51−4.50 (m, 2 H), 4.38 (d, J = 11.4 Hz, 1 H), 4.06−3.98 (m, 4 H), 3.88−3.87 (m, 1 H), 3.65−3.54 (m, 3 H), 2.74−2.62 (m, 4 H), 2.15 (s, 3 H), 1.63−1.58 (m, 4 H), 1.40−1.32 (m, 4 H), 1.19 (s, 9 H), 0.93−0.87 (m, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.56, 177.17, 172.05, 137.77, 137.26, 128.62, 128.58, 128.50, 128.28, 128.23, 128.09, 128.05, 128.01, 96.97, 77.15, 73.10, 71.71, 70.31, 68.21, 68.12, 67.34, 66.09, 38.18, 32.28. 32.21, 30.00, 28.17, 27.33, 18.78, 18.75, 13.77, 13.74. ^{31}P NMR (120 MHz, $CDCl_3$): δ −2.12. ESI-MS: m/z (M + Na)$^+$ calcd 757.3323, obsd 757.3313.

***n*-Pentenyl 3,6-Di-*O*-benzyl-4-*O*-levulinoyl-2-*O*-pivaloyl-*β*-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-*β*-D-glucopyranoside 15.** Glycosyl phosphate **3** (1.83 g, 2.49 mmol) and monosaccharide **14**[29] (1.44 g, 2.81 mmol) were coevaporated three times with toluene, dissolved in CH_2Cl_2 (60 mL), and cooled to −78 °C. TBSOTf (0.83 mL, 3.61 mmol) was added and the mixture was warmed slowly to −60 °C. After 1 h Et_3N (5 mL) was added and the mixture was poured into a saturated solution of $NaHCO_3$ (100 mL). The aqueous phase was extracted twice with CH_2Cl_2, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (3:1 hexane/EtOAc) to afford 2.12 g (82%) of **15** as a colorless oil. $[\alpha]_D$: −1.03 (c = 1.28, CH_2Cl_2). IR (thin film): 3438, 2970, 2932, 2871, 1738, 1367, 1277 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.20 (m, 20 H), 5.76−5.38 (m, 1 H), 5.59 (d, J = 3.0 Hz, 1 H), 5.10 (dd, J = 10.0, 8.1 Hz, 1 H), 4.95−5.04 (m, 4 H), 4.77 (d, J = 12.1 Hz, 1 H), 4.69 (d, J = 11.4 Hz, 1 H), 4.56 (d, J = 10.7 Hz, 1 H), 4.46−4.36 (m, 4 H), 4.32−4.29 (m, 2 H), 4.07 (app t, J = 9.3 Hz, 1 H), 3.89−3.83 (m, 1 H), 3.77−3.70 (m, 2 H), 3.65−3.60 (m, 1 H), 3.54−3.51 (m, 1 H), 3.47−3.42 (m, 1 H), 3.38−3.28 (m, 4 H), 2.73−2.49 (m, 4 H), 2.08 (s, 3 H), 2.13−2.06 (m, 2 H), 1.72−1.64 (m, 2 H), 1.18 (s, 9 H), 1.15 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.85, 176.97, 176.75, 172.11, 138.89, 138.26, 138.12, 138.02, 137.63, 128.73, 128.65, 128.57, 128.41, 128.36, 128.26, 128.19, 128.03, 127.89, 127.87, 127.81, 127.69, 127.47, 127.39, 75.39, 75.31, 74.62, 73.76, 72.39, 72.24, 71.41, 71.15, 69.07, 68.05, 67.44, 66.31, 38.93, 38.89, 38.15, 30.21, 29.87, 28.93, 28.10, 27.43, 27.33.

***n*-Pentenyl 3,6-Di-*O*-benzyl-2-*O*-pivaloyl-*β*-D-galacto-pyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-*β*-D-gluco-pyranoside 16.** Disaccharide **15** (1.98 g, 1.91 mmol) was dissolved in CH_2Cl_2 (100 mL). A solution of hydrazine acetate (193 mg, 2.10 mmol) in MeOH (10 mL) was added, and the mixture was stirred for 1 h at room temperature and concentrated. The residue was purified by flash chromatography (4:1 hexane/EtOAc), yielding 1.70 g (95%) of **16** as a colorless oil. $[\alpha]_D$: +13.5 (c = 0.80, CH_2Cl_2). IR (thin film): 2928, 1738, 1134, 1062 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39−7.19 (m, 20 H), 5.83−5.76 (m, 1 H), 5.20 (dd, J = 9.8, 8.1 Hz, 1 H), 5.05−4.95 (m, 4 H), 4.76 (d, J = 12.1 Hz, 1 H), 4.65 (d, J = 11.8 Hz, 1 H), 4.56 (d, J = 10.9 Hz, 1 H), 4.51 (d, J = 11.8 Hz, 1 H), 4.47−4.38 (m, 3 H), 4.36 (d, J = 8.0 Hz, 1 H), 4.31 (d, J = 11.9 Hz, 1 H), 4.05 (app t, J = 9.3 Hz, 1 H), 4.02−4.01 (m, 1 H), 3.89−3.83 (m, 1 H), 3.63 (app t, J = 9.1 Hz, 1 H), 3.57 (dd, J = 9.5, 6.6 Hz, 1 H), 3.47−3.31 (m, 5 H), 2.25 (br s, 1 H), 2.13−2.06 (m, 2 H), 1.68−1.64 (m, 4 H), 1.19 (s, 9 H), 1.18 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.08, 176.82, 139.00, 138.31, 138.29, 138.21, 137.50, 128.69, 128.63, 128.57, 128.24, 128.17, 127.95, 127.90, 127.88, 127.80, 127.69, 127.28, 114.99, 101.51, 99.79, 81.05, 79.42, 75.40, 75.35, 74.74, 73.76, 73.74, 73.35, 72.51, 71.57, 71.15, 69.09, 68.46, 68.18, 65.78, 38.98, 38.91, 30.24, 28.96, 27.47, 27.34. ESI-MS: m/z (M + Na)$^+$ calcd 961.4709, obsd 961.4725.

Allyl 4,6-Di-*O*-benzyl-3-*O*-*p*-methoxybenzyl-α/*β*-D-galactopyranoside 18. To a solution of di-*O*-benzyl galactal **11**[34] (1.26 g, 3.86 mmol) in DMF (20 mL) were added NaH (176 mg, 4.4 mmol), *p*-methoxybenzyl chloride (600 *μ*L, 4.4 mmol), and TBAI (70 mg, 0.19 mmol) at 0 °C. The reaction was stirred for 16 h at room temperature, diluted with EtOAc, washed three times with water, and dried over $MgSO_4$. The organic phase was concentrated in vacuo and the crude residue was purified by flash chromatography (6:1 hexanes/EtOAc) to afford 1.65 g (97%) of **17**[17] as a colorless oil. Compound **17** (1.65 g, 3.70 mmol) was dissolved in CH_2Cl_2 (30 mL) and cooled to 0 °C. A solution of DMDO (0.08 M in acetone, 60 mL, 4.8 mmol) was added and the mixture was stirred for 10 min and then concentrated in vacuo at 0 °C. The resulting residue was dissolved in allyl alcohol (30 mL) and stirred at room temper-

ature for 16 h. The solution was concentrated and the crude product was purified by flash chromatography (3:1 hexanes/EtOAc) to afford 1.52 g (79%, α:β = 1:5) of **18** as a colorless oil. IR (thin film): 3460, 2914, 2869, 2107, 1612, 1513, 1454, 1248, 1078 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, β-anomer): δ 7.39−7.28 (m, 14 H), 6.91 (app d, J = 8.6 Hz, 2 H), 5.98−5.92 (m, 1 H), 5.32 (dd, J = 17.2, 1.4 Hz, 1 H), 5.21 (app d, J = 10.4 Hz, 1 H), 4.91 (d, J = 11.6 Hz, 1 H), 4.71−4.59 (m, 2 H), 4.52−4.44 (m, 2 H), 4.42−4.36 (m, 1 H), 4.32 (d, J = 7.7 Hz, 1 H), 4.16−4.12 (m, 1 H), 4.00−3.97 (m, 1 H), 3.93 (app d, J = 2.5 Hz, 1 H), 3.38 (s, 3 H), 3.66−3.59 (m, 2 H), 3.44 (dd, J = 9.8, 2.8 Hz, 1 H), 2.42 (br s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.75, 138.92, 138.26, 130.48, 129.29, 128.88, 128.69, 128.62, 128.34, 128.26, 128.23, 128.00, 118.25, 114.35, 114.30, 102.42, 82.05, 75.09, 74.38, 74.16, 73.99, 73.14, 72.45, 71.60, 70.39, 69.15, 55.71, 21.51, 14.64. ESI-MS: m/z $(M + Na)^+$ calcd 543.2359, obsd 543.2359.

Allyl 2,4,6-Tri-*O*-benzyl-3-*O*-*p*-methoxybenzyl-α/*β*-D-galactopyranoside 19. To a solution of **18** (1.5 g, 2.9 mmol) in DMF (20 mL) were added NaH (140 mg, 3.5 mmol) and benzyl bromide (420 μL, 3.5 mmol) at 0 °C. The mixture was stirred for 4 h and then quenched with water, diluted with EtOAc, and washed twice with water and once with brine. The organic phase was dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (6:1 hexanes/EtOAc) to afford 1.60 g (71%, α:β = 1:5) of **19** as a white solid. IR (thin film): 2915, 2867, 2360, 2341, 1513, 1454, 1248, 1099, 1077 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, β-anomer): δ 7.43−7.28 (m, 19 H), 6.90 (d, J = 11.6 Hz, 1 H), 6.89 (d, J = 11.5 Hz, 1 H), 6.01−5.93 (m, 1 H), 5.35 (dd, J = 18.0, 2.0 Hz, 1 H), 5.20 (dd, J = 12.2, 1.4 Hz, 1 H), 4.97 (d, J = 11.7 Hz, 1 H), 4.96 (d, J = 10.8 Hz, 1 H), 4.80 (d, J = 10.8 Hz, 1 H), 4.47−4.42 (m, 3 H), 4.17−4.13 (m, 1 H), 3.90−3.86 (m, 1 H), 3.84 (s, 3 H), 3.61 (dd, J = 6.3, 3.0 Hz, 1 H), 3.57−3.52 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.56, 139.21, 139.08, 138.34, 134.63, 131.04, 129.64, 129.58, 128.86, 128.80, 128.71, 128.67, 128.59, 128.44, 128.32, 128.22, 128.16, 127.98, 127.95, 117.47, 103.38, 82.31, 80.02, 75.70, 74.86, 73.97, 73.84, 73.39, 73.15, 69.34, 68.63, 55.70. ESI-MS: m/z $(M + Na)^+$ calcd 633.2823, obsd 633.2828.

Allyl 2,4,6-Tri-*O*-benzyl-3-*O*-levulinoyl-α/*β*-D-galactopyranoside 20. To a solution of **19** (1.20 g, 1.96 mmol) in CH_2Cl_2 (20 mL) were added water (1.0 mL) and DDQ (556 mg, 2.45 mmol). The reaction was stirred for 1 h at room temperature and then poured into a saturated solution of $NaHCO_3$ and extracted three times with CH_2Cl_2. The organic phases were combined, dried over $MgSO_4$, filtered, and concentrated. The crude residue was dissolved in CH_2Cl_2 (20 mL), and levulinic acid (318 mg, 2.74 mmol), DIC (490 μL, 3.14 mmol), and DMAP (24 mg, 0.20 mmol) were added. The mixture was stirred for 16 h at room temperature and then diluted with CH_2Cl_2, washed with H_2O and saturated aqueous $NaHCO_3$, dried over $MgSO_4$, and filtered. The solvent was removed in vacuo and the residue was purified by flash chromatography (3:1 → 2:1 hexanes/EtOAc) to afford 1.07 g (93%, α:β = 1:5) of **20** as a colorless oil. IR (thin film): 2920, 1738, 1718, 1361, 1209, 1158, 1074 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, β-anomer): δ 7.38−7.28 (m, 15 H), 5.98−5.93 (m, 1 H), 5.35 (dd, J = 17.2, 1.6 Hz, 1 H), 5.20 (dd, J = 10.5, 1.4 Hz, 1 H), 4.97−4.91 (m, 2 H), 4.73−4.66 (m, 2 H), 4.57−4.42 (m, 5 H), 4.17−4.14 (m, 1 H), 3.96 (app d, J = 2.9 Hz, 1 H), 3.84 (dd, J = 10.2, 7.7 Hz, 1 H), 3.69−3.76 (m, 1 H), 3.62−3.55 (m, 2 H), 2.76−2.39 (m, 4 H), 2.15 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.74, 172.64, 138.99, 138.70, 138.25, 134.39, 128.85, 128.77, 128.67, 128.63, 128.54, 128.46, 128.40, 128.31, 128.24, 128.20, 128.12, 128.02, 127.97, 117.63, 103.21, 77.30, 75.59, 75.34, 75.10, 74.82, 73.89, 73.79, 73.57, 70.63, 68.78, 38.19, 30.24, 28.38, 28.30. ESI-MS: m/z $(M + Na)^+$ calcd 611.2615, obsd 611.2619.

2,4,6-Tri-*O*-benzyl-3-*O*-levulinoyl-α-D-galactopyranosyl Trichloracetimidate 21. Compound **20** (906 mg, 1.54 mmol) was dissolved in AcOH (9 mL). Water (300 μL) was added, followed by NaOAc (290 mg, 3.54 mmol) and $PdCl_2$ (314 mg, 1.77 mmol), and the mixture was stirred for 16 h at room temperature. The reaction mixture was diluted with EtOAc and washed with water, saturated aqueous $NaHCO_3$, and brine. The organic phase was dried over $MgSO_4$, filtered, and concentrated to give the desired lactol as a pale yellow oil. The crude lactol was dissolved in CH_2Cl_2 (10 mL), and trichloroacetonitrile (5 mL) and DBU (10 μL) were added. The mixture was stirred for 1 h at room temperature and concentrated. The resulting residue was purified by flash chromatography (2:1 hexanes/EtOAc, 2% Et_3N) to yield 794 mg (76%) of compound **21** as a colorless oil. $[\alpha]_D$: +67.9 (c = 1.90, CH_2Cl_2). IR (thin film): 3337, 2920, 2871, 1739, 1718, 1672, 1353, 1289, 1155, 1103, 1074, 1027 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.57 (s, 1 H), 7.36−7.28 (m, 15 H), 6.54 (d, J = 3.5 Hz, 1 H), 5.39 (dd, J = 10.5, 2.9 Hz, 1 H), 4.76 (d, J = 11.3 Hz, 1 H), 4.73 (d, J = 10.3 Hz, 1 H), 4.64 (d, J = 12.1 Hz, 1 H), 4.57 (d, J = 11.4 Hz, 1 H), 4.50 (d, J = 11.8 Hz, 1 H), 4.43 (d, J = 11.8 Hz, 1 H), 4.30 (app t, J = 6.6 Hz, 1 H), 4.24 (dd, J = 10.5, 3.5 Hz, 1 H), 4.17 (app d, J = 2.3 Hz, 1 H), 3.59−3.56 (m, 2 H), 2.81−2.75 (m, 1 H), 2.66−2.40 (m, 3 H), 2.17 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.80, 172.66, 161.71, 138.58, 138.36, 138.11, 128.83, 128.76, 128.67, 128.63, 128.54, 128.39, 128.24, 128.19, 128.15, 128.12, 127.95, 95.02, 91.63, 75.68, 75.32, 73.77, 73.62, 73.18, 72.80, 71.85, 68.21, 60.83, 38.18, 30.25, 28.32. ESI-MS: m/z $(M + Na)^+$ calcd 714.1399, obsd 714.1370.

Dibutyl 2,4,6-Tri-*O*-benzyl-3-*O*-levulinoyl-*β*-D-galactopyranoside Phosphate 4. Glycosyl trichloroacetimidate **21** (425 mg, 0.613 mmol) was dissolved in CH_2Cl_2 (5 mL) and cooled to 0 °C. Dibutyl phosphate (135 μL, 0.675 mmol) was added and the mixture was stirred for 1 h and concentrated. The residue was purified by flash chromatography (1:1 hexane/EtOAc, 2% Et_3N) to afford 410 mg (90%) of **4** as a colorless oil. $[\alpha]_D$: +28.8 (c = 0.92, CH_2Cl_2). IR (thin film): 2927, 1717, 1494, 1262, 1050 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.36−7.27 (m, 15 H), 5.18 (app t, J = 7.0 Hz, 1 H), 4.96 (dd, J = 10.2, 3.1 Hz, 1 H), 4.86 (d, J = 11.6 Hz, 1 H), 4.72 (d, J = 11.6 Hz, 1 H), 4.67 (d, J = 11.6 Hz, 1 H), 4.56 (d, J = 11.6 Hz, 1 H), 4.47 (d, J = 11.8 Hz, 1 H), 4.42 (d, J = 11.8 Hz, 1 H), 4.10−3.98 (m, 5 H), 3.91 (dd, J = 10.2, 7.8 Hz, 1 H), 3.84−3.80 (m, 1 H), 3.61−3.59 (m, 2 H), 2.70−2.32 (m, 4 H), 2.13 (s, 3 H), 1.63−1.56 (m, 4 H) 1.38−1.24 (m, 4 H), 0.89 (t, J = 7.4 Hz, 3 H) 0.86 (t, J = 7.4 Hz, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.38, 172.25, 138.38, 138.29, 137.78, 128.58, 128.44, 128.42, 128.17, 127.95, 127.84, 127.83, 127.77, 99.13, 77.00, 75.21, 75.16, 74.88, 74.22, 73.85, 73.55, 67.87, 67.77, 37.86, 32.29, 32.25, 29.93, 27.92, 18.72, 13.75, 13.72. ^{31}P NMR (120 MHz, $CDCl_3$): δ −1.66. ESI-MS: m/z $(M + Na)^+$ calcd 763.3218, obsd 763.3227.

***n*-Pentenyl 2,4,6-Tri-*O*-benzyl-3-*O*-levulinoyl-α-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-*β*-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-*β*-D-glucopyranoside 22. Procedure A.** Disaccharide **16** (980 mg, 0.945 mmol) and glycosyl phosphate **4** (2.39 g, 3.22 mmol) were coevaporated three times with toluene, dissolved in CH_2Cl_2/Et_2O (1:4, 50 mL), and cooled to −78 °C. TBSOTf (740 μL, 3.2 mmol) was added and the mixture was stirred for 2 h while warming to −20 °C. Triethylamine (5 mL) was added and the mixture was concentrated under reduced pressure. The residue was purified by flash chromatography (4:1 → 3:1 hexane/EtOAc) to afford 1.10 g (79%) of **22** as a colorless oil.

Procedure B. Disaccharide **16** (78 mg, 0.083 mmol) and trichloroacetimidate **21** (105 mg, 0.166 mmol) were coevaporated three times with toluene, dissolved in CH_2Cl_2 (4 mL), and cooled to 0 °C. TMSOTf (5 μL, 0.025 mmol) was added and the mixture was stirred for 40 min at 0 °C. Triethylamine (50 μL) was added and the mixture was concentrated under reduced pressure. The residue was purified by flash chromatography (4:1 → 3:1 hexane/EtOAc) to afford 66 mg (54%) of **22** as a colorless oil.

$[\alpha]_D$: +23.7 (c = 0.91, CH_2Cl_2). IR (thin film): 2930, 2870, 1740, 1132, 1095, 1054 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ

7.40−7.16 (m, 35 H), 5.88−5.81 (m, 1 H), 5.40−5.35 (m, 2 H), 5.16 (d, J = 12.1 Hz, 1 H), 5.08−5.00 (m, 4 H), 4.81 (d, J = 12.1 Hz, 1 H), 4.80 (d, J = 12.1 Hz, 1 H), 4.65−4.51 (m, 8 H), 4.41−4.33 (m, 3 H), 4.23−4.22 (m, 2 H), 4.15−4.16 (m, 1 H), 4.13−4.06 (m, 5 H), 3.92−3.81 (m, 3 H), 3.71−3.67 (m, 1 H), 3.52−3.41 (m, 5 H), 3.32 (dd, J = 10.4, 2.4 Hz, 1 H), 3.12 (dd, J = 8.9, 4.9 Hz, 1 H), 2.57−2.54 (m, 1 H), 2.49−2.31 (m, 3 H), 2.17−2.14 (m, 2 H), 2.11 (s, 3 H), 1.72−1.69 (m, 2 H), 1.22 (s, 9 H), 1.18 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.64, 176.88, 176.54, 171.64, 139.56, 138.98, 138.70, 138.48, 138.41, 138.37, 138.33, 138.01, 128.60, 128.57, 128.53, 128.44, 128.31, 128.30, 128.22, 128.08, 127.99, 127.97, 127.89, 127.84, 127.79, 127.73, 127.71, 127.47, 127.45, 126.90, 114.96, 104.41, 101.45, 100.79, 81.29, 80.27, 76.35, 75.88, 75.41, 75.29, 75.13, 74.88, 74.65, 73.68, 73.63, 73.41, 73.24, 73.12, 72.62, 71.87, 71.31, 69.08, 68.66, 68.36, 67.70, 67.49, 38.93, 38.88, 37.97, 30.27, 29.99, 28.98, 28.00, 27.56, 27.31. ESI-MS: m/z (M + Na)$^+$ calcd 1491.7013, obsd 1491.7052.

***n*-Pentenyl 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-*β*-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-*β*-D-glucopyranoside 23.** To a deep blue solution of sodium in liquid ammonia (ca. 7 mL) was added trisaccharide **22** (125 mg, 0.085 mmol) in dry THF (5 mL) under N_2 at −78 °C. After 45 min the reaction was quenched with MeOH (5 mL) and most of the ammonia was removed with a stream of N_2. The mixture was diluted with MeOH, treated with Dowex 50-X8 ion-exchange resin (washed and dried), filtered, and rinsed thoroughly with MeOH. The solution was concentrated in vacuo, and the resulting residue was dissolved in pyridine (3 mL) and treated with Ac_2O (2 mL) in the presence of DMAP (one crystal) at room temperature for 18 h. Flash chromatography of the crude material (1:1 → 1:2 hexanes/EtOAc) afforded 36 mg (43%) of **23** as a colorless oil. $[\alpha]_D$: +44.9 (c = 1.20, CH_2Cl_2). IR (thin film): 2926, 1750, 1700, 1653, 1558, 1540, 1495, 1373, 1230, 1050 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.80−5.76 (m, 1 H), 5.60 (d, J = 1.8 Hz, 1 H), 5.40 (dd, J = 11.0, 2.9 Hz, 1 H), 5.24−5.17 (m, 2 H), 5.11 (dd, J = 10.5, 8.1 Hz, 1 H), 5.04−4.96 (m, 3 H), 4.90 (m, 1 H), 4.73 (app d, J = 10.8 Hz, 1 H), 4.54−4.27 (m, 4 H), 4.18−4.09 (m, 4 H), 4.02 (app s, 1 H), 3.87−3.77 (m, 4 H), 3.78−3.62 (m, 1 H), 3.52−3.46 (m, 1 H) 2.14 (s, 3 H), 2.13 (s, 3 H), 2.09−2.06 (m, 23 H), 2.13 (s, 3 H), 1.71−1.62 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.69, 170.51, 170.47, 170.10, 169.72, 169.69, 169.54, 168.87, 137.81, 115.07, 101.10, 100.53, 99.63, 73.14, 72.81, 72.45, 71.79, 71.74, 70.21, 69.30, 68.93, 68.82, 67.85, 67.09, 67.04, 62.23, 61.26, 60.39, 60.23, 53.44, 29.82, 28.56, 20.95, 20.88, 20.72, 20.69, 20.65, 20.61, 20.52. ESI-MS: m/z (M + Na)$^+$ calcd 1015.3265, obsd 1015.3253.

3-*O*-Acetyl-2-azido-4,6-di-*O*-benzyl-2-deoxy-α/*β*-D-galactopyranosyl Nitrate 25. Galactal **24**[40] (3.03 g, 8.22 mmol) was dissolved in CH_3CN (60 mL) and cooled to −15 °C. CAN (13.5 g, 24.7 mmol) and NaN_3 (800 mg, 12.3 mmol) were added, and the mixture was stirred vigorously using a mechanical stirrer. After 4 h the reaction mixture was diluted with ice-cold Et_2O, washed twice with ice−water, dried over Na_2SO_4, and concentrated. The crude residue was purified by flash chromatography (5:1 hexanes/EtOAc) to afford 1.7 g (45%) of **25** (α:β = 4:1) as a colorless oil. IR (thin film): 2922, 2116, 1748, 1652, 1280, 1223, 1102, 1028 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, selected peaks): δ 6.30 (d, J = 4.1 Hz, 1 H, α H-1), 5.54 (d, J = 8.8 Hz, 1 H, β H-1), 5.19 (dd, J = 11.3, 2.9 Hz, 1 H, α H-3), 4.86 (dd, J = 11.0, 3.0 Hz, 1 H, β H-3), 4.29 (dd, J = 11.3, 4.2 Hz, 1 H, α H-2), 4.18 (app d, J = 2.9 Hz, 1 H, α H-4), 4.07 (app d, J = 2.9 Hz, 1 H, β H-4), 4.00 (dd, J = 11.0, 8.8 Hz, 1 H, β H-2). ESI-MS: m/z (M + Na)$^+$ calcd 495.1486, obsd 495.1469.

3-*O*-Acetyl-2-azido-4,6-di-*O*-benzyl-2-deoxy-D-galactose 26. To a solution of **25** (1.42 g, 3.00 mmol) in CH_3CN (30 mL) were added thiophenol (900 μL, 9.00 mmol) and DIEA (525 μL, 3.00 mmol) at 0 °C. After 90 min the reaction mixture was concentrated under reduced pressure and the crude residue purified by flash chromatography (6:1 → 2:1 hexanes/EtOAc) to give 1.16 g (91%, α:β = 2:1) of **26** as a white solid. IR (thin film): 3399, 3031, 2872, 2112, 1745, 1231, 1045 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, selected peaks): δ 5.38 (d, J = 3.4 Hz, 1 H, α H-1), 5.32 (dd, J = 11.0, 2.9 Hz, 1 H, α H-3), 4.74 (dd, J = 10.8, 3.1 Hz, 1 H, β H-3), 4.06 (app d, J = 2.3 Hz, α H-4), 3.94 (app d, J = 3.3 Hz, 1 H, β H-4), 3.92 (dd, J = 11.1, 3.5 Hz, α H-2), 3.07 (br s, 1 H, OH). ESI-MS: m/z (M + Na)$^+$ calcd 450.1636, obsd 450.1628.

Dimethylthexylsilyl 3-*O*-Acetyl-2-azido-4,6-di-*O*-benzyl-2-deoxy-*β*-D-galactopyranoside 27. To 1.16 g (2.70 mmol) of **26** in DMF (25 mL) were added imidazole (551 mg, 8.10 mmol) and thexyldimethylsilyl chloride (TDS−Cl) (800 μL, 4.07 mmol). The mixture was stirred at room temperature for 12 h, diluted with EtOAc, and washed with water, saturated aqueous $NaHCO_3$, water, and brine. The organic phase was dried over $MgSO_4$, concentrated, and purified by flash chromatography (8:1 hexanes/EtOAc) to afford 1.48 g (96%) of **27** as a colorless oil. $[\alpha]_D$: +2.4 (c = 1.32, CH_2Cl_2). IR (thin film): 2927, 2112, 1749, 1653, 1558, 1455, 1259, 1090 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49−7.22 (m, 10 H), 4.70 (dd, J = 11.1, 2.7 Hz, 1 H), 4.63−4.40 (m, 5 H), 3.94 (app s, 1 H), 3.74 (dd, J = 8.0, 2.4 Hz, 1 H), 3.66−3.59 (m, 3 H), 2.04 (s, 3 H), 1.69 (m, 1 H), 0.90 (m, 12 H), 0.21 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.25, 138.08, 137.95, 137.74, 137.70, 129.34, 128.61, 128.46, 128.43, 128.38, 128.18, 128.15, 128.07, 127.86, 127.79, 127.74, 126.05, 97.31, 75.30, 75.24, 75.05, 73.58, 73.53, 73.47, 73.33, 72.41, 68.48, 68.23, 67.38, 63.83, 33.80, 24.81, 20.87, 19.95, 19.83, 18.50, 18.40, 1.03, −1.91, −3.25, −3.27. ESI-MS: m/z (M + Na)$^+$ calcd 592.2813, obsd 592.2805.

Dimethylthexylsilyl 3-*O*-Acetyl-4,6-di-*O*-benzyl-2-deoxy-2-trichloroacetamido-*β*-D-galactopyranoside 28. To a solution of **27** (1.34 g, 2.35 mmol) in EtOH (20 mL) were added $NaBH_4$ (444 mg, 11.8 mmol) and $NiCl_2$ (56 mg, 0.24 mmol). The solution was stirred for 90 min at room temperature then neutralized with AcOH and concentrated to dryness. The residue was precipitated with CH_2Cl_2, filtered over a pad of Celite, and concentrated. To a solution of the crude amine in CH_2Cl_2 (20 mL) was added Et_3N (975 μL, 7.00 mmol) and trichloroacetyl chloride (310 μL, 2.80 mmol) at 0 °C. The reaction mixture was stirred for 20 min at 0 °C and then diluted with CH_2Cl_2 and washed with water, saturated aqueous $NaHCO_3$, and water. The organic phase was dried over $MgSO_4$ and concentrated. The resulting residue was dissolved in pyridine (10 mL) and treated with Ac_2O (5 mL). After 12 h the reaction mixture was concentrated, coevaporated with toluene, and purified by flash chromatography (4:1 hexanes/EtOAc) to yield 648 mg (40%) of **28** as a colorless oil. $[\alpha]_D$: −5.3 (c = 0.89, CH_2Cl_2). IR (thin film): 2926, 2862, 1717, 1653, 1558, 1540, 1403, 1050 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.27 (m, 10 H), 6.67 (d, J = 9.0 Hz, 1 H), 5.19 (dd, J = 11.3, 2.3 Hz, 1 H), 4.85 (d, J = 7.8 Hz, 1 H), 4.75 (d, J = 11.7 Hz, 1 H), 4.60 (d, J = 11.7 Hz, 1 H), 4.53 (d, J = 11.7 Hz, 1 H), 4.47 (d, J = 11.7 Hz, 1 H), 4.31−4.24 (m, 1 H), 3.98 (app s, 1 H), 3.77−3.74 (m, 1 H), 3.68 (app t, J = 8.8 Hz, 1 H), 3.64−3.62 (m, 1 H), 2.00 (s, 3 H), 1.65−1.62 (m, 1 H), 0.88−0.85 (m, 12 H), 0.20 (s, 3 H), 0.16 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.34, 161.98, 138.38, 138.19, 129.44, 128.87, 128.78, 128.68, 128.25, 128.19, 96.52, 93.02, 75.37, 74.06, 73.98, 73.92, 68.73, 55.86, 34.23, 25.16, 21.22, 20.45, 20.36, 18.98, 18.96, −1.22, −2.86. ESI-MS: m/z (M + Na)$^+$ calcd 710.1845, obsd 710.1867.

3-*O*-Acetyl-4,6-di-*O*-benzyl-2-deoxy-2-trichloroacetamido-α-D-galactopyranosyl Trichloroacetimidate 30. To a solution of compound **28** (740 mg, 1.07 mmol) in dry THF (10 mL) were added AcOH (75 μL, 1.3 mmol) and a 1.0 M solution of tetrabutylammonium fluoride in THF (1.3 mL, 1.3 mmol). The mixture was stirred at room temperature for 20 h, diluted with EtOAc, washed with saturated aqueous $NaHCO_3$, water, and brine, dried over $MgSO_4$, and concentrated. Purification of the resulting residue by flash chromatography (8:1 → 4:1 hexanes/EtOAc) yielded 530 mg (91%) of **29** as a colorless oil. To a solution of lactol **29** (527 mg, 0.96

mmol) in CH_2Cl_2 (10 mL) was added trichloroacetonitrile (5 mL) and DBU (10 μL). The mixture was stirred at room temperature for 2 h and then concentrated. Purification of the crude residue by flash chromatography (4:1 hexanes/EtOAc) yielded 461 mg (70%) of **30** as a colorless foam. $[\alpha]_D$: +65.1 (*c* = 0.83, CH_2Cl_2). IR (thin film): 2926, 1717, 1684, 1558, 1494, 1452, 1403, 1050 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.73 (s, 1 H), 7.39−7.27 (m, 10 H), 6.93 (d, *J* = 8.9 Hz, 1 H), 6.47 (d, *J* = 3.5 Hz, 1 H), 5.42 (dd, *J* = 11.3, 2.7 Hz, 1 H), 4.90−4.87 (m, 1 H), 4.82 (d, *J* = 11.4 Hz, 1 H), 4.62 (d, *J* = 11.4 Hz, 1 H), 4.52−4.49 (m, 2 H), 4.44 (d, *J* = 11.7 Hz, 1 H), 4.25 (dd, *J* = 7.8, 5.7 Hz, 1 H), 4.12 (d, *J* = 2.4 Hz, 1 H), 3.70 (app t, *J* = 9.0 Hz, 1 H), 3.61 (dd, *J* = 9.1, 5.4 Hz, 1 H), 2.06 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.86, 162.44, 160.67, 138.06, 137.94, 128.89, 128.87, 128.58, 128.39, 128.34, 128.28, 95.32, 92.46, 91.22, 77.64, 75.65, 74.06, 73.92, 72.47, 70.95, 67.80, 50.92, 21.28. ESI-MS: *m*/*z* $(M + Na)^+$ calcd 710.9763, obsd 710.9763.

Dibutyl 3-*O*-Acetyl-4,6-di-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-galactopyranosyl Phosphate 5. To a solution of imidate **30** (453 mg, 0.66 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added dibutyl phosphate (150 μL, 0.72 mmol). The mixture was stirred for 1 h and then directly loaded onto a short column of silica gel and eluted with 1:1 hexanes/EtOAc to afford 360 mg (74%) of phosphate **5** as a white solid. $[\alpha]_D$: +13.8 (*c* = 0.82, CH_2Cl_2). IR (thin film): 2928, 1718, 1540, 1494, 1454, 1260, 1028 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 9.5 Hz, 1 H), 7.35−7.26 (m, 10 H), 5.53 (app t, *J* = 7.8 Hz, 1 H), 5.25 (d, *J* = 10.9 Hz, 1 H), 4.71 (d, *J* = 11.6 Hz, 1 H), 4.63−4.55 (m, 1 H), 4.50 (d, *J* = 11.2 Hz, 1 H), 4.47 (d, *J* = 10.9 Hz, 1 H), 4.38 (d, *J* = 11.7 Hz, 1 H), 4.09 (m, 2 H), 4.02−3.99 (m, 2 H), 3.82 (app s, 2 H), 3.64−3.60 (m, 1 H), 3.53−3.49 (m, 1 H), 2.01 (s, 3 H), 1.64−1.59 (m, 4 H), 1.38−1.36 (m, 4 H), 0.94−0.88 (m, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.41, 163.73, 162.42, 137.60, 128.35, 128.29, 128.19, 127.82, 127.70, 127.53, 96.77, 96.72, 92.62, 91.97, 74.92, 73.31, 73.04, 72.81, 68.34, 68.27, 68.14, 68.10, 68.03, 67.66, 52.72, 52.63, 31.93, 31.86, 20.68, 18.49, 18.46, 13.49. ^{31}P NMR (120 MHz, $CDCl_3$): δ −2.62. ESI-MS: *m*/*z* $(M + Na)^+$ calcd 760.1582, obsd 760.1559.

***n*-Pentenyl 2,4,6-Tri-*O*-benzyl-α-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside 31**. Trisaccharide **22** (1.10 g, 0.746 mmol) was dissolved in CH_2Cl_2 (20 mL). A solution of hydrazine acetate (122 mg, 1.33 mmol) in MeOH (4 mL) was added and the mixture was stirred for 12 h. The mixture was diluted with CH_2Cl_2 (100 mL) and washed twice with water, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (4:1 → 2:1 hexane/EtOAc) to afford 634 mg (62%) of **31** as a colorless oil. $[\alpha]_D$: +25.1 (*c* = 1.00, CH_2Cl_2). IR (thin film): 3030, 2871, 1737, 1130, 1094 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.37−7.16 (m, 35 H), 5.83−5.67 (m, 1 H), 5.27 (dd, *J* = 10.4, 7.9 Hz, 1 H), 5.14 (d, *J* = 11.9 Hz, 1 H), 5.04−4.94 (m, 4 H), 4.78 (d, *J* = 12.2 Hz, 1 H), 4.77 (d, *J* = 12.1 Hz, 1 H), 4.66 (d, *J* = 11.3 Hz, 1 H), 4.56−4.45 (m, 6 H), 4.38−4.34 (m, 2 H), 4.24−4.20 (m, 3 H), 4.12−3.99 (m, 5 H), 3.96−3.95 (m, 1 H), 3.88−3.81 (m, 1 H), 3.73−3.79 (m, 3 H), 3.62 (app t, *J* = 9.0 Hz, 1 H), 3.50−3.34 (m, 5 H), 3.27 (dd, *J* = 10.4, 2.5 Hz, 1 H), 3.07 (dd, *J* = 8.8, 4.9 Hz, 1 H), 2.12−2.05 (m, 2 H), 1.78−1.62 (m, 3 H), 1.17 (s, 9 H), 1.12 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.90, 176.74, 139.44, 139.01, 138.62, 138.36, 138.32, 138.29, 138.24, 138.13, 128.61, 128.42, 128.39, 128.31, 128.28, 128.21, 128.17, 128.11, 127.92, 127.86, 127.75, 127.68, 127.60, 127.46, 127.30, 127.16, 114.96, 101.47, 100.19, 99.94, 81.35, 80.03, 75.40, 75.33, 75.30, 74.60, 74.48, 73.68, 73.51, 73.31, 73.12, 73.12, 72.36, 71.75, 71.30, 70.09, 69.08, 68.94, 68.30, 67.69, 67.55, 30.23, 28.93, 28.93, 27.25. ESI-MS: *m*/*z* $(M + Na)^+$ calcd 1393.6645, obsd 1393.6612.

***n*-Pentenyl 3-*O*-Acetyl-4,6-di-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-galactopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside 32.** Trisaccharide **31** (308 mg, 0.230 mmol) and glycosyl phosphate **5** (196 mg, 0.270 mmol) were coevaporated three times with toluene, dissolved in CH_2Cl_2 (4 mL), and cooled to −78 °C. TMSOTf (50 μL, 0.270 mmol) was added and the mixture was stirred for 30 min. Triethylamine (200 μL) was added and the mixture was directly purified by flash chromatography (4:1 → 2:1 hexane/EtOAc) to afford 405 mg (93%) of **32** as a white solid. $[\alpha]_D$: −15.2 (*c* = 1.00, CH_2Cl_2). IR (thin film): 1734, 1521, 1455, 1364, 1231, 1093 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.46−7.18 (m, 45 H), 6.54 (d, *J* = 9.8 Hz, 1 H), 5.85−5.78 (m, 1 H), 5.36 (dd, *J* = 9.9, 8.3 Hz, 1 H), 5.06−4.96 (m, 4 H), 4.84−4.74 (m, 6 H), 4.66−4.47 (m, 8 H), 4.38−4.02 (m, 17 H), 4.02−3.99 (m, 2 H), 3.89 (app s, 1 H), 3.90−3.80 (m, 2 H), 3.78−3.51 (m, 3 H), 3.48−3.35 (m, 4 H), 3.28 (app d, *J* = 10.2 Hz, 1 H), 3.05 (dd, *J* = 8.5, 5.1 Hz, 1 H), 2.12−2.08 (m, 2 H), 2.00 (s, 3 H), 1.71−1.66 (m, 2 H), 1.18 (s, 9 H), 1.26 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.27, 171.13, 163.83, 162.32, 139.08, 138.55, 138.50, 138.46, 138.43, 138.37, 129.72, 129.15, 129.04, 128.93, 128.89, 128.86, 128.83, 128.65, 128.63, 128.45, 128.40, 128.29, 128.25, 128.21, 128.15, 128.13, 128.03, 127.94, 127.92, 127.85, 127.80, 127.57, 127.42, 115.26, 102.34, 101.73, 101.00, 92.84, 80.41, 80.00, 79.64, 77.72, 77.64, 75.48, 75.39, 75.27, 75.15, 74.89, 74.24, 73.96, 73.93, 73.85, 73.80, 73.61, 73.50, 73.38, 73.04, 73.01, 72.33, 72.16, 71.84, 71.76, 69.34, 69.13, 68.48, 68.17, 67.93, 67.64, 53.65, 39.19, 39.09, 30.49, 29.21, 27.76, 27.67, 27.58, 21.32. ESI-MS: *m*/*z* $(M + Na)^+$ calcd 1920.7315, obsd 1920.7340.

***n*-Pentenyl 4,6-Di-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-galactopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside 33.** To a solution of tetrasaccharide **32** (305 mg, 0.160 mmol) in MeOH (15 mL) was added a solution of NaOMe in MeOH (180 μL, 0.80 mmol, 25% by wt). The reaction mixture was stirred at room temperature for 1 h and then quenched with Dowex 50-X8 ion-exchange resin, filtered, and concentrated. The crude residue was purified by flash chromatography (3:1 hexanes/EtOAc) to afford 262 mg (88%) of tetrasaccharide **33** as a white solid. $[\alpha]_D$: −6.6 (*c* = 1.10, CH_2Cl_2). IR (thin film): 2870, 1735, 1454, 1366, 1094 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.45−7.18 (m, 45 H), 6.37 (d, *J* = 8.7 Hz, 1 H), 5.86−5.76 (m, 1 H), 5.37 (app t, *J* = 8.2 Hz, 1 H), 5.04−4.90 (m, 5 H), 4.80−4.65 (m, 6 H), 4.56−4.30 (m, 8 H), 4.24 (app s, 1 H), 4.16−4.00 (m, 11 H), 3.86−3.67 (m, 6 H), 3.66−3.57 (m, 2 H), 3.44−3.28 (m, 5 H), 3.17 (app d, *J* = 10.5 Hz, 1 H), 3.08 (dd, *J* = 8.3, 5.4 Hz, 1 H), 2.34 (br s, 1 H), 1.87−1.89 (m, 2 H), 1.88 (s, 9 H), 1.69−1.64 (m, 2 H), 1.13 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.84, 176.81, 139.44, 139.31, 138.79, 138.31, 138.24, 138.20, 138.15, 138.09, 129.44, 128.72, 128.66, 128.61, 128.58, 128.38, 128.24, 128.18, 128.09, 128.04, 127.97, 127.93, 127.86, 127.73, 127.66, 127.60, 127.38, 127.25, 114.98, 101.66, 101.43, 100.30, 100.07, 92.47, 79.83, 79.59, 79.20, 75.61, 75.51, 75.27, 75.14, 73.78, 73.71, 73.64, 73.48, 73.36, 73.17, 72.93, 72.81, 72.30, 71.64, 71.42, 69.03, 68.26, 67.87, 67.85, 67.42, 56.52, 38.93, 38.83, 30.22, 28.94, 28.30, 27.52, 27.32, 22.89, 14.43. ESI-MS: *m*/*z* $(M + Na)^+$ calcd 1878.7209, obsd 1878.7262.

Dibutyl 2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl Phosphate 6. Tri-*O*-benzyl galactal **12** (644 mg, 1.55 mmol) was dissolved in CH_2Cl_2 (15 mL) and cooled to 0 °C. DMDO (0.08 M in acetone, 30 mL, 2.4 mmol) was added and the reaction was stirred for 10 min. The solvent was evaporated at 0 °C, and the resulting residue was dissolved in CH_2Cl_2 (15 mL) and cooled to −78 °C. Dibutyl phosphate (340 μL, 1.7 mmol) was added and the mixture was stirred for 10 min. After warming to 0 °C DMAP (758 mg, 6.20 mmol) and acetyl chloride (220 μL, 3.10 mmol) were added, and the reaction mixture was stirred for 2 h and concentrated. Purification of the crude residue by flash chromatography (1:1

hexane/EtOAc) afforded 769 mg (73%) of phosphate **6** as a colorless oil. $[\alpha]_D$: +25.9 (c = 0.93, CH_2Cl_2). IR (thin film): 2927, 1751, 1558, 1494, 1452, 1403, 1050 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.54−7.28 (m, 15 H), 5.46 (dd, J = 10.0, 8.0 Hz, 1 H), 5.16 (app t, J = 7.5 Hz, 1 H), 4.96 (d, J = 11.5 Hz, 1 H), 4.69 (d, J = 12.4 Hz, 1 H), 4.62 (d, J = 11.4 Hz, 1 H), 4.53 (d, J = 12.2 Hz, 1 H), 4.45 (app s, 2 H), 4.07−3.95 (m, 5 H), 3.71−3.65 (m, 2 H), 3.62−3.55 (m, 2 H), 2.05 (s, 3 H), 1.62−1.40 (m, 4 H), 1.38−1.35 (m, 4 H), 0.95−0.87 (m, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.48, 138.24, 137.61, 137.59, 128.44, 128.22, 127.85, 127.64, 127.51, 127.37, 96.97, 79.64, 74.63, 74.13, 73.49, 72.20, 72.08, 67.94, 67.87, 67.81, 32.08, 32.01, 31.94, 20.92, 18.55, 13.55, 13.53. ^{31}P NMR (120 MHz, $CDCl_3$): δ −2.26. ESI-MS: m/z $(M + Na)^+$ calcd 707.2956, obsd 707.2931.

***n*-Pentenyl 2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-*β*-D-galactopyranosyl-(1→3)-4,6-di-*O*-benzyl-2-deoxy-2-trichloroacetamido-*β*-D-galactopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-*β*-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-*β*-D-glucopyranoside 36.** Tetrasaccharide **33** (89 mg, 48 μmol) and glycosyl phosphate **6** (66 mg, 96 μmol) were coevaporated three times with toluene, dissolved in CH_2Cl_2 (4 mL), and cooled to −50 °C. TMSOTf (18 μL, 96 μmol) was added and the mixture was stirred for 20 min. Triethylamine (100 μL) was added and the mixture was directly purified by flash chromatography (4:1 hexanes/EtOAc) to afford 99 mg (88%) of pentasaccharide **36** as a colorless foam. $[\alpha]_D$: +1.8 (c = 1.00, CH_2Cl_2). IR (thin film): 2926, 1734, 1700, 1653, 1558, 1495, 1455, 1400, 1050 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.35−7.18 (m, 60 H), 6.22 (d, J = 8.9 Hz, 1 H), 5.84−5.77 (m, 1 H), 5.45 (app t, J = 8.6 Hz, 1 H), 5.32 (app t, J = 8.8 Hz, 1 H), 5.04−4.96 (m, 6 H), 4.86−3.53 (m, 48 H), 3.43−3.36 (m, 5 H), 3.26−3.24 (m, 2 H), 3.15−3.13 (m, 1 H), 2.10−2.06 (m, 2 H), 2.06 (s, 3 H), 1.70−1.65 (m, 2 H), 1.15 (s, 9 H), 1.12 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.55, 176.37, 169.76, 160.94, 139.34, 139.18, 139.02, 138.63, 138.57, 138.45, 138.40, 138.06, 137.87, 137.74, 137.65, 128.74, 128.52, 128.49, 128.37, 128.34, 128.31, 128.26, 128.21, 128.13, 128.07, 127.99, 127.91, 127.88, 127.84, 127.81, 127.73, 127.66, 127.58, 127.52, 127.41, 127.35, 127.11, 127.02, 126.90, 114.75, 101.24, 101.15, 100.76, 100.10, 92.68, 79.64, 78.06, 77.00, 76.49, 75.88, 75.07, 74.81, 74.77, 74.49, 73.87, 73.58, 73.46, 73.24, 73.16, 72.96, 72.72, 72.33, 71.84, 71.43, 71.10, 70.79, 68.94, 68.80, 68.46, 68.40, 67.60, 55.20, 38.67, 38.60, 30.02, 29.68, 29.26, 28.75, 28.10, 27.30, 27.10, 22.43, 21.10, 13.98. ESI-MS: m/z $(M + Na)^+$ calcd 2352.9251, obsd 2352.9288.

***n*-Pentenyl 3,4,6-Tri-*O*-benzyl-*β*-D-galactopyranosyl-(1→3)-4,6-di-*O*-benzyl-2-deoxy-2-trichloroacetamido-*β*-D-galactopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-*β*-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-*β*-D-glucopyranoside 37**. To a solution of pentasaccharide **36** (98 mg, 42 μmol) in MeOH (3 mL) was added a solution of NaOMe in MeOH (48 μL, 21 μmol, 25% by wt). The reaction mixture was stirred at room temperature for 12 h and then quenched with Dowex 50-X8 ion-exchange resin, filtered, and concentrated. The crude residue was purified by flash chromatography (4:1 hexanes/EtOAc) to afford 73 mg (76%) of pentasaccharide **37** as a colorless foam. $[\alpha]_D$: −0.3 (c = 1.00, CH_2Cl_2). IR (thin film): 2926, 1734, 1558, 1494, 1403, 1261, 1050 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.38−7.16 (m, 60 H), 6.51 (d, J = 8.5 Hz, 1 H), 5.84−5.74 (m, 1 H), 5.32 (app t, J = 8.4 Hz, 1 H), 4.99−4.88 (m, 7 H), 4.76−4.25 (m, 22 H), 4.18−3.74 (m, 17 H), 3.60−3.54 (m, 8 H), 3.41−3.34 (m, 5 H), 3.26−3.24 (m, 2 H), 3.10 (dd, J = 8.6, 5.2 Hz, 1 H), 2.44 (br s, 1 H), 2.09−2.06 (m, 2 H), 1.67−1.65 (m, 2 H), 1.16 (s, 9 H), 1.12 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.55, 176.42, 162.11, 139.26, 139.16, 139.01, 138.66, 138.61, 138.38, 138.38, 138.26, 138.05, 138.03, 137.88, 137.73, 128.97, 128.55, 128.47, 128.42, 128.39, 128.34, 128.24, 128.15, 128.07, 128.00, 127.93, 127.91, 127.83, 127.76, 127.67, 127.61, 127.52, 127.40, 127.35, 127.10, 127.05, 127.01, 114.75, 104.39, 101.17, 100.07, 99.99, 92.57, 80.99, 79.80, 79.68, 79.56, 78.25, 75.81, 75.55, 75.06, 74.88, 74.59, 74.47, 73.35, 73.92, 73.87, 73.57, 73.46, 73.34, 73.28, 73.22, 72.93, 72.85, 72.71, 72.39, 72.26, 71.70, 71.40, 71.15, 68.91, 68.79, 68.72, 68.25, 68.15, 67.82, 67.47, 38.68, 38.59, 31.90, 31.56, 30.02, 29.67, 29.34, 29.25, 28.74, 28.10, 27.30, 27.10, 22.63, 22.42, 21.05, 14.17, 14.12, 13.97. ESI-MS: m/z $(M + Na)^+$ calcd 2310.9146, obsd 2310.9136.

***n*-Pentenyl 2,3,4,6-Tetra-*O*-acetyl-*β*-D-galactopyranosyl-(1→3)-4,6-di-*O*-acetyl-2-deoxy-2-acetamido-*β*-D-galactopyranosyl-(1→3)-2,4,6-tri-*O*-acetyl-α-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-*β*-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-*β*-D-glucopyranoside 38.** Pentasaccharide **37** (35 mg, 15 μmol), Bu_3SnH (50 μL, 160 μmol), and a catalytic amount of AIBN were dissolved in dry toluene (3 mL), and the solution was vigorously stirred for 20 min under a stream of N_2. After heating to 100 °C for 1 h, another 20 μL of Bu_3SnH and a catalytic amount of AIBN were added. After 1 h the reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by flash chromatography (10:1 → 4:1 → 2:1 hexanes/EtOAc) to afford 18 mg (55%) of the desired product. To a deep blue solution of sodium in liquid ammonia (ca. 7 mL) was added the above compound in dry THF (3 mL) under N_2 at −78 °C. After 45 min, the reaction was quenched with MeOH (4 mL) and most of the ammonia was removed with a stream of N_2. The mixture was diluted with MeOH, treated with Dowex 50-X8 ion-exchange resin (washed and dried), filtered, and rinsed with a solution of NH_3 in MeOH. The solution was concentrated in vacuo and coevaporated with toluene. The resulting residue was dissolved in pyridine (2 mL) and treated with Ac_2O (1 mL) in the presence of DMAP (one crystal) at room temperature for 20 h. Flash chromatography of the crude material (2:1 EtOAc/hexanes → 100% EtOAc) gave 5 mg (40%) of pentasaccharide **38** as a white solid. IR (thin film): 1745, 1548, 1370, 1229, 1066 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 5.85−5.75 (m, 1 H), 5.67 (d, J = 7.2 Hz, 1 H), 5.61 (app s, 1 H), 5.42 (app s, 1 H), 5.36 (app d, J = 2.1 Hz, 1 H), 5.32−4.89 (m, 10 H), 4.77 (app d, J = 9.4 Hz, 1 H), 4.70 (app d, J = 8.4 Hz, 1 H), 4.63 (app d, J = 7.7 Hz, 1 H), 4.55 (d, J = 7.6 Hz, 1 H), 4.48 (app d, J = 8.0 Hz, 1 H), 4.44−4.37 (m, 2 H), 4.24−4.02 (m, 9 H), 3.96−3.93 (m, 1 H), 3.89−3.86 (m, 2 H), 3.81−3.77 (m, 2 H), 3.65−3.62 (m, 2 H), 3.52−3.48 (m, 1 H), 3.28−3.23 (m, 1 H), 2.16−1.96 (m, 48 H), 1.75−1.65 (m, 2 H), 1.61 (s, 3 H). ESI-MS: m/z $(M + Na)^+$ calcd 1590.5115, obsd 1590.5170.

***n*-Pentenyl 2-*O*-Benzyl-3,4-di-*O*-pivaloyl-α-L-fucopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-*β*-D-galactopyranosyl-(1→3)-4,6-di-*O*-benzyl-2-deoxy-2-trichloroacetamido-*β*-D-galactopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-*β*-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-*β*-D-glucopyranoside 1**. Pentasaccharide **37** (54 mg, 24 μmol) and fucosyl phosphate **7** (44 mg, 71 μmol) were coevaporated three times with toluene, dissolved in CH_2Cl_2 (2 mL), and cooled to −50 °C. TMSOTf (13 μL, 71 μmol) was added and the mixture was stirred for 45 min while warming to −20 °C. Triethylamine (200 μL) was added and the mixture was directly purified by flash chromatography (8:1 → 5:1 hexanes/EtOAc) to afford 42 mg (66%) of hexasaccharide **1** as a colorless foam. $[\alpha]_D$: −20.6 (c = 1.00, CH_2Cl_2). IR (thin film): 2926, 1734, 1558, 1494, 1403, 1262 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, J = 6.7 Hz, 1 H), 7.38−7.15 (m, 60 H), 7.03−7.00 (m, 5 H), 5.86−5.72 (m, 1 H), 5.65 (d, J = 2.6 Hz, 1 H), 5.51 (app d, J = 10.6 Hz, 1 H), 5.30 (app t, J = 9.1 Hz, 1 H), 5.22 (app s, 1 H), 5.17−5.13 (m, 2 H), 5.07−4.86 (m, 7 H), 4.78−3.92 (m, 38 H), 3.92−3.58 (m, 10 H), 3.47−3.38 (m, 7 H), 3.24−3.18 (m, 2 H), 2.09−2.07 (m, 2 H), 1.67−1.64 (m, 2 H), 1.60 (s, 9 H), 1.15 (s, 9 H), 1.11 (s, 9 H), 1.04 (s, 9 H), 0.70 (d, J = 6.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.46, 177.26, 177.03, 176.69, 162.79, 140.06, 139.30, 139.18, 139.04, 138.78, 138.63, 138.56, 138.37, 138.24, 138.21, 128.95, 128.93, 128.86, 128.78, 128.75, 128.71, 128.62,

128.58, 128.55, 128.49, 128.40, 128.35, 128.27, 128.24, 128.07, 128.02, 127.97, 127.91, 127.84, 127.76, 127.69, 127.52, 127.45, 127.41, 127.34, 127.19, 115.19, 102.74, 101.52, 101.16, 100.91, 100.06, 96.93, 84.12, 80.68, 78.51, 78.16, 77.65, 76.66, 76.51, 75.69, 75.56, 75.44, 74.96, 74.85, 74.72, 74.52, 74.44, 74.00, 73.88, 73.72, 73.37, 73.11, 73.05, 72.39, 72.15, 71.94, 71.81, 71.75, 70.54, 69.25, 69.09, 68.86, 68.59, 68.31, 65.67, 39.30, 39.14, 39.08, 32.02, 30.50, 29.22, 27.73, 27.63, 27.57, 27.51, 23.09, 15.74, 14.57. ESI-MS: m/z $(M + 2Na)^{2+}$ calcd 1369.0618, obsd 1369.0602.

***n*-Pentenyl 2,3,4-Tri-*O*-acetyl-α-L-fucopyranosyl-(1→2)-3,4,6-tri-*O*-acetyl-*β*-D-galactopyranosyl-(1→3)-2-acetamido-4,6-di-*O*-acetyl-2-deoxy-*β*-D-galactopyranosyl-(1→3)-2,4,6-tri-*O*-acetyl-α-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-*β*-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-*β*-D-glucopyranoside 39.**[33] Hexasaccharide **1** (21 mg, 7.8 μmol), Bu_3SnH (25 μL, 80 μmol), and a catalytic amount of AIBN were dissolved in dry toluene (3 mL), and the solution was vigorously stirred for 20 min under a stream of N_2. After heating to 100 °C for 1 h, another 25 μL of Bu_3SnH and a catalytic amount of AIBN were added. After 1.5 h the reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by flash chromatography (10:1 → 4:1 → 2:1 hexanes/EtOAc) to afford 12 mg (60%) of the desired product. To a deep blue solution of sodium in liquid ammonia (ca. 7 mL) was added the above compound in dry THF (3 mL) under N_2 at −78 °C. After 45 min the reaction was quenched with MeOH (4 mL) and most of the ammonia was removed with a stream of N_2. The mixture was diluted with MeOH, treated with Dowex 50-X8 ion-exchange resin (washed and dried), filtered, and rinsed with a solution of NH_3 in MeOH. The solution was concentrated in vacuo and coevaporated with toluene. The resulting residue was dissolved in pyridine (2 mL) and treated with Ac_2O (1 mL) in the presence of DMAP (one crystal) at room temperature for 16 h. Flash chromatography of the crude material (2:1 EtOAc/hexanes → 100% EtOAc) afforded 4 mg (40%) of hexasaccharide **39** as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.69 (d, J = 6.8 Hz, 1 H), 5.82−5.75 (m, 1 H), 5.61 (app s, 1 H), 5.48 (app d, J = 3.3 Hz, 1 H), 5.41 (app d, J = 2.4 Hz, 1 H), 5.31−4.85 (m, 12 H), 4.78−4.74 (m, 1 H), 4.54−4.40 (m, 6 H), 4.37−4.35 (m, 1 H), 4.26 (dd, J = 10.5, 2.5 Hz, 1 H), 4.21−3.96 (m, 8 H), 3.90−3.73 (m, 5 H), 3.64−3.60 (m, 1 H), 3.52−3.46 (m, 1 H), 3.08−3.04 (m, 1 H), 2.16−1.90 (m, 53 H), 1.68−1.64 (m, 2 H), 1.60 (s, 3 H), 1.15 (d, J = 6.2 Hz, 3 H). ESI-MS: m/z $(M + Na)^+$ calcd 1820.5906, obsd 1820.5949.[33]

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Supporting Information Available: ^{1}H NMR and ^{13}C NMR spectral data for all described compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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