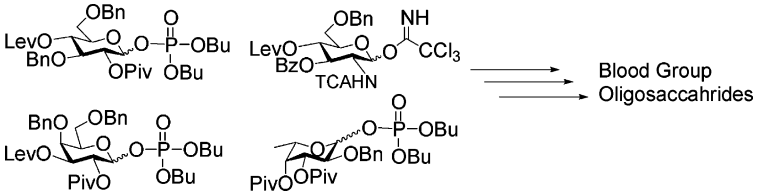
JOC*Article*

Solution Syntheses of Protected Type II Lewis Blood Group Oligosaccharides: Study for Automated Synthesis

Kerry Routenberg Love and Peter H. Seeberger*
Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, and Laboratorium für Organische Chemie, ETH-Hönggerberg, 8093, Zürich, Switzerland

seeberger@org.chem.ethz.ch

Received December 30, 2004



Glycosyl phosphate and trichloroacetimidate monosaccharide building blocks were used in a stepwise solution-phase synthesis of three Lewis blood group oligosaccharides. The syntheses were conducted to establish general routes for the automated assembly of the oligosaccharide portion of biologically important glycolipids. The H-type II pentasaccharide, Le^x pentasaccharide, and Le^y hexasaccharide were prepared in high yield. These syntheses served to evaluate the utility and limitations of the 2-(azidomethyl)benzoate ester (AZMB) for the construction of complex carbohydrates. Development of a glucosamine building block containing a *N*-trichloroacetamide group to mask the C2 amine improved coupling yields and was key for completion of the Le^x and Le^y structures.

Introduction

The serological differences in human blood were first examined at the turn of the 20th century.[1] It was found that antigen specificity was inherited and carbohydrate-containing secretory substances termed the Lewis blood group antigens were discovered.[2] The ABO related antigens (Figure 1) are the terminal carbohydrate portions of glycan chains located on the erythrocyte surface. The H-type II antigen causes agglutination of O-type erythrocytes and is the precursor to the A and B antigens, these antigens being the α-(1→3) addition of an *N*-acetyl galactosamine or galactose residue, respectively.[3] Derivatization of the H-type II antigen to include an α-(1→3) fucose residue on the central *N*-acetyl glucosamine leads to the formation of type II antigens, namely Le^x and Le^y antigens.

Elucidation of the biological roles of complex carbohydrates, such as the Lewis blood group oligosaccharides, has led to the development of carbohydrate-based therapeutic agents for the treatment of parasitic infections[4] and autoimmune disorders[5] and as cancer vaccines.[6]

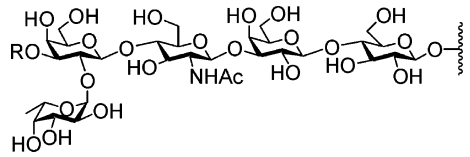


FIGURE 1. Structure of the ABO blood antigens.

More detailed biochemical and biophysical studies of carbohydrates require access to discrete, isomerically pure oligosaccharides. While oligosaccharides can be accessed by enzymatic degradation of naturally occurring oligosaccharides,[7] chemoenzymatic synthesis,[8] and chemical synthesis,[9] access to complex saccharides remains difficult for nonspecialists.

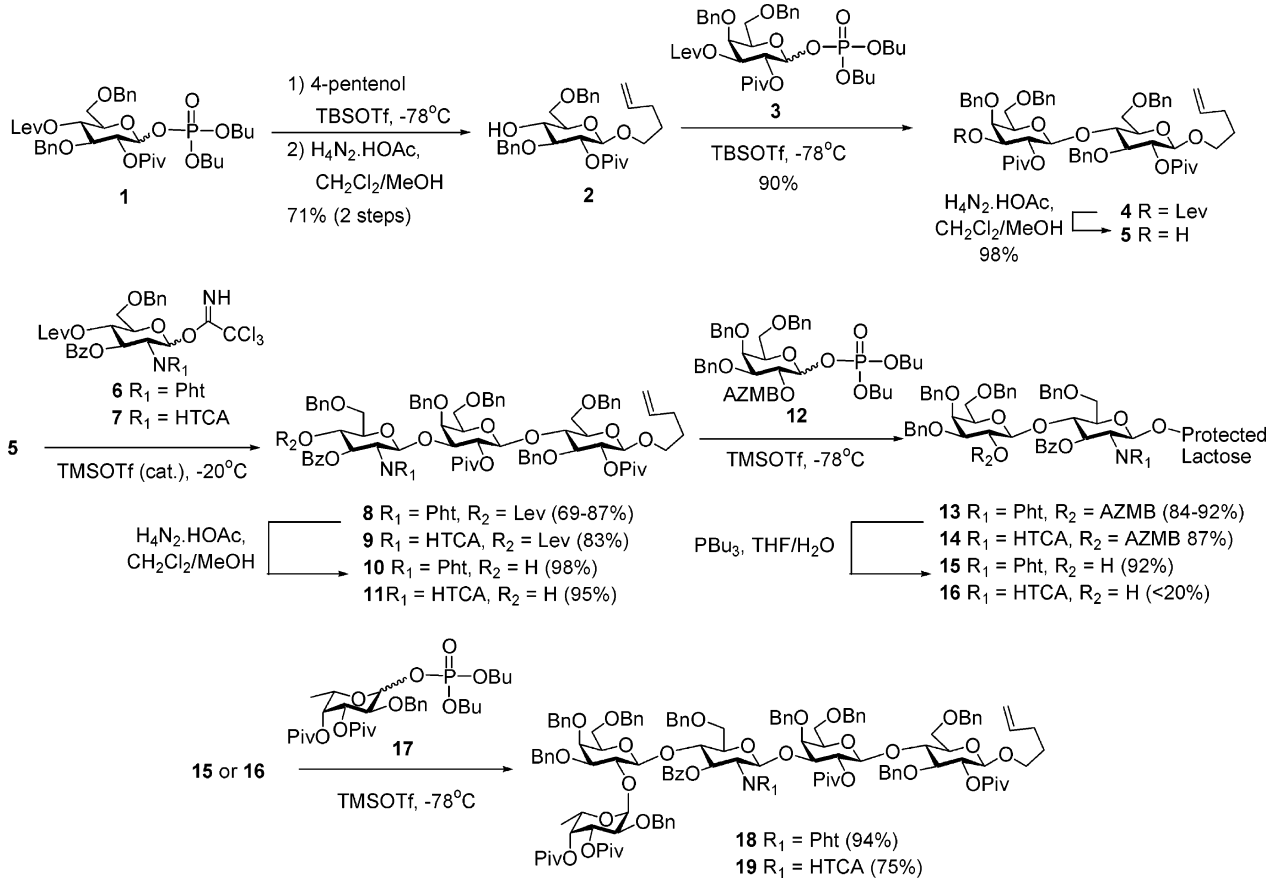
The introduction of the first oligosaccharide synthesizer was a step toward a general method for carbohy-

* Corresponding author: fax (41) 1-633-1235; tel (41) 1-633-2103.

(1) Landsteiner, K. *Zbt. Bakt.* **1900**, *27*, 357−362.
(2) Watkins, W. M. *Trends Glycosci. Glycotechnol.* **1999**, *11*, 391−411.
(3) Watkins, W. M.; Morgan, W. J. M. *Vox Sang.* **1955**, *5*, 1−14.
(4) Schofield, L.; Hewitt, M. C.; Evans, K.; Siomos, M. A.; Seeberger, P. H. *Nature* **2002**, *418*, 785−789.
(5) Chmiela, M.; Wadstrom, T.; Folkesson, H.; Malecka, I. P.; Czkwianianc, E.; Rechcinski, T.; Rudnicka, W. *Immunol. Lett.* **1998**, *61*, 119−125.
(6) Williams, L. J.; Harris, C. R.; Glunz, P. W.; Danishefsky, S. J. *Tetrahedron Lett.* **2000**, *41*, 9505−9508.
(7) Venkataraman, G.; Shriver, Z.; Raman, R.; Sasisekharan, R. *Science* **1999**, *286*, 537−542.
(8) Koeller, K. M.; Wong, C. H. *Chem. Rev.* **2000**, *100*, 4465−4493.
(9) Nicolaou, K. C.; Mitchell, H. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 1576−1624.

10.1021/jo047723b CCC: $30.25
Published on Web 03/23/2005

SCHEME 1. Synthesis of a Protected H-type II Pentasaccharide with Two Modes of Amine Protection: the Phthaloyl Group (Pht) and the Trichloroacetamide Group (TCA)



drate assembly much like the methods already available for peptide and nucleic acid assembly.[10] A growing number of oligosaccharides have been synthesized by automation[11] but the method has to be extended to eventually include all classes of glycoconjugates. The Lewis oligosaccharides, representatives of a large class of intricate carbohydrates, were used to identify key building blocks and establish synthetic strategies for automated synthesis.[12] Our earlier linear synthesis of a H-type II pentasaccharide[13] did not translate well to automated oligosaccharide assembly, as only low yields of the desired product were obtained.[14]

Here, we describe the solution-phase syntheses of the three type II Lewis oligosaccharides in protected form: H-type II pentasaccharide, Le^x pentasaccharide, and Le^y hexasaccharide. The strictly linear assembly strategy relies on glycosyl phosphates and glycosyl trichloroacetimidate monosaccharide building blocks in anticipation of automated assembly.

Results and Discussion

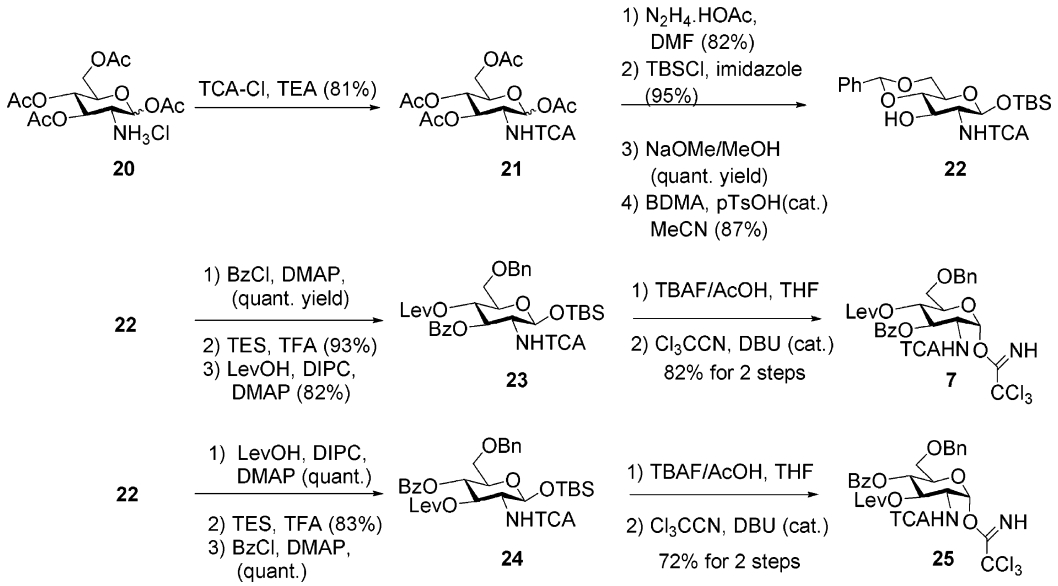
The synthesis of lactose disaccharide **5** built on earlier advances[13] and was readily accomplished using glucosyl phosphate **1**[13] and galactosyl phosphate **3**,[13] two reliable monomers (Scheme 1). The variable yields for solution-phase glycosylations of **5** when glucosamine trichloroacetimidate **6** was used prompted a triple glycosylation on solid support with a total of 30 equiv of monosaccharide building block over a 3 h period.[14] Was this indeed a "difficult" coupling or a matter of a suboptimal glucosamine building block? A more detailed study of the incorporation of glucosamine by coupling with lactose **5** was warranted. Identification of a new glucosamine building block was necessary to reliably access structures such as the Lewis antigens in solution and by automated solid-phase synthesis.

The trichloroacetamide (TCA) group has been used previously as an amine protecting group in the synthesis of complex oligosaccharides.[15−17] Its remarkable base stability and flexibility make it an attractive candidate to mask amines during automated oligosaccharide assembly. The TCA group is readily converted to the naturally displayed *N*-acetate at the end of a synthesis by a hydrogen−halogen exchange reaction.[15]

Synthesis of glucosamine building block **7** commenced with the installation of the TCA group on the amine of known glucosamine **20**[18,19] to furnish **21** (Scheme 2). An

(10) Plante, O. J.; Palmacci, E. R.; Seeberger, P. H. *Science* **2001**, *291*, 1523−1527.
(11) Palmacci, E. R.; Plante, O. J.; Hewitt, M. C.; Seeberger, P. H. *Helv. Chim. Acta* **2003**, *86*, 3975−3990.
(12) Love, K. R.; Seeberger, P. H. *Angew. Chem., Int. Ed.* **2004**, *43*, 602−605.
(13) Love, K. R.; Andrade, R. B.; Seeberger, P. H. *J. Org. Chem.* **2001**, *66*, 8165−8176.
(14) Love, K. R. Dissertation, Massachusetts Institute of Technology, Cambridge, MA, 2004.
(15) Blatter, G.; Beau, J. M.; Jacquinet, J. C. *Carbohydr. Res.* **1994**, *260*, 189−202.
(16) Blatter, G.; Jacquinet, J. C. *Carbohydr. Res.* **1996**, *288*, 109−125.
(17) Mulard, L. A.; Ughetto-Monfrin, J. *J. Carbohydr. Chem.* **2000**, *19*, 193−220.
(18) Marra, A.; Sinay, P. *Carbohydr. Res.* **1990**, *200*, 319−337.
(19) Bergmann, M.; Zervas, L. *Berichte* **1931**, *64*, 975.

SCHEME 2. Synthesis of Glucosamine Trichloroacetimidates 7 and 25

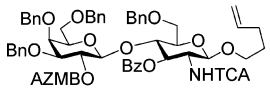
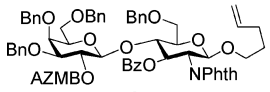


anomeric silyl protecting group was put in place before treatment with sodium methoxide to remove all three remaining acetates and subsequent protection as the 4,6-benzylidene to give **22**. Protection of the C-3 hydroxyl group of **22** as the benzoate ester, followed by regioselective opening of the benzylidene, and protection of the C-4 hydroxyl by a levulinyl ester yielded **23**. Glycoside **23** was then converted to glycosyl trichloroacetimidate **7** in 82% yield over two steps. Intermediate **22** was readily converted into another glucosamine building block **25** for the facile derivatization of the C-3 position by establishing another protecting group pattern. Following the strategy employed for building block **7**, glucosamine trichloroacetimidate **25** was synthesized beginning with protection of the C-3 position of intermediate **22**. Here, a levulinate ester was introduced (Scheme 2). Regioselective benzylidene opening to the C-6 position is followed by benzoylation of the C-4 hydroxyl, furnishing fully protected glucosamine **24**. Anomeric silyl cleavage of **24** and treatment with trichloroacetonitrile and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) generated trichloroacetimidate **25**.

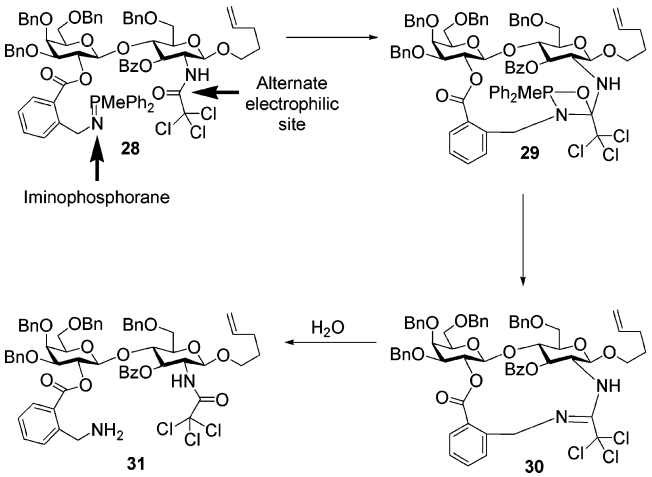
Activation of glycosyl trichloroacetimidate **7** (1.8 equiv) with trimethylsilyl trifluoromethanesulfonate (TMSOTf) at −20 °C resulted in efficient coupling with lactose **5** in 5 min as indicated by thin-layer chromatography (TLC) to yield 83% of the desired trisaccharide **9** (Scheme 1). The levulinate ester of trisaccharide **9** was readily cleaved in 95% yield by use of a solution of hydrazine acetate. Coupling of galactosyl phosphate building block **12** that contains a 2-azidomethyl benzoate (AZMB) to mask the C-2 hydroxyl with deprotected trisaccharide **11** gave 87% of the desired tetrasaccharide **14**. Repeated attempts to remove the AZMB group from tetrasaccharide **14** using the Staudinger conditions we had established earlier [13] (3 equiv of PBu_3 and 5 equiv of water in tetrahydrofuran, THF) furnished the desired product **16** in less than 20% yield.

The unsatisfactory yields for removal of the AZMB group from tetrasaccharide **14** prompted us to investigate possible incompatibilities of the functional groups on the glucosamine building block when treated under Staudinger conditions. Treatment of peracetylated *N*-TCA-protected glucosamine with tributyl phosphine and water in THF did not affect the starting material, thus demonstrating that the TCA group was stable under reducing conditions. By use of model compounds **26** and **27**, containing either TCA- or phthalimide-protected amines, respectively, a series of conditions for AZMB removal were examined (Table 1). During these studies, a side product stemming from **26** exhibited a broadened ^{1}H NMR spectrum indicative of an amine. Further analysis pointed to an internal O to P rearrangement of the intermediate iminophos-

TABLE 1. Removal of the AZMB Group from Model Disaccharides

Compound	Deprotection conditions	Yield
 **26**	5 equiv. PBu_3 3 equiv. H_2O THF	decomposition
26	5 equiv. PBu_3 3 equiv. H_2O MeCN	no reaction
26	5 equiv. $PMePh_2$ 3 equiv. H_2O THF	< 60% (crude)
26	5 equiv. $PMePh_2$ THF/H_2O 5:1	60%
 **27**	5 equiv. $PMePh_2$ 3 equiv. H_2O THF	70%
27	5 equiv. PBu_3 THF/H_2O 5:1	60%
27	5 equiv. $PMePh_2$ THF/H_2O 5:1	72%

SCHEME 3. Proposed Internal Iminophosphorane Rearrangement for Model Disaccharide 26



phorane **28**, rather than the expected hydrolysis of this species by water (Scheme 3).[20] While uncommon, this kind of rearrangement is not without precedent, as the internal rearrangement of a similar iminophosphorane containing a neighboring ester has been utilized for cell surface engineering.[21]

In **26**, the amide group may act as an alternative electrophilic site for the addition of the iminophosphorane that results in the formation of a four-membered ring transition state (**29**), as the amide oxygen attacks the nearby phosphorane. Collapse of this intermediate yields the methyldiphenyl phosphine oxide as well as imine **30**, which is hydrolyzed in the presence of water to the corresponding amine (**31**). This proposed mechanism would also explain the difference in isolated yields between the two model compounds, as the amide bond is more electrophilic in the case of the TCA-protected amine in **26**. Attempts to minimize this intramolecular side reaction by varying the electron density of the phosphine and the concentration of water were unsuccessful.

The difficulties observed in AZMB removal from model compounds **26** and **27** corresponded with similar problems in AZMB removal from tetrasaccharide **14** (Scheme 1). Changing the phosphine from PBu_3 to the more electron-rich $PMePh_2$ did, however, enable the isolation of tetrasaccharide **16** in 42% yield. While acceptable during the course of a solution-phase synthesis, this poor-yielding deprotection would be the demise of a solid-phase oligosaccharide assembly. Furthermore, a second product resulting from the migration of the C-3 benzoyl ester of the glucosamine to the newly liberated C-2 hydroxyl of the neighboring galactose residue was isolated from this reaction. Benzoate migration confirms the close spatial proximity of these two rings, lending more support for the proposed iminophosphorane rearrangement mechanism. Migration was suppressed when reductions were performed in a 5:1 mixture of THF/water, but the yield of **16** was not increased. Completion of the H-type II pentasaccharide by fucosylation of **16** with fucosyl phosphate **17** provided **19** in 75% yield.

(20) Gololobov, Y. G.; Kasukhin, L. F. *Tetrahedron* **1992**, *48*, 1353–1406.

(21) Saxon, E.; Bertozzi, C. R. *Science* **2000**, *287*, 2007–2010.

The AZMB group is attractive due to the mild conditions used for its removal, but these results demonstrate that this protecting group must be employed wisely in order to avoid spatial juxtaposition with amide-protected amines. Incompatibilities due to internal rearrangement of the iminophosphorane may arise if AZMB is placed in the vicinity of other electrophilic functional groups.

Consciousness of the incompatibilities between the C-2 AZMB group on the terminal galactose residue and amino-protecting groups led to the use of more traditional esters for protection of the terminal galactose residue in the Lewis series. Glycosylation to form branched Lewis oligosaccharides must occur first on the C-3 hydroxyl of glucosamine, followed by coupling to the C-4 hydroxyl group in order to achieve proper sterics and acceptor reactivity with the desired protecting group pattern.[12] Building block **25** was used for this purpose, equipped with a C-3 levulinate ester that can be removed selectively.

The assembly of the three target oligosaccharides commenced with the addition of glucosamine building block **25** to lactose **5**. Levulinate ester cleavage at the C-3 position with hydrazine acetate in a solution of methanolic dichloromethane rendered trisaccharide **33** (Scheme 4). Fucosylation of trisaccharide **33** with phosphate building block **17** afforded tetrasaccharide **34**. Removal of the terminal C-4 benzoate ester by the action of sodium methoxide and galactosylation with building block **36** completed the protected Le^x pentasaccharide **37**. Removal of the C-2 benzoate ester from the terminal galactose residue was accompanied by a partial loss of the pivaloyl esters from fucose to result in pentasaccharide intermediate **38** in lower than desired yield (47%). Addition of fucosyl phosphate **17** to pentasaccharide **35** resulted in the procurement of Le^y hexasaccharide **39** in 95% yield.

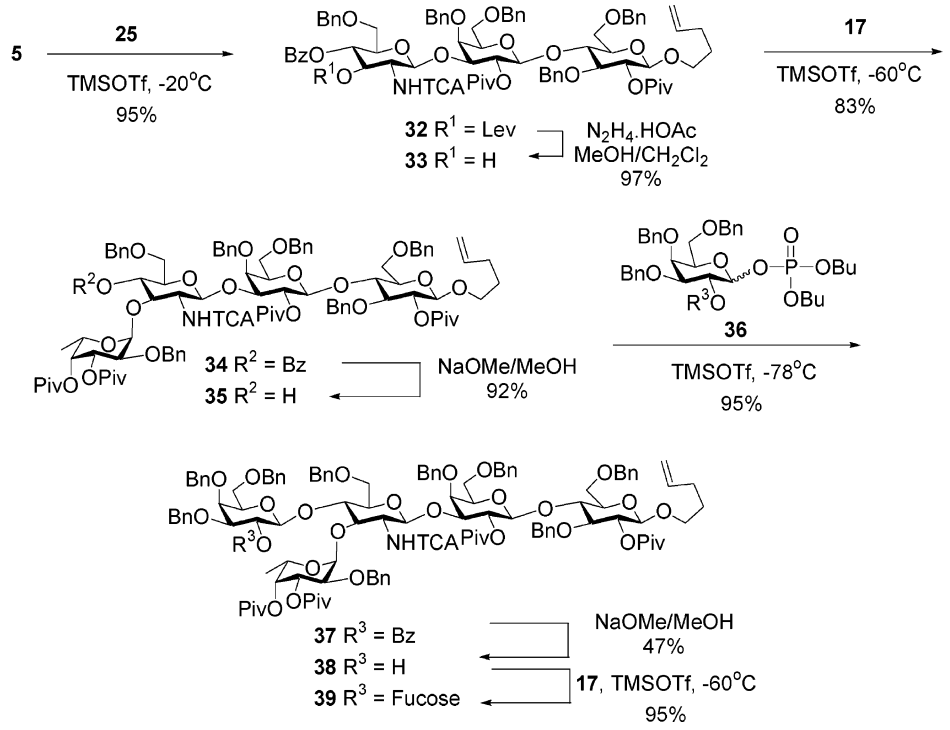
Conclusions

We have demonstrated the solution-phase syntheses of the type II Lewis oligosaccharides, H-type II, Le^x and Le^y, using a set of robust and reliable monosaccharide building blocks. By keeping in mind the constraints of automated solid-phase synthesis, all protecting-group manipulations and couplings used only homogeneous solutions. The AZMB protecting group served well in the completion of the H-type II pentasaccharide, but limitations of this mode of protection were exposed when AZMB was juxtaposed with amides. Adjustments to the synthetic route enabled the rapid synthesis of the branched Le^x and Le^y oligosaccharides using levulinate and benzoate esters as temporary protecting groups.

Experimental Section

3-*O*-Benzoyl-6-*O*-benzyl-2-deoxy-4-*O*-levulinyl-2-trichloroacetamido-β-D-glucopyranosyl Trichloroacetimidate 7. A solution of **23** (390 mg, 0.536 mmol) in THF (6 mL) was cooled to 0 °C. To this solution were added tetrabutylammonium fluoride (TBAF) (563 μL of a 1.0 M solution in THF) and acetic acid (32 μL, 0.563 mmol) simultaneously dropwise. After 90 min, the solution was diluted with water (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated to yield 3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-4-*O*-levulinyl-2-trichloroacetamido-β-D-glucopyranose (328 mg, quant yield) as a

SCHEME 4. Synthesis of Le^x Pentasaccharide 37 and Le^y Hexasaccharide 39



yellow foam, which was used without further purification. $[\alpha]_D$ +16.70° (c = 3.21, CH_2Cl_2); IR (thin film) 3414, 2919, 1745, 1721, 1272 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97−7.95 (m, 2H), 7.58−7.54 (m, 1H), 7.46−7.41 (m, 2H), 7.37−7.30 (m, 5H), 7.20 (d, J = 9.0 Hz, 1H), 5.66 (dd, J = 10.7 and 9.7 Hz, 1H), 5.42 (br s, 1H), 5.31 (t, J = 9.9 Hz, 1H), 4.60 (d, J = 11.9 Hz, 1H), 4.56 (d, J = 11.9 Hz, 1H), 4.38−4.29 (m, 2H), 4.18 (br s, 1H), 3.63 (dd, J = 4.7 and 3.6 Hz, 2H), 2.65−2.39 (m, 3H), 2.34−2.27 (m, 1H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.3, 171.7, 167.1, 162.1, 137.6, 133.8, 130.2, 129.0, 128.7, 128.6, 128.4, 128.1, 92.1, 91.2, 73.9, 71.2, 69.1, 68.8, 68.8, 54.6, 38.0, 29.8, 28.0; ESI-MS m/z (M + Na)$^+$ calcd 638.0722, obsd 638.0726.

3-*O*-Benzoyl-6-*O*-benzyl-2-deoxy-4-*O*-levulinyl-2-trichloroacetamido-β-D-glucopyranose (286 mg, 0.465 mmol) was azeotroped with toluene (3 × 3 mL) and then dried under vacuum for 1 h. The residue was dissolved in CH_2Cl_2 (5 mL) and 1 mL of trichloroacetonitrile was added, followed by DBU (7 μL, 0.0465 mmol). After 10 min, the solution was concentrated in vacuo and the crude residue was purified by flash silica gel chromatography (20% EtOAc/hexanes) to give **7** (291 mg, 82%) as a yellow foam. $[\alpha]_D$ +9.55° (c = 1.21, CH_2Cl_2); IR (thin film) 3346, 1922, 1722, 1712, 1272 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 7.98−7.96 (m, 2H), 7.62−7.58 (m, 1H), 7.45 (app t, J = 7.9 Hz, 2H), 7.38−7.27 (m, 6H), 6.61 (d, J = 3.4 Hz, 1H), 5.73−5.65 (m, 2H), 4.58 (d, J = 11.9 Hz, 1H), 4.55−4.51 (m, 2H), 4.23−4.19 (m, 1H), 3.72 (dd, J = 11.2 and 2.6 Hz, 1H), 3.66 (dd, J = 11.2 and 3.6 Hz, 1H), 2.63−2.55 (m, 2H), 2.40−2.31 (m, 2H), 2.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.2, 206.1, 199.1, 188.7, 186.4, 171.5, 167.7, 162.3, 160.3, 137.8, 134.1, 130.2, 128.8, 128.6, 128.6, 128.3, 128.0, 94.1, 91.9, 90.9, 78.0, 73.8, 72.1, 71.1, 67.7, 67.5, 54.6, 38.0, 29.7, 27.9; ESI-MS m/z (M + Na)$^+$ calcd 780.9818, obsd 780.9810.

***n*-Pentenyl 3-*O*-Benzoyl-6-*O*-benzyl-4-*O*-levulinyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside 9.** Lactose acceptor 5 (60 mg, 0.064 mmol) and glucosamine imidate 7 (98 mg, 0.129 mmol) were coevaporated in toluene (3 × 1 mL) and then dried under vacuum for 1 h. Dichloromethane was added (2 mL) and the solution was cooled to −20 °C. TMSOTf (1 μL, 0.0064 mmol) was added, and the reaction mixture turned pink. The reaction was stirred at −20 °C for 30 min, until the lactose was nearly consumed. Triethylamine was added to quench the mixture and the solution was slowly warmed to room temperature. The solution was concentrated, and the crude product was purified by flash silica column chromatography (25% EtOAc/hexanes) to afford 9 (82 mg, 83% yield). $[\alpha]_D$ −31.46° (c = 0.48 CH_2Cl_2); IR (thin film) 2924, 1741, 1726, 1273, 1068 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (app d, J = 8.4 Hz, 2H), 7.56 (app t, J = 7.4 Hz, 1H), 7.41 (app t, J = 7.8 Hz, 2H), 7.32−7.23 (m, 20H), 7.15−7.10 (m, 3H), 7.03 (app t, J = 7.1 Hz, 2H), 6.75 (d, J = 9.0 Hz, 1H), 5.82−5.73 (m, 1H), 5.38−5.28 (m, 3H), 5.02−4.92 (m, 5H), 4.74 (d, J = 12.0 Hz, 1H), 4.67 (d, J = 8.2 Hz, 1H), 4.57 (d, J = 17.9 Hz, 1H), 4.54 (d, J = 18.0 Hz, 1H), 4.50 (d, J = 11.2 Hz, 1H), 4.45 (d, J = 12.0 Hz, 1H), 4.44 (d, J = 10.6 Hz, 1H), 4.35−4.29 (m, 3H), 4.20−4.16 (m, 2H), 4.00 (t, J = 9.1 Hz, 1H), 3.95−3.90 (m, 2H), 3.84 (dt, J = 9.5 and 6.4 Hz, 1H), 3.77−3.65 (m, 5H), 3.54 (t, J = 9.0 Hz, 1H), 3.49−3.39 (m, 3H), 3.35−3.29 (m, 2H), 2.62−2.41 (m, 3H), 2.35−2.28 (m, 1H), 2.12−2.01 (m, 2H), 2.02 (s, 3H), 1.67−1.60 (m, 2H), 1.25 (s, 9H), 1.16 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.1, 176.8, 176.8, 171.6, 166.9, 162.4, 139.0, 138.9, 138.3, 138.2, 138.1, 137.8, 133.9, 130.2, 129.0, 128.7, 128.6, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.6, 127.1, 115.0, 101.4, 100.3, 99.6, 92.1, 91.3, 81.0, 77.4, 76.4, 75.5, 75.4, 74.8, 74.7, 74.3, 73.8, 73.8, 73.7, 73.5, 72.6, 72.4, 71.1, 69.4, 69.2, 69.1, 69.0, 68.7, 68.2, 56.5, 39.1, 38.9, 38.0, 30.2, 29.7, 29.0, 27.9, 27.8, 27.3; ESI-MS m/z (M + Na)$^+$ calcd 1558.5433, obsd 1558.5476.

***n*-Pentenyl 3-*O*-Benzoyl-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside 11.** A solution of hydrazine acetate (5 mg, 0.070 mmol) in MeOH (0.1 mL) was added to a solution of 9 (98 mg, 0.064 mmol) in CH_2Cl_2 (1 mL) and the resulting solution was stirred overnight at room temperature. The reaction mixture was diluted with CH_2Cl_2 (5 mL) and concentrated in vacuo. The crude product was purified by flash silica gel chromatography (20% EtOAc/hexanes) to yield 87 mg (95%) of 11. $[\alpha]_D$ −20.89° (c = 1.25, $CHCl_3$); IR (thin film) 3672, 3621, 3015, 2964, 1733 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (app d, J = 8.4 Hz, 2H), 7.57 (app t, J = 7.4 Hz, 1 H), 7.43 (app t, J = 7.9 Hz, 1H), 7.36−7.23 (m, 20H), 7.15−7.10

(m, 3H), 7.02 (app t, J = 7.5 Hz, 2H), 6.76 (d, J = 9.1 Hz, 1H), 5.82−5.73 (m, 1H), 5.30 (app t, J = 9.0 Hz, 1H), 5.18 (dd, J = 10.9 and 9.0 Hz, 1H), 5.02−4.91 (m, 5H), 4.76 (d, J = 12.0 Hz, 1H), 4.67−4.58 (m, 3H), 4.49−4.43 (m, 3H), 4.37−4.28 (m, 3H), 4.24−4.17 (m, 2H), 4.05−3.97 (m, 2H), 3.93−3.83 (m, 6H), 3.71 (d, J = 2.4 Hz, 2H), 3.66−3.61 (m, 1H), 3.54 (t, J = 9.2 Hz, 1H), 3.50−3.40 (m, 3H), 3.35−3.30 (m, 2H), 3.17 (d, J = 2.8 Hz, 1H), 2.11−2.04 (m, 2H), 1.69−1.63 (m, 2H), 1.25 (s, 9H), 1.16 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 176.9, 167.7, 162.6, 139.0, 138.8, 138.3, 138.1, 137.4, 134.0, 130.2, 128.9, 128.7, 128.7, 128.6, 128.6, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.6, 127.1, 115.0, 101.4, 100.2, 99.6, 92.1, 81.0, 77.4, 76.5, 75.7, 75.6, 75.4, 75.0, 74.8, 74.6, 74.0, 73.8, 73.7, 72.4, 71.2, 70.2, 69.1, 68.2, 55.9, 39.1, 38.9, 31.8, 30.2, 28.9, 27.8, 27.3, 22.9, 14.4; ESI-MS m/z $(M + Na)^+$ calcd 1460.5065, obsd 1460.5040.

***n*-Pentenyl 2-*O*-[2-(Azidomethyl)benzoyl]-3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl-(1→4)-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside 14.** Trisaccharide acceptor 11 (48 mg, 0.033 mmol) and galactosyl phosphate 12 (53 mg, 0.066 mmol) were coevaporated in toluene (3 × 2 mL) and then dried under vacuum for 2 h. Dichloromethane (1.5 mL) was added and the solution was cooled to −78 °C. TMSOTf (10 μL, 0.59 mmol) was added and the reaction mixture was stirred for 30 min at −78 °C. The reaction mixture was quenched by addition of TEA and slowly warmed to room temperature. The solution was concentrated and the crude residue was purified by flash silica gel chromatography (10% EtOAc/hexanes) to yield 54 mg (87%) of 14. $[\alpha]_D$ −5.59° (c = 1.68, $CHCl_3$); IR (thin film) 3015, 2923, 2103, 1728, 1077 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (app d, J = 7.2 Hz, 2H), 7.86 (app d, J = 7.7 Hz, 1H), 7.61−7.53 (m, 3H), 7.49 (app t, J = 7.5 Hz, 1H), 7.37−7.07 (m, 41H), 7.00 (app t, J = 7.2 Hz, 2H), 6.76 (d, J = 9.3 Hz, 1H), 5.82−5.73 (m, 1H), 5.50 (dd, J = 10.1 and 8.0 Hz, 1H), 5.31 (dd, J = 10.8 and 8.7 Hz, 1H), 5.26 (dd, J = 10.1 and 8.0 Hz, 1H), 5.04−4.90 (m, 6H), 4.87 (d, J = 11.6 Hz, 1H), 4.71 (d, J = 11.5 Hz, 2H), 4.66−4.57 (m, 3H), 4.53−4.40 (m, 6H), 4.35−4.25 (m, 5H), 4.23−4.19 (m, 1H), 4.18−4.13 (m, 5H), 3.98 (dd, J = 9.4 Hz, 1H), 3.92 (d, J = 2.1 Hz, 1H), 3.85−3.78 (m, 3H), 3.66 (d, J = 2.7 Hz, 2H), 3.60 (dd, J = 11.7 and 4.3 Hz, 1 H), 3.55−3.50 (m, 3H), 3.47 (dd, J = 10.2 and 2.6 Hz, 1H), 3.43−3.38 (m, 3H), 3.32−3.24 (m, 3H), 3.16 (dd, J = 9.0 and 4.4 Hz, 1H), 3.01 (dd, J = 8.3 and 4.3 Hz, 1H), 2.11−2.04 (m, 2H), 1.68−1.62 (m, 2H), 1.22 (s, 9H), 1.15 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 176.6, 165.0, 162.5, 139.1, 138.7, 138.3, 138.2, 138.0, 137.9, 137.7, 133.2, 131.2, 130.1, 130.0, 129.7, 128.7, 128.7, 128.6, 128.5, 128.5, 128.4, 128.3, 128.1, 128.1, 128.0, 127.9, 127.8, 127.6, 127.5, 127.0, 115.0, 99.7, 92.2, 81.1, 80.1, 77.4, 76.6, 75.5, 74.7, 73.8, 73.7, 73.5, 73.3, 72.5, 71.5, 69.1, 68.4, 67.2, 56.4, 53.2, 39.1, 38.9, 30.3, 29.9, 29.0, 27.8, 27.4, 11.2; ESI-MS m/z $(M + Na)^+$ calcd 2051.7434, obsd 2051.7404.

***n*-Pentenyl 3,4,6-Tri-*O*-benzyl-β-D-galactopyranosyl-(1→4)-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside 16.** *Method A*: A solution of 14 (55 mg, 0.027 mmol) in THF (2 mL) was treated with water (5 μL, 0.27 mmol), followed by tri-*n*-butyl phosphine (34 μL, 0.135 mmol), and the mixture was stirred at room temperature. After 1 h, the reaction mixture was diluted with dichloromethane (10 mL) and washed with saturated aqueous $NaHCO_3$, brine, and water (20 mL each). The organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude residue was purified by flash silica gel chromatography (20% EtOAc/hexanes) to yield 7 mg (15%) of 16. $[\alpha]_D$ −33.08° (c = 1.10, CH_2Cl_2); IR (thin film) 3672, 3621, 3015, 2964, 1733 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (app d, J = 7.1 Hz, 2H), 7.49 (app t, J = 7.5 Hz, 2H), 7.37−7.06 (m, 39H), 7.03 (app t, J = 7.5 Hz, 2H), 6.75 (d, J = 9.3 Hz, 1H), 5.82−5.74 (m, 1H), 5.36−5.28 (m, 2H), 5.05−4.90 (m, 7H), 4.74 (d, J = 11.8 Hz, 2H), 4.66−4.42 (m, 14H), 4.38−4.29 (m, 5H), 4.24−4.16 (m, 4H), 4.06 (s, 2H), 4.02−3.97 (m, 3H), 3.90−3.78 (m, 8H), 3.58−3.52 (m, 2H), 3.46−3.40 (m, 4H), 3.34−3.31 (m, 2H), 3.25 (dd, J = 7.1 and 2.7 Hz, 1H), 3.20 (t, J = 9.1 Hz, 1H), 3.05 (dd, J = 8.6 and 4.4 Hz, 1H), 2.74 (dd, J = 8.5 and 4.5 Hz, 1H), 2.11−2.06 (m, 2H), 1.69−1.62 (m, 2H), 1.23 (s, 9H), 1.16 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.1, 176.8, 176.7, 166.5, 166.5, 164.4, 162.5, 139.1, 139.0, 139.0, 139.0, 138.9, 138.3, 138.3, 138.2, 137.9, 137.8, 137.7, 133.5, 130.0, 129.8, 129.7, 129.7, 128.6, 128.6, 128.6, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.9, 127.9, 127.8, 127.7, 127.5, 127.5, 127.1, 127.0, 115.0, 104.4, 101.4, 101.1, 100.6, 99.7, 99.5, 81.9, 81.0, 77.9, 77.4, 76.6, 76.6, 76.4, 75.6, 75.5, 75.5, 75.4, 75.4, 74.9, 74.9, 74.7, 74.6, 74.0, 73.9, 73.7, 73.7, 73.4, 73.2, 72.5, 72.2, 72.2, 71.8, 71.8, 69.0, 68.5, 68.4, 68.3, 67.3, 66.5, 56.3, 55.3, 39.2, 39.1, 38.9, 30.2, 29.0, 27.8, 27.4, 27.1; ESI-MS m/z $(M + 2Na)^{2+}$ calcd 957.8452, obsd 957.8425.

Method B: A solution of **14** (219 mg, 0.107 mmol) in THF (3 mL) was treated with water (20 μL, 1.07 mmol), followed by methyldiphenyl phosphine (120 μL, 0.650 mmol), and the mixture was stirred at room temperature. After 2 h, the reaction mixture was diluted with water (20 mL) and extracted with dichloromethane (3 × 20 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated. The crude residue was purified by flash silica gel chromatography (25→40% EtOAc/ hexanes) to yield 81 mg (42%) of **16**.

α-Pentenyl 2-*O*-Benzyl-3,4-di-*O*-pivaloyl-α-L-fucopyranosyl-(1→2)-3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl-(1→4)-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside 19. Tetrasaccharide acceptor 16 (17 mg, 0.0095 mmol) and fucosyl phosphate 17 (12 mg, 0.019 mmol) were coevaporated in toluene (3 × 1 mL) and then dried under vacuum for 45 min. Dichloromethane (1 mL) was added and the solution was cooled to −78 °C, and then TMSOTf (3 μL, 0.0019 mmol) was added. The solution was warmed to −25 °C over 50 min, then quenched by addition of TEA, and allowed to warm to room temperature. The solution was concentrated and the crude residue was purified by flash silica gel chromatography (10% EtOAc/hexanes) to yield 16 mg (crude, 75%) of 19. $[\alpha]_D$ −53.45° (c = 1.56, CH_2Cl_2); IR (thin film) 3378, 3029, 2978, 2875, 1735 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (app d, J = 7.2 Hz, 2H), 7.36−7.01 (m, 46H), 6.95 (app d, J = 6.5 Hz, 2H), 6.79 (d, J = 9.2 Hz, 1H), 5.84−5.74 (m, 1H), 5.62 (d, J = 3.4 Hz, 1H), 5.38−5.29 (m, 3H), 5.25−5.23 (m, 1H), 5.12 (dd, J = 10.9 and 9.3 Hz, 1H), 4.98−4.89 (m, 5H), 4.77−4.57 (m, 8H), 4.53−4.43 (m, 6H), 4.41−4.26 (m, 10H), 4.22−4.16 (m, 2H), 4.12−4.08 (m, 1H), 4.06−3.94 (m, 5H), 3.87−3.78 (m, 4H), 3.75 (m, 1H), 3.71 (dd, J = 11.0 and 4.5 Hz, 1H), 3.61−3.38 (m, 7H), 3.38−3.35 (m, 1H), 3.31 (dd, J = 9.1 and 5.4 Hz, 2H), 3.24 (dd, J = 8.8 and 4.9 Hz, 1H), 3.03 (t, J = 8.8 Hz, 1H), 2.14−2.05 (m, 2H), 1.71−1.63 (m, 2H), 1.26 (s, 9H), 1.18 (s, 9H), 1.16 (s, 9H), 1.14 (s, 9H), 1.11 (d, J = 6.5 Hz, 3H), ^{13}C NMR (125 MHz, $CDCl_3$): δ 177.9, 177.7, 177.6, 177.0, 176.9, 167.0, 162.5, 139.1, 139.0, 138.9, 138.4, 138.4, 138.3, 138.3, 138.2, 138.0, 138.0, 137.8, 137.6, 132.9, 130.2, 130.1, 128.8, 128.7, 128.7, 128.6, 128.6, 128.6, 128.4, 128.3, 128.3, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6., 127.6, 127.5, 127.4, 127.0, 126.5, 114.5, 101.4, 100.7, 100.7, 99.8, 97.7, 97.1, 92.3, 92.0, 84.0, 81.1, 78.4, 77.9, 77.4, 76.6, 76.2, 76.2, 75.6, 75.0, 74.9, 74.6, 73.9, 73.9, 73.7, 73.7, 73.6, 73.6, 73.4, 73.2, 73.1, 73.0, 73.0, 72.9, 72.5, 72.2, 71.8, 71.6, 71.3, 71.1, 70.5, 70.4, 70.3, 69.7, 69.0, 68.7, 68.5, 67.7, 67.5, 65.5, 65.1, 56.2, 39.3, 39.3, 39.2, 39.0, 38.9, 30.3, 29.1, 27.8, 27.5, 27.5, 27.4, 27.4, 16.4, 16.2, 15.8; ESI-MS m/z $(M + Na)^+$ calcd 2296.9206, obsd 2296.9187.

Acetyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside 21. Acetyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-amino-β-D-glucopyranoside (10 g, 23.5 mmol) was dissolved in CH_2Cl_2 (100 mL) and cooled to 0 °C. To this solution was

added triethylamine (6.6 mL, 47.0 mmol) followed by trichloroacetyl chloride (3.4 mL, 30.6 mmol). After 15 min, the solution was diluted with CH_2Cl_2 (150 mL) and washed with water (100 mL) and saturated aqueous $NaHCO_3$ (2 × 150 mL). The organic extracts were dried over Na_2SO_4, filtered, and concentrated to a brown residue. The crude residue was recrystallized twice in 25% EtOAc/hexanes to yield 10.9 g (81%) of **21**. Characterization data were consistent with previously reported data.[15]

***t*-Butyldimethylsilyl 4,6-*O*-Benzylidene-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside 22.** A solution of **21** (2.32 g, 4.7 mmol) in *N*,*N*-dimethylformamide (DMF) (50 mL) was treated with hydrazine acetate (0.53 g, 7.1 mmol). After 3 h, the reaction mixture was diluted with 100 mL of ethyl acetate and washed with saturated aqueous $NaHCO_3$, brine, and water (50 mL each). The organic layer was dried over Na_2SO_4 and filtered, and the filtrate was concentrated to give 1.76 g (83%) of 3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetimido-D-glucopyranose (α/β mixture) as a white solid, which was used without further purification.

A solution of 3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-D-glucopyranose (6.58 g, 14.6 mmol) in DMF (50 mL) was treated with imidazole (2.00 g, 29.2 mmol) and *tert*-butyldimethylsilyl chloride (2.64 g, 17.5 mmol). After 3 h, the reaction mixture was diluted with water (100 mL) and the solution was extracted with ethyl acetate (3 × 100 mL). The combined organic extracts were washed with water, saturated aqueous $NaHCO_3$, brine, 5% aqueous HCl, and again with water (100 mL each). The organic extracts were dried over Na_2SO_4, filtered, and concentrated. The crude residue was purified by flash silica gel chromatography (40% EtOAc/hexanes) to yield 7.81 g (95%) of *tert*-butyldimethylsilyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside as a clear oil. Characterization data were consistent with previously reported data.[15]

A solution of *tert*-butyldimethylsilyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (4.04 g, 7.20 mmol) in methanol (50 mL) was treated with sodium methoxide (164 μL of a 25% solution by weight, 0.72 mmol) at room temperature. After 2 h, the reaction mixture was diluted with methanol (50 mL) and the pH was lowered to 6 by addition of Dowex acidic resin. The solution was filtered, and the filtrate was concentrated in vacuo to yield 3.50 g (quant yield) of *tert*-butyldimethylsilyl 2-deoxy-2-trichloroacetamido-β-D-glucopyranoside as a white foam, which was used without further purification.

A solution of *tert*-butyldimethylsilyl 2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (3.50 g, 7.20 mmol) in acetonitrile (50 mL) was treated with benzaldehyde dimethyl acetal (2.93 mL, 19.4 mmol) and *p*-toluenesulfonic acid (34 mg, 0.18 mmol). After 1 h, the reaction mixture was diluted with ethyl acetate (100 mL) and washed with saturated aqueous $NaHCO_3$, brine, and water (100 mL each). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by flash silica gel chromatography (5→40% EtOAc/hexanes) to yield 3.50 g (93%) of **22** as a clear oil. Characterization data were consistent with previously reported data.[15]

***t*-Butyldimethylsilyl 3-*O*-Benzoyl-6-*O*-benzyl-2-deoxy-4-*O*-levulinyl-2-trichloroacetamido-β-D-glucopyranoside 23.** A solution of **22** (1.58 g, 3.00 mmol) in CH_2Cl_2 (30 mL) was treated with DMAP (0.73 g, 4.50 mmol), followed by benzoyl chloride (0.52 mL, 4.50 mmol) After 4 h, the reaction mixture was diluted with CH_2Cl_2 (100 mL) and washed with a 5% aqueous HCl solution and water (50 mL each), dried over Na_2SO_4, filtered, and concentrated to a yellow oil. The crude residue was purified by flash silica gel chromatography (5% MeOH/CH_2Cl_2) to yield *tert*-butyldimethylsilyl 3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (1.73 g, 92%). $[\alpha]_D$ −65.53° (*c* = 1.92, CH_2Cl_2); IR (thin film) 3354, 2930, 2859, 1704, 1100 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02−7.99 (m, 1H), 7.71 (d, *J* = 9.8 Hz, 1H), 7.61−7.56 (m, 1H), 7.47−7.41 (m, 4H), 7.34−7.31 (m, 3H), 5.85 (d, *J* = 11.2 Hz, 1H), 5.54 (s, 1H), 4.92 (d, *J* = 7.9 Hz, 1H), 4.38−4.31 (m, 1H), 3.95−3.87 (m, 2H), 3.71 (t, *J* = 10.1 Hz, 1H), 3.55 (dt, *J* = 9.6 and 5.0 Hz, 1H), 0.89 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 162.6, 137.3, 130.2, 129.0, 128.7, 128.3, 126.1, 101.1, 96.6, 92.5, 79.3, 72.7, 68.5, 66.4, 58.3, 25.7, 17.9, −3.8, −5.3; ESI-MS *m/z* $(M + Na)^+$ calcd 652.1062, obsd 652.1064.

A solution of dry *tert*-butyldimethylsilyl 3-*O*-benzoyl-4,6-*O*-benzylidene-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (1.54 g, 2.40 mmol) in CH_2Cl_2 (25 mL) was treated with triethylsilane (1.92 mL, 12.0 mmol) and cooled to 0 °C. After 10 min, trifluoroacetic acid (0.92 mL, 12.0 mmol) was added slowly dropwise to the solution. The reaction mixture was left to slowly warm to room temperature. After 2.5 h, the solution was diluted with CH_2Cl_2 (50 mL) and washed with saturated aqueous $NaHCO_3$ (2 × 50 mL) and water (50 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude residue was purified by flash silica gel chromatography (30% EtOAc/hexanes) to give *tert*-butyldimethylsilyl 3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (1.40 g, 93%) as a white solid. $[\alpha]_D$ −18.42° (*c* = 6.90, CH_2Cl_2); IR (thin film) 3488, 3347, 2928, 2863, 1701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02−7.99 (m, 2H), 7.59−7.55 (m, 1H), 7.44−7.39 (m, 3H), 7.37−7.30 (m, 4H), 5.66 (dd, *J* = 10.8 and 9.1 Hz, 1H), 4.94 (d, *J* = 7.9 Hz, 1H), 4.58 (dd, *J* = 18.3 and 11.9 Hz, 2H), 4.25−4.18 (m, 1H), 3.99−3.96 (m, 1H), 3.81−3.73 (m, 3H), 3.31 (d, *J* = 4.0 Hz, 1H), 0.89 (s, 9H), 0.14 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 162.4, 137.8, 133.9, 130.2, 129.1, 128.7, 128.1, 128.8, 96.1, 92.6, 75.9, 74.0, 71.3, 70.6, 57.7, 25.7, 18.0, −3.9, −5.1; ESI-MS *m/z* $(M + Na)^+$ calcd 654.1219, obsd 654.1218.

Levulinic acid (238 mg, 2.06 mmol) and DMAP (240 mg, 1.96 mmol) were dissolved in 10 mL of CH_2Cl_2 and cooled to 0 °C. After 10 min, DIPC (0.34 mL, 2.16 mmol) was added with vigorous stirring. After an additional 5 min, a solution of *tert*-butyldimethylsilyl 3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (1.24 g, 1.96 mmol) in 10 mL of CH_2Cl_2 was added to the levulinic acid solution via cannula and the mixture was left to slowly warm to room temperature. After 12 h, the reaction mixture was diluted with EtOAc and flushed through a plug of silica gel. The filtrate was concentrated and the residue was purified by flash silica gel chromatography (25→40% EtOAc/hexanes) to afford 1.16 g (81%) of **23** as a clear oil. $[\alpha]_D$ −18.05° (*c* = 0.82, CH_2Cl_2); IR (thin film) 3353, 2929, 2858, 1748, 1719, 1703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.96−7.94 (m, 2H), 7.58−7.53 (m, 1H), 7.40 (app t, *J* = 7.9 Hz, 1H), 7.33−7.26 (m, 6H), 5.71 (app t, *J* = 9.8 Hz, 1H), 5.33 (t, *J* = 9.8 Hz, 1H), 5.00 (d, *J* = 7.9 Hz, 1H), 4.56 (s, 2H), 4.27−4.20 (m, 1H), 3.93−3.88 (m, 1H), 3.69 (dd, *J* = 10.8 and 2.7 Hz, 1H), 3.64 (dd, *J* = 10.7 and 6.0 Hz, 1H), 2.47−2.38 (m, 3H), 2.30−2.25 (m, 1H), 1.94 (s, 3H), 0.90 (s, 9H), 0.16 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.9, 171.8, 167.3, 162.2, 138.3, 133.9, 130.2, 128.8, 128.6, 128.4, 127.8, 127.7, 96.1, 92.4, 73.8, 73.6, 72.9, 69.4, 58.1, 37.8, 29.6, 27.9, 25.7, 18.0, −3.9, −5.2; ESI-MS *m/z* $(M + Na)^+$ calcd 752.1587, obsd 752.1579.

***t*-Butyldimethylsilyl 4-*O*-Benzoyl-6-*O*-benzyl-2-deoxy-3-*O*-levulinyl-2-trichloroacetamido-β-D-glucopyranoside 24.** Levulinic acid (410 mg, 3.70 mmol) and DMAP (452 mg, 3.53 mmol) were dissolved in 15 mL of CH_2Cl_2 and cooled to 0 °C. After 10 min, DIPC (0.53 mL, 3.36 mmol) was added with vigorous stirring. After an additional 5 min, a solution of **22** (1.76 g, 3.36 mmol) in 10 mL of CH_2Cl_2 was added to the levulinic acid solution via cannula and the mixture was left to slowly warm to room temperature. After 12 h, the reaction mixture was diluted with EtOAc and flushed through a plug of silica gel. The filtrate was concentrated and the residue was purified by flash silica gel chromatography (10→25% EtOAc/hexanes) to afford 1.76 g (84%) of *tert*-butyldimethylsilyl 4,6-*O*-benzylidine-2-deoxy-3-*O*-levulinyl-2-trichloroacetamido-β-D-

glucopyranoside as a clear oil. Characterization data were consistent with published data.[22]

A solution of dry *tert*-butyldimethylsilyl 4,6-*O*-benzylidene-2-deoxy-3-*O*-levulinyl-2-trichloroacetamido-β-D-glucopyranoside (1.76 g, 2.82 mmol) in CH_2Cl_2 (20 mL) was treated with triethylsilane (2.70 mL, 16.9 mmol) and cooled to 0 °C. After 10 min, trifluoroacetic acid anhydride (0.4 mL, 2.82 mmol) and trifluoroacetic acid (1.08 mL, 14.1 mmol) was added slowly dropwise to the solution. The reaction mixture was left to slowly warm to room temperature and after 1 h was diluted with CH_2Cl_2 (50 mL) and washed with saturated aqueous $NaHCO_3$ (2 × 100 mL) and water (100 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated. The crude residue was purified by flash silica gel chromatography (40% EtOAc/hexanes) to give *t*-butyldimethylsilyl 6-*O*-benzyl-2-deoxy-3-*O*-levulinyl-2-trichloroacetamido-β-D-glucopyranoside (1.47 g, 83%). Characterization data were consistent with published data.[22]

A solution of *tert*-butyldimethylsilyl 6-*O*-benzyl-2-deoxy-3-*O*-levulinyl-2-trichloroacetamido-β-D-glucopyranoside (1.47 g, 2.35 mmol) in CH_2Cl_2 (20 mL) was treated with DMAP (0.574 g, 4.70 mmol), followed by benzoyl chloride (0.40 mL, 3.52 mmol). After 12 h, the reaction mixture was diluted with 100 mL of a 25% EtOAc/hexanes solution and filtered throught a pad of silica. The filtrate was concentrated and the crude residue was purified by flash silica gel chromatography (25%) to EtOAc/hexanes yield **24** (1.72 g, quant yield) as a white solid. Characterization data were consistent with published data.[22]

4-*O*-Benzoyl-6-*O*-benzyl-2-deoxy-3-*O*-levulinyl-2-trichloroacetamido-β-D-glucopyranosyl trichloroacetimidate 25. A solution of **24** (1.72 g, 2.35 mmol) in THF (20 mL) was cooled to 0 °C. To this solution were added TBAF (2.6 mL of a 1.0 M solution in THF) and acetic acid (150 μL, 2.60 mmol) simultaneously dropwise. After 90 min, the solution was diluted with water (70 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were washed once with saturated aqueous $NaHCO_3$ (100 mL), dried over Na_2SO_4, filtered, and concentrated to yield 4-*O*-benzoyl-6-*O*-benzyl-2-deoxy-3-*O*-levulinyl-2-trichloroacetamido-D-glucopyranose (α/β mixture, 1.32 g, 91%) as a yellow foam, which was used without further purification.

4-*O*-Benzoyl-6-*O*-benzyl-2-deoxy-3-*O*-levulinyl-2-trichloroacetamido-D-glucopyranose (1.32 g, 2.15 mmol) was azeotroped with toluene (3 × 3 mL) and then dried under vacuum for 1 h. The residue was dissolved in CH_2Cl_2 (10 mL) and trichloroacetonitrile (10 mL), and DBU was added (32 μL, 0.215 mmol). After 10 min, the solution was concentrated in vacuo and the crude residue was purified by flash silica gel chromatography (10→15→25% EtOAc/hexanes) to give **25** (1.08, 66%) as a yellow foam. Characterization data were consistent with published data.[22]

***n*-Pentenyl 4-*O*-Benzoyl-6-*O*-benzyl-3-*O*-levulinyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside 32.** Lactose acceptor 5 (20 mg, 0.0212 mmol) and glucosamine imidate 25 (32 mg, 0.0424 mmol) were coevaporated in toluene (3 × 1 mL) and then dried under vacuum for 2 h. Dichloromethane was added (1.5 mL) and the solution was cooled to −30 °C. TMSOTf (1 μL, 0.0064 mmol) was added, and the reaction was allowed to warm to 0 °C over 30 min. The reaction mixture was quenched with TEA and the solution was slowly warmed to room temperature. The solution was concentrated, and the crude product was purified by flash silica column chromatography (25% EtOAc/hexanes) to afford 32 (27 mg, 80%). $[\alpha]_D$ −28.42° (c = 1.19, CH_2Cl_2); IR (thin film) 3346, 3031, 2971, 1735, 1066 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (app t, J = 7.1 Hz, 2H), 7.60 (app t, J = 7.4 Hz, 1H), 7.46 (app t, J = 7.9 Hz, 2H), 7.34−7.10 (m, 23H), 7.04 (app t, J = 7.5 Hz, 1H), 6.69 (d, J = 8.7 Hz, 1H), 5.82−5.74 (m, 1H), 5.39−5.28 (m, 3H), 5.03−4.93 (m, 5H), 4.73 (d, J = 4.7 Hz, 1H), 4.71 (s, 1H), 4.53−4.43 (m, 5H), 4.35 (d, J = 8.0 Hz, 2H), 4.32 (d, J = 11.9 Hz, 1H), 4.20 (d, J = 11.7 Hz, 1H), 4.07−4.00 (m, 2H), 3.94−3.91 (m, 2H), 3.86−3.79 (m, 2H), 3.70−3.63 (m, 4H), 3.56 (t, J = 9.0 Hz, 1H), 3.48−3.40 (m, 3H), 3.36−3.31 (m, 2H), 2.57 (app t, J = 6.5 Hz, 2H), 2.43 (app t, J = 6.5 Hz, 2H), 2.13−2.03 (m, 2H), 1.69−1.63 (m, 2H), 1.25 (s, 9H), 1.17 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.8, 176.9, 176.8, 172.7, 165.5, 162.4, 139.0, 139.0, 138.3, 138.2, 138.2, 137.5, 133.8, 130.1, 129.2, 128.7, 128.7, 128.6, 128.4, 128.3, 128.1, 128.0, 127.9, 127.6, 127.1, 115.0, 101.4, 100.0, 99.6, 92.3, 81.0, 77.4, 76.5, 75.6, 74.8, 74.6, 74.5, 73.9, 73.8, 73.5, 72.4, 72.1, 69.9, 69.4, 69.1, 68.4, 68.3, 56.7, 39.1, 38.9, 38.0, 30.3, 29.6, 29.0, 28.2, 27.8, 27.4; ESI-MS m/z (M + Na)$^+$ calcd 1558.5433, obsd 1558.5437.

***n*-Pentenyl 4-*O*-Benzoyl-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside 33.** A solution of hydrazine acetate (5 mg, 0.070 mmol) in MeOH (0.2 mL) was added to a solution of **32** (76 mg, 0.050 mmol) in CH_2Cl_2 (2 mL), and the resulting solution was stirred overnight at room temperature. The reaction mixture was diluted with CH_2Cl_2 (5 mL) and concentrated in vacuo. The crude product was purified by flash silica gel chromatography (30% EtOAc/hexanes) to yield 69 mg (97%) of **33**. $[\alpha]_D$ −16.84° (c = 0.40, CH_2Cl_2); IR (thin film) 3367, 2918, 1734, 1718, 1059 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (app t, J = 7.2 Hz, 2H), 7.63 (app t, J = 7.4 Hz, 1H), 7.48 (app t, J = 7.9 Hz, 3H), 7.38−7.04 (m, 25H), 5.89−5.77 (m, 1H), 5.34−5.30 (m, 1H), 5.21 (t, J = 9.4 Hz, 1H), 5.06−4.96 (m, 4H), 4.89 (d, J = 11.4 Hz, 1H), 4.77 (d, J = 12.1 Hz, 1H), 4.65 (d, J = 8.1 Hz, 1H), 4.58−4.48 (m, 6H), 4.43−4.35 (m, 3H), 4.26 (d, J = 11.7 Hz, 1H), 4.10−3.97 (m, 5H), 3.87 (dt, J = 9.6 and 6.2 Hz, 1H), 3.80−3.57 (m, 8H), 3.52−3.36 (m, 5H), 2.25−2.05 (m, 2H), 1.72−1.67 (m, 2H), 1.26 (s, 9H), 1.20 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.7, 176.8, 171.4, 166.3, 164.3, 162.5, 154.9, 138.9, 138.8, 138.3, 138.1, 137.8, 137.7, 137.5, 136.8, 133.7, 133.5, 130.1, 129.4, 129.3, 129.0, 128.9, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.7, 127.1, 121.0, 115.0, 102.5, 101.4, 99.3, 99.1, 98.2, 98.0, 92.5, 92.2, 80.9, 77.4, 77.0, 76.7, 76.1, 75.6, 75.4, 74.7, 74.5, 74.4, 74.0, 73.9, 73.8, 73.7, 73.7, 73.5, 73.4, 73.0, 72.3, 71.7, 71.6, 71.2, 69.8, 69.3, 69.1, 68.2, 68.0, 67.3, 60.6, 59.9, 39.1, 38.9, 30.2, 29.5, 28.9, 28.3, 27.6, 27.3, 27.1, 22.6, 21.3, 14.4, 14.2; ESI-MS m/z (M + Na)$^+$ calcd 1460.5065, obsd 1460.5060.

***n*-Pentenyl 2-*O*-Benzyl-3,4-di-*O*-pivaloyl-α-L-fucopyranosyl-(1→3)-4-*O*-benzoyl-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside 34.** Trisaccharide acceptor 33 (66 mg, 0.045 mmol) and fucosyl phosphate 17 (56 mg, 0.091 mmol) were coevaporated in toluene (3 × 2 mL) and then dried under vacuum for 2 h. Dichloromethane (2 mL) was added and the solution was cooled to −60 °C. TMSOTf (10 μL, 0.59 mmol) was added and the reaction mixture was allowed to warm to −30 °C over 30 min. The reaction mixture was quenched by addition of TEA and slowly warmed to room temperature. The solution was concentrated and the crude residue was purified by flash silica gel chromatography (10→20% EtOAc/hexanes) to yield 62 mg (83%) of 34. $[\alpha]_D$ −27.64° (c = 1.25, CH_2Cl_2); IR (thin film) 3351, 3031, 2973, 1736, 1094 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (app d, J = 7.5 Hz, 2H), 7.58 (app t, J = 7.4 Hz, 1H), 7.43 (app t, J = 7.9 Hz, 2H), 7.37−7.10 (m, 33H), 7.04 (app t, J = 7.1 Hz, 2H), 6.78 (d, J = 7.2 Hz, 1H), 5.82−5.73 (m, 1H), 5.34−5.30 (m, 1H), 5.25 (app t, J = 9.6 Hz, 1H), 5.21 (dd, J = 10.7 and 3.1 Hz, 1 H), 5.10−5.08 (m, 1H), 5.02−4.90 (m, 6H), 4.79 (d, J = 3.4 Hz, 1H), 4.72 (d, J = 12.3 Hz, 1H), 4.69 (d, J = 11.9 Hz, 1H), 4.57 (d, J = 11.5 Hz, 1H), 4.50−4.42 (m, 5H), 4.34−4.29 (m, 2H), 4.21 (app t, J = 8.7 Hz, 1H), 4.19 (d, J = 11.8 Hz, 1H), 4.05−3.93 (m, 4H), 3.83 (dt, J = 9.6 and 6.3 Hz, 1H), 3.79−3.74 (m, 1H), 3.70−3.53 (m, 8H), 3.47−

(22) Palmacci, E. R. Dissertation, Massachusetts Institute of Technology, Cambridge, MA, 2003.

3.30 (m, 5H), 2.11−2.04 (m, 2H), 1.68−1.62 (m, 2H), 1.23 (s, 9H), 1.17 (s, 9H), 1.11 (s, 18H), 0.66 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.3, 177.3, 176.8, 176.2, 165.5, 162.1, 139.3, 139.0, 138.3, 138.3, 138.3, 138.1, 137.6, 133.4, 130.0, 129.9, 128.8, 128.8, 128.6, 128.6, 128.5, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.1, 115.0, 101.4, 99.9, 99.7, 99.3, 92.4, 81.1, 78.1, 77.4, 75.5, 74.8, 74.6, 74.0, 73.9, 73.8, 73.7, 73.7, 73.6, 72.8, 72.5, 71.2, 70.7, 69.9, 69.0, 68.4, 66.4, 59.0, 39.1, 39.0, 38.9, 38.8, 30.3, 29.0, 27.6, 27.4, 27.4, 15.4; ESI-MS: m/z $(M + Na)^+$ calcd 1864.7264, obsd 1864.7322.

***n*-Pentenyl 2-*O*-Benzyl-3,4-di-*O*-pivaloyl-α-L-fucopyranosyl-(1→3)-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D -galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside 35.** A solution of 34 (49 mg, 0.027 mmol) in methanol (1.5 mL) was treated with sodium methoxide (30 μL of a 25% solution by weight, 5 equiv) at room temperature. After 90 min the solution was diluted with 10 mL of methanol and acidified to pH 6 by addition of Amberlite acidic resin. The solution was filtered and the filtrate was concentrated. The crude residue was filtered through a plug of silica with a 25% EtOAc/hexanes solution and concentrated to furnish 39 mg of the tetrasaccharide 35 (85%). $[\alpha]_D$ −36.59° (c = 0.60, CH_2Cl_2); IR (thin film) 3431, 3031, 2973, 1735, 1066 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.21 (m, 25H), 7.16 (app d, J = 7.1 Hz, 2H), 7.11 (app t, J = 7.3 Hz, 1H), 7.02 (app t, J = 7.6 Hz, 2H), 6.69 (d, J = 7.7 Hz, 1 H), 5.84−5.74 (m, 1H), 5.33−5.27 (m, 3H), 5.03−4.93 (m, 6H), 4.75−4.69 (m, 3H), 4.62 (d, J = 12.1 Hz, 1H), 4.59−4.44 (m, 5H), 4.40−4.29 (m, 4H), 4.18 (d, J = 11.8 Hz, 1 H), 4.11 (br s, 1H), 4.03−3.91 (m, 3H), 3.86−3.72 (m, 6H), 3.68−3.51 (m, 7H), 3.48−3.39 (m, 3H), 3.35−3.30 (m, 2H), 2.11−2.04 (m, 2H), 1.69−1.63 (m, 2H), 1.22 (s, 9H), 1.20 (s, 9H), 1.17 (s, 18H), 1.07 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 177.3, 176.8, 176.5, 162.1, 139.2, 138.9, 138.3, 138.3, 138.1, 138.0, 137.7, 129.8, 128.8, 128.7, 128.6, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 128.0, 128.0, 127.9, 127.9, 127.8, 127.5, 127.0, 115.0, 101.4, 99.8, 99.5, 98.5, 92.6, 91.9, 82.8, 81.1, 77.9, 77.4, 76.6, 75.5, 75.5, 75.2, 74.7, 73.8, 73.7, 73.6, 73.3, 72.4, 71.0, 70.6, 69.8, 69.6, 69.0, 68.3, 67.0, 57.0, 39.2, 39.0, 38.9, 30.2, 29.5, 29.0, 28.3, 27.6, 27.3, 22.7, 16.1, 14.2; ESI-MS m/z $(M + Na)^+$ calcd 1760.7002, obsd 1760.7031.

Dibutyl 2-*O*-Benzoyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl Phosphate 36. Tri-*O*-benzyl-D-galactal (995 mg, 2.39 mmol) was azeotroped with toluene (3 × 3 mL) and then dried under vacuum for 1 h. Dichloromethane (20 mL) was added and the solution was cooled to 0 °C before a solution of dimethyldioxirane in acetone (50 mL, 0.08 M) was added. The reaction mixture was stirred for 15 min at 0 °C, and then the volatiles were removed in vacuo. The residue was dried under vacuum for 5 min at 0 °C, and then 20 mL of CH_2Cl_2 was added and the reaction mixture was cooled to −78 °C and stirred for 10 min. To the reaction vessel was added a solution of dibutyl phosphate (570 μL, 2.87 mmol) in CH_2Cl_2 (10 mL) via cannula, and the reaction mixture was warmed to 0 °C after 5 min. DMAP (1.17 g, 9.56 mmol) and benzoyl chloride (0.55 mL, 4.78 mmol) were added and the solution was left to warm to room temperature over 1 h. The reaction mixture was diluted with a solution of 25% EtOAc/hexanes (50 mL), filtered, and concentrated. The crude product was purified by flash silica column chromatography (25→40% EtOAc/hexanes) to afford **36** (1.28 mg, 73% yield). $[\alpha]_D$ +39.88° (c = 2.13, CH_2Cl_2); IR (thin film) 3337, 2961, 1732, 1268, 1028 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (app d, J = 7.1 Hz, 2H), 7.59 (app t, J = 7.5 Hz, 1H), 7.45 (app t, J = 7.9 Hz, 2H), 7.39−7.15 (m, 15H), 5.74 (dd, J = 10.1 and 8.1 Hz, 1H), 5.32 (app t, J = 7.6 Hz, 1H), 5.01 (d, J = 11.5 Hz, 1H), 4.67−4.64 (m, 2H), 4.49 (d, J = 12.4 Hz, 1H), 4.46 (s, 2H), 4.05−3.95 (m, 3H), 3.78−3.60 (m, 6H), 1.59−1.54 (m, 2H), 1.35−1.22 (m, 4H), 1.03−0.97 (m, 2H), 0.87 (t, J = 7.4 Hz, 3 H), 0.67 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 138.5, 137.9, 137.5, 133.4, 130.1, 130.0, 128.7, 128.6, 128.5, 128.1, 128.0, 128.0, 127.9, 97.3, 79.5, 74.9, 74.5, 73.8, 72.5, 72.0, 71.8, 71.7, 68.1, 68.1, 68.0, 68.0, 67.9, 32.2, 32.2, 32.0, 31.9, 18.7, 18.4, 13.8, 13.6; ^{31}P NMR (120 MHz, $CDCl_3$) δ −2.04; ESI-MS m/z $(M + Na)^+$ calcd 769.3112, obsd 769.3116.

***n*-Pentenyl 2-O-Benzoyl-3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl(1→4)-[2-*O*-benzyl-3,4-di-*O*-pivaloyl-α-L-fucopyranosyl-(1→3)]-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside 37.** Tetrasaccharide acceptor 35 (48 mg, 0.028 mmol) and galactosyl phosphate 36 (40 mg, 0.055 mmol) were coevaporated in toluene (3 × 2 mL) and then dried under vacuum for 2 h. Dichloromethane (2 mL) was added and the solution was cooled to −60 °C. TMSOTf (10 μL, 0.55 mmol) was added and the reaction mixture was allowed to warm to −20 °C over 30 min. The reaction mixture was quenched by addition of TEA and slowly warmed to room temperature. The solution was concentrated and the crude residue was purified by flash silica gel chromatography (10→20% EtOAc/ hexanes) to yield 65 mg (98%) of 37. $[\alpha]_D$ −11.72° (c = 0.30, CH_2Cl_2); IR (thin film) 3421, 3031, 2971, 1734, 1718 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, J = 7.7 and 1.3 Hz, 2H), 7.46−7.12 (m, 46H), 7.04 (app t, J = 7.0 Hz, 2H), 6.86 (d, J = 8.3 Hz, 1H), 5.83−5.74 (m, 1H), 5.48 (dd, J = 10.0 and 8.0 Hz, 1H), 5.32 (d, J = 10.4 Hz, 1H), 5.30 (d, J = 10.7 Hz, 1H), 5.24−5.19 (m, 2H), 5.03−4.95 (m, 4H), 4.85 (d, J = 11.5 Hz, 1H,) 4.83 (d, J = 11.5 Hz, 1H), 4.74 (d, J = 12.0 Hz, 1H), 4.68−4.59 (m, 5H), 4.56−4.54 (m, 2H), 4.48−4.33 (m, 13H), 4.22−4.19 (m, 2H), 4.07 (d, J = 11.8 Hz, 1 H), 4.04 (d, J = 2.6 Hz, 1H), 4.00 (t, J = 9.4 Hz, 1H), 3.96−3.91 (m, 2H), 3.87−3.81 (m, 4H), 3.72 (d, J = 2.6 Hz, 2H), 3.65−3.40 (m, 9H), 3.37−3.34 (m, 2H), 3.29−3.20 (m, 3H), 2.12−2.05 (m, 2H), 1.69−1.61 (m, 2H), 1.20 (s, 9H), 1.19 (s, 9H), 1.17 (s, 9H), 1.11 (s, 9H), 0.98 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 177.1 176.9, 176.7, 165.5, 161.7, 139.2, 139.1, 138.3, 138.3, 137.9, 137.9, 137.6, 130.0, 130.0, 129.9, 129.9, 129.2, 129.1, 128.7, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.2, 128.2, 128.2, 128.1, 128.0, 127.8, 127.7, 127.4, 127.0, 115.0, 101.4, 100.1, 100.0, 99.9, 96.5, 92.3, 91.2, 81.1, 79.5, 78.1, 77.9, 77.4, 76.1, 75.7, 74.9, 74.7, 74.5, 73.9, 73.8, 73.6, 73.6, 73.3, 73.1, 72.8, 72.5, 72.4, 72.3, 71.9, 71.4, 71.4, 71.0, 70.3, 69.8, 69.0, 68.7, 68.4, 67.8, 65.5, 58.2, 39.2, 39.0, 38.9, 38.8, 30.2, 29.5, 29.0, 28.3, 27.7, 27.4, 27.4, 27.3, 22.7, 15.7, 14.4, 14.2; ESI-MS: m/z $(M + Na)^+$ calcd 2296.9200, obsd 2296.9263.

***n*-Pentenyl2-*O*-Benzyl-3,4-di-*O*-pivaloyl-α-L-fucopyranosyl-(1→2)-3,4,6-tri-O-benzyl-β-D-galactopyranosyl(1→4)-[2-*O*-benzyl-3,4-di-*O*-pivaloyl-α-L-fucopyranosyl-(1→3)]-6-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-galactopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-D-glucopyranoside 35.** A solution of 37 (55 mg, 0.024 mmol) in methanol (1.5 mL) was treated with sodium methoxide (28 μL of a 25% solution by weight, 10 equiv) at room temperature. After 2.5 h the solution was diluted with 10 mL of methanol and acidified to pH 6 by addition of Dowex resin. The solution was filtered, and the filtrate was concentrated and purified by column to give 25 mg of pentasaccharide **38**.

Pentasaccharide acceptor **38** (20 mg, 0.0092 mmol) and fucosyl phosphate 17 (12 mg, 0.018 mmol) were coevaporated in toluene (3 × 1 mL) and then dried under vacuum for 2 h. Dichloromethane (1 mL) was added and the solution was cooled to −50 °C. TMSOTf (5 μL, 0.018 mmol) was added and the reaction mixture was allowed to warm to −20 °C over 30 min. The reaction mixture was quenched by addition of TEA and slowly warmed to room temperature. The solution was concentrated and the crude residue was purified by flash silica gel chromatography (5→10→17→25% EtOAc/hexanes) to yield 22 mg (95%) of hexasaccharide **39**. $[\alpha]_D$ −51.33° (c = 1.38, CH_2Cl_2); IR (thin film) 3487, 3050, 2937, 1741, 1720 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.01 (m, 46H), 6.99 (app t, J = 7.7 Hz, 2H), 6.90 (app d, J = 6.6 Hz, 2H), 6.60 (d, J = 7.6 Hz, 1H), 5.81−5.75 (m, 1H), 5.66 (d, J = 3.5 Hz, 1H), 5.37−5.27

(m, 4H), 5.24 (d, J = 3.6 Hz, 1H), 5.19 (dd, J = 10.7 and 3.3 Hz, 1H), 5.05 (d, J = 7.3 Hz, 1H), 5.01−4.98 (m, 1H), 4.97−4.93 (m, 3H), 4.91−4.85 (m, 2H), 4.75−4.62 (m, 7H), 4.60 (d, J = 7.8 Hz, 1H,) 4.55 (d, J = 12.1 Hz, 1H), 4.51 (d, J = 12.2 Hz, 1H), 4.48−4.36 (m, 6H), 4.34−4.31 (m, 2H), 4.29−4.25 (m, 2H), 4.21−4.16 (m, 2H), 4.14−4.11 (m, 1H), 4.08−4.01 (m, 2H), 3.98−3.95 (m, 1H), 3.92−3.86 (m, 3H), 3.83−3.79 (m, 2H), 3.74−3.67 (m, 3H), 3.55 (t, J = 8.8 Hz, 1H), 3.45−3.40 (m, 3H), 3.36−3.25 (m, 4H), 2.09−2.04 (m, 2H), 1.67−1.61 (m, 2H), 1.21 (s, 9H), 1.20 (s, 9H), 1.17 (s, 9H), 1.16 (s, 9H), 1.15 (s, 18H), 1.11 (d, J = 6.5 Hz, 3H), 0.99 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.9, 177.5, 177.2, 177.0, 176.8, 176.4, 161.4, 139.2, 139.1, 138.8, 138.4, 138.4, 138.3, 138.3, 138.2, 138.1, 137.7, 130.0, 129.6, 128.7, 128.6, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6, 127.6, 127.5, 127.4, 127.3, 127.2, 127.0, 126.4, 114.9, 101.4, 99.9, 99.9, 97.6, 97.5, 84.1, 81.2, 75.6, 75.6, 75.5, 75.3, 75.1, 74.7, 74.5, 74.3, 73.9, 73.8, 73.7, 73.7, 73.6, 73.4, 73.4, 73.3, 73.3, 73.1, 73.0, 72.6, 72.2, 71.9, 71.5, 71.2, 70.8, 70.2, 69.0, 68.4, 67.9, 65.4, 65.3, 39.2, 39.1, 39.0, 38.9, 38.8, 30.3, 29.0, 27.6, 27.5, 27.5, 27.4, 27.4, 27.3, 15.8, 15.8; ESI-MS m/z $(M + Na)^+$ calcd 2597.1137, obsd 2597.1087.

Acknowledgment. This research was supported by GlaxoSmithKline (Scholar award to P.H.S.), the Swiss National Science Foundation (SNF), the Alfred P. Sloan Foundation (Fellowship to P.H.S.), Merck (Academic Development Award to P.H.S.) and ETH Zürich.

Supporting Information Available: General experimental methods and compound characterization data, including ^{1}H NMR, ^{13}C NMR, and ^{31}P NMR spectral data for all described compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JO047723B