The identity of the decarbonylation product, undecane, was verified by comparison with an authentic sample (Aldrich) using the OV-101 column and was additionally confirmed by comparison on a 50-m HP-1 (cross-linked methylsilicone gum phase) capillary column where it could be distinguished clearly from undecene. The absence of undecene was checked by taking the GC of the final reaction mixtures on the capillary column. Dodecanal-d_1 and heptanal-d_1 were prepared using the modified Rosenmund reduction method of dodecanoyl chloride developed by Burgstahler.[17] The preparation was done with 16 mL of dodecanoyl chloride, purchased from Aldrich and distilled before use. Prolonged reaction times were necessary (48 h) for completion of the reaction. The product was identified by GC, FTIR, NMR, and GC-MS. All rhodium reactions were conducted under inert atmosphere. High-purity argon was passed through purification towers containing MnO and 4A molecular sieves before being bubbled through catalytic reaction solutions.

All NMR spectra were obtained with a Varian XL-200 spectrometer. IR spectra were obtained with a Mattson Cygnus 100 spectrophotometer. A Varian 3400 GC interfaced with a Finnigan-Mat 8230 high-resolution magnetic sector mass spectrometer, using electron ionization (70 eV), was used for all GC-MS analyses.

Catalytic reactions (eq 5) were carried out in a bubbler constructed of a cell (9-cm length, 2.5-cm diameter) fused to a Vigreux condenser (15 cm) on top of which was attached an inlet/outlet adapter. The inlet was fitted with a Kontes high-vacuum stopcock and extended through a glass capillary tube through the condenser to the bottom of the cell. The outlet was also fitted with a similar stopcock, used to adjust the flow rate, and joined to a flow meter. A GC sampling port (an Ace-Thred adjustable electrode adapter) was placed near the outlet. In a typical experiment, 4 mL of solution is placed in the cell, the flow rate of purified argon is adjusted, and the condenser is cooled with water at 0 °C. To monitor the reaction, the cell is taken out of the oil bath and is immediately placed in an ice bath to quench the reaction. The reaction solution is shaken so as to dissolve any material which might be on the inner walls of the condenser and a sample is taken for GC analysis.

The stoichiometric reaction (eq 2) was monitored by FTIR. Two procedures were followed. The reaction was carried out either (a) in a thermostated IR cell or (b) in an Ace-Thred-fitted cell immersed in a thermostated oil bath. Samples were then transferred by syringe into an IR cell. The reason for the use of the latter procedure was to ensure that temperatures in both the stoichiometric and the catalytic cases were identical. The results from both procedures were in good agreement. The concentration of the alkane (using both procedures) was derived from the concentration of $Rh(PMe_3)_2(CO)Cl$ product and calculated using eq 9,

$$[R'H] = \tfrac{1}{2}\{20\text{ mM} - y \pm [(-20\text{ mM} + y)^2 - 8y(10\text{ mM} + y - y/K_{eq})]^{1/2}\} \quad (9)$$

where y is the concentration of $Rh(PMe_3)_2(CO)Cl$ (mM) as determined spectroscopically. This expression was derived from eq 2 and the equilibrium in ref 8 for a 10 mM initial concentration of **2** (the solution obtained by subtracting the radical expression is used for the early stages of the reaction). The equilibrium constant, $K_{eq} = 0.4$, was determined by adding substoichiometric amounts of carbon monoxide to solutions of **2** and then monitoring the concentrations of $Rh(PMe_3)_2(CO)Cl$ and **2**. This value was in agreement with that obtained by monitoring reaction 2 before completion. We were also able to use an alternative expression to determine the stoichiometric reaction rate, eq 10, where x is the

$$[R'H] = 20\text{ mM} - 2(x + y) \quad (10)$$

spectroscopically determined concentration of **2**. Equation 10 gave results in agreement with eq 9, but the determination of small changes in [2] introduced additional scatter into the data and we therefore relied on eq 9.

C-O stretching frequencies (cm^{-1}) in the infrared spectrum are as follows (dodecanal solvent; extinction coefficient in parentheses in units of M^{-1} cm^{-1}): **1**, 2001 (2200), 2086 (1500); **2**, 1975 (3900); $Rh(PMe_3)_2(CO)Cl$, 1960.5 (2100); $Rh_2(PMe_3)(CO)_3Cl_2$, 2089 (ca. 2400), 2019 (ca. 2500), 1990 (ca. 1800).

Acknowledgment. Financial support from the donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged. A.S.G. thanks the Camille and Henry Dreyfus Foundation for a Distinguished New Faculty Grant. We thank Johnson-Matthey for generous loans of rhodium trichloride. Mr. Kuochen Shih is thanked for experimental assistance.

Registry No. 1, 31340-72-4; **2**, 49634-24-4; dodecanol, 112-53-8; undecane, 1120-21-4; deuterium, 7782-39-0.

Total Synthesis of (-)-Hikizimycin Employing the Strategy of Two-Directional Chain Synthesis

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Abstract: Hikizimycin (anthelmycin) is a nucleoside antibiotic and anthelmintic agent that represents the most structurally complex member of the long-chain carbohydrate class of natural products. The undecose moiety of hikizimycin was constructed efficiently by employing the strategy of two-directional chain synthesis. A description of this approach, including the advantages and challenges, is provided. In addition, the methods that were utilized to solve the remaining problems associated with the synthesis of hikizimycin are reported. The synthesis confirms the assigned structure of the natural product.

Introduction

Hikizimycin (also named anthelmycin) is a nucleoside disaccharide that was isolated from the fermentation broth of *Streptomyces* A-5[1] and *Streptomyces longissimus*[2] and shown to possess significant anthelmintic activity against a variety of common parasites.[3] Hikizimycin belongs to an important class of natural products that incorporate, within their structure, long-chain carbohydrate moieties.[4] These molecules, which include tunicamycins,[5] herbicidins,[6] and neuraminic acids,[7] have stimulated much interest due to their complex structures and to their ability to exert a profound influence on a variety of biological processes. Hikizimycin is comprised of a cytosine base, a 3-

† Present address: Department of Chemistry, Columbia University, New York, NY 10027.

(1) Uchida, K.; Ichikawa, T.; Shimauchi, Y.; Ishikura, T.; Ozaki, A. *J. Antibiot.* **1971**, *24*, 259.
(2) Hamill, R. L.; Hoehn, M. M. *J. Antibiot.* **1964**, *17*, 100.
(3) Hikizimycin has also been shown to exibit antibacterial properties: Uchida, K.; Wolf, H. *J. Antibiot.* **1974**, *27*, 783.
(4) See: (a) Isono, K. *J. Antibiot.* **1988**, *41*, 1711. (b) Danishefsky, S. J.; DeNinno, M. P. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 15.
(5) *Tunicamycin*; Tamura, G., Ed.; Japan Scientific Soc.: Tokyo, 1982.
(6) Arai, M.; Haneishi, T.; Kitahara, N.; Enokita, R.; Kawakubo, K.; Kondo, Y. *J. Antibiot.* **1976**, *29*, 863.
(7) (a) Schauer, R. *Adv. Carbohydr. Chem. Biochem.* **1982**, *40*, 131. (b) Schauer, R. *The Sialic Acids*; Springer-Verlag: Vienna, 1982.

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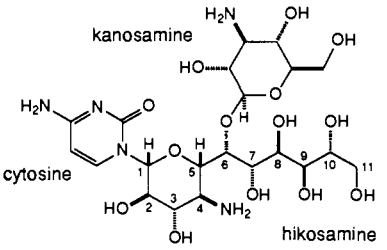


Figure 1. Structure of hikizimycin (anthelmycin) and its components.

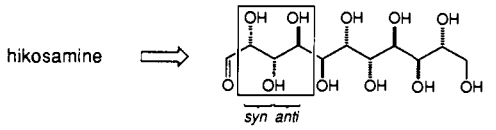


Figure 2. Retrosynthesis of the hikosamine fragment.

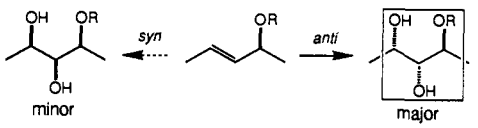


Figure 3. Diastereoselectivity of osmylation reactions.[13]

amino-3-deoxyglucose sugar (kanosamine), and a 4-aminoundecose sugar (hikosamine), and by virtue of this fully oxidized 11-carbon core, hikizimycin may be considered the most complex representative of this class of natural products (Figure 1).

In our laboratory is an ongoing program aimed at demonstrating the versatility of two-directional chain synthesis for the efficient construction of stereochemically complex structures. An attractive feature of this strategy is that the nascent chain is simultaneously homologated at both termini, thus resulting in a reduction in the number of synthetic steps and greater material throughput, as well as high levels of enantiomeric purity of the products. Recognition of the appropriate symmetries inherent in target compounds, the choice of highly stereoselective transformations, and a method to achieve terminus group differentiation are important considerations for the success of this strategy.[8] Its application has resulted in the syntheses of a number of complex natural products.[9] An analysis of the undecose moiety of hikizimycin suggested a synthesis employing two-directional chain synthesis.[10,11]

Replacing the C4 amino group with a hydroxyl group with inversion of configuration and rendering the structure in the aldose form yielded a retron displaying a repeating syn-anti arrangement of vicinal hydroxyl groups (Figure 2). Past syntheses of long-chain sugars have shown that osmylation[12] is an effective method for introducing vicinal diol functionalities. Osmylations of *E*-olefins yield *syn*-diols, while *Z*-olefins yield *anti*-diols. In addition, allylic ether systems often react with high facial selectivity to dispose the newly created hydroxyl groups anti (or erythro) to the preexisting alkoxy or hydroxy group (Figure 3). The latter stereochemical insight was obtained by Kishi and co-workers in the course of their investigations of palytoxin; the resulting empirical rule governing the stereochemical outcome of such reactions has proven to be a highly reliable method for stereoselective synthesis.[13] The C_2 symmetry of the C2–C11 fragment suggested a two-directional approach employing two sets of olefination/osmylation operations, each with double processing, and use of the C6 and C7 stereocenters as initial stereocontrolling elements (Figure 4). The C1 carbonyl group had to be accommodated by departing from the simultaneous two-directional approach at some point of the synthesis. Monofunctionalization of one of the two homotopic ends of the C_2 symmetric C2–C9 fragment followed by a sequential two-directional synthesis resulted in a satisfactory solution. Reported herein is the full account of the first total synthesis of hikizimycin.[10]

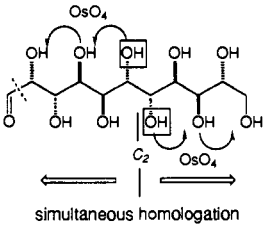
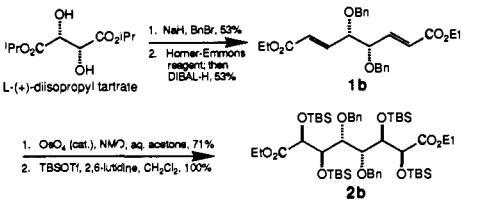
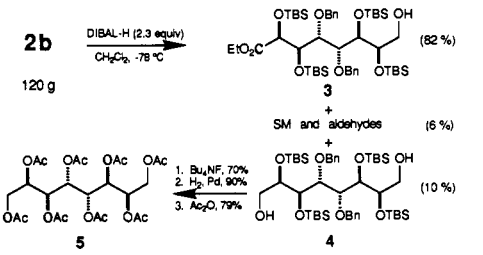


Figure 4. Two-directional strategy applied to the hikosamine retron. Without the formyl group (dotted line), a C_2 axis of symmetry is present.

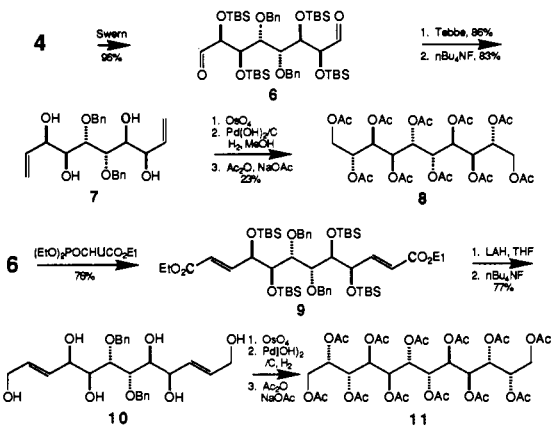
Scheme I



Scheme II



Scheme III



Results and Discussion

1. Two-Directional Approach to the Undecose Chain. The synthesis began with L-(+)-diisopropyl tartrate, which provided

(8) Description of this strategy: Schreiber, S. L. *Chem. Scr.* **1987**, *27*, 563.

(9) For the use of two-directional chain synthesis in synthetic studies, see the following references. (a) Mycoticins: Schreiber, S. L.; Goulet, M. T.; Schulte, G. *J. Am. Chem. Soc.* **1987**, *109*, 4718. Schreiber, S. L.; Goulet, M. T. *J. Am. Chem. Soc.* **1987**, *109*, 8120. (b) (+)-KDO and Riboflavin: Smith, D. B.; Wang, Z.; Schreiber, S. L. *Tetrahedron* **1990**, *46*, 4793. (c) Teurilene: Kiessling, L. K. Ph.D. Thesis, Yale University, New Haven, CT, February, 1989. (d) FK506: Schreiber, S. L.; Sammakia, T.; Uehling, D. E. *J. Org. Chem.* **1989**, *54*, 15. Nakatsuka, M.; Ragan, J. A.; Sammakia, T.; Smith, D. B.; Uehling, D. E.; Schreiber, S. L. *J. Am. Chem. Soc.* **1990**, *112*, 5583. (e) Streptovaricin A: Schreiber, S. L.; Wang, Z.; Schulte, G. *Tetrahedron Lett.* **1988**, *29*, 4085. Wang, Z.; Schreiber, S. L. *Tetrahedron Lett.* **1990**, *31*, 31.

(10) For a preliminary account of this work, see: Ikemoto, N.; Schreiber, S. L. *J. Am. Chem. Soc.* **1990**, *112*, 9657.

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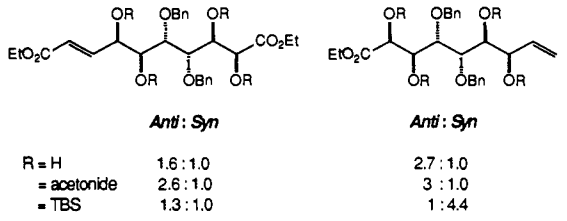
(12) Review: Schröder, M. *Chem. Rev.* **1980**, *80*, 187.

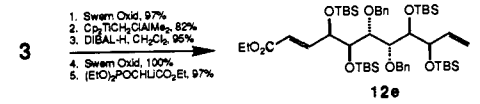
(13) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron* **1984**, *40*, 2247.



R = H	1.6 : 1.0	2.7 : 1.0
= acetonide	2.6 : 1.0	3 : 1.0
= TBS	1.3 : 1.0	1 : 4.4

Figure 5. Selectivities in the osmylation[15] of model substrates.

Scheme IV



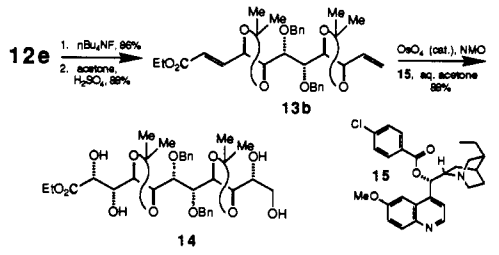
the C6 and C7 stereocenters (Scheme I). Benzylation of the hydroxyl groups followed by a one-pot reduction/homologation procedure[14] furnished the α,β-unsaturated ester **1b**. Bis-hydroxylation with catalytic osmium tetraoxide and excess *N*-methylmorpholine *N*-oxide (NMO)[15] yielded the tetraol **2a** with high selectivity.[16] The product was obtained after workup as a pure crystalline solid and was thus freed from the minor diastereomers arising from the *E,Z* isomer of **1b** and the minor "syn" mode of addition. The tetraol was protected as its tetra(*tert*-butyldimethylsilyl ether) **2b**. By this sequence of four reactions, the synthesis of the eight-carbon chain with four new, fully protected stereocenters was achieved efficiently on a multigram scale (124 g).

Terminus differentiation of the C_2-symmetric chain was achieved at this stage by effecting a monofunctionalization of the two homotopic ester groups of **2b** (Scheme II). The alcohol **3** was prepared efficiently and with surprisingly good selectivity by treatment of **2b** with DIBAL-H, added slowly at −78 °C.[17] The overreduction product **4** was useful for confirming the "anti" selectivity of the first set of osmylation reactions. Desilylation and debenzylation of **4** afforded an octitol, which was peracetylated to yield compound **5**: its melting point and optical rotation were comparable to those of octa-*O*-acetyl-D-*threo*-L-*galacto*-octitol[18] with the stereochemistry shown.

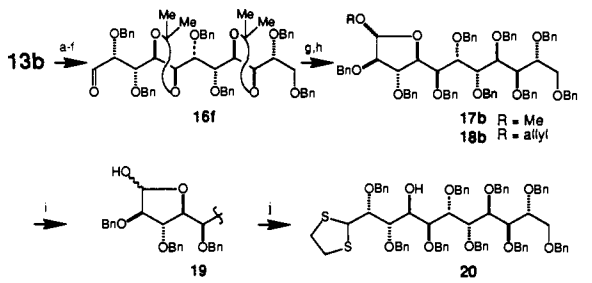
Other long-chain alditol derivatives were prepared rapidly by applying the olefination/osmylation tactic[19] in two directions (Scheme III). The diol **4** was converted to the dialdehyde **6** by Swern oxidation[20] and olefinated with the Tebbe reagent.[21] Desilylation to the diene **7** followed by a bis-osmylation in the presence of a chiral amine catalyst (vide infra), debenzylation, and peracetylation afforded, after HPLC separation of minor diastereomers, deca-*O*-acetyl-D-*manno*-D-*manno*-decitol (**8**). Similarly, bis-olefination of **6** with the Horner–Emmons reagent to the bis-α,β-unsaturated ester **9**, followed by DIBAL-H reduction and desilylation afforded **10**. Osmylation, debenzylation, and peracetylation as above yielded dodeca-*O*-acetyl-L-*threo*-L-*galacto*-L-*galacto*-dodecitol (**11**).

The undecose chain of hikosamine was constructed sequentially in two directions (Scheme IV). Swern oxidation of **3** followed

Scheme V



Scheme VI[a]



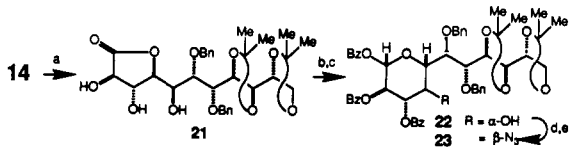
[a] (a) DIBAL-H, CH_2Cl_2 (92%). (b) TBDPSCl, imidazole, DMF (100%). (c) OsO_4, NMO, aqueous acetone (63%). (d) NaH, BnBr, DMF, 0 °C. (e) TBAF, THF (80%, two steps). (f) Oxalyl chloride, DMSO (97%). (g) 3% HCl, MeOH, 8 h, reflux (64%). (h) NaH, BnBr, DMF. (i) R = Me: Me_2BBr, CH_2Cl_2, −78 to −40 °C; R = allyl: Pd/C, *p*-TsOH. (j) $HSCH_2CH_2SH$, *p*-TsOH, CH_2Cl_2, 50 °C, (50%, three steps, for R = Me).

by Tebbe olefination established the terminal vinyl group. This olefination procedure, which is used more conventionally with ketones and esters, proved superior to the Wittig-type reagents with this aldehyde. The α,β-unsaturated ester moiety at the other end of the chain was fashioned by a reduction, oxidation, and Horner–Emmons olefination sequence to furnish **12e**. Unlike the first set of osmylation reactions, the reaction with **12e** displayed poor diastereoselectivity and yielded a mixture of compounds. Studies with model systems showed that acetonides imparted better anti selectivity, while silyl ether protecting groups offered lower or opposite stereoselectivities (Figure 5). The *tert*-butyldimethylsilyl groups of **12e** were therefore removed and replaced with acetonides to afford **13b** (Scheme V).

The inherent anti selectivity offered by **13b** was still only marginal, and better selectivity was desired. On the basis of a report by Sharpless on the use of cinchona alkaloid derivatives (dihydroquinine and dihydroquinidine acetates)[22] to achieve enantiofacial selectivity with stoichiometric osmylation reactions of prochiral olefins, we had earlier established the feasibility of employing such chiral ligands in boosting the internal diastereofacial selectivity of chiral olefinic compounds[23] under catalytic conditions (NMO).[24] Thus, catalytic osmylation was conducted with **13b** in the presence of a dihydroquinine *p*-chlorobenzoate **15**, a more effective catalyst than the acetate,[25,26] to afford the tetraol **14** with good diastereoselectivity.[27] In 11 steps, all per-

(14) Takacs, J. M.; Helle, M. A.; Seely, F. L. *Tetrahedron Lett.* **1986**, *27*, 1257.
(15) VanRheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973.
(16) The diastereofacial selectivity at each olefin was determined to be 12.9:1 on the basis of HPLC ratios of the acetylated products following osmylation of HPLC-purified olefin **1b**.
(17) Studies with related compounds revealed the importance of the protecting group on the success of this reaction. TBS groups adjacent to the ester moieties afforded good selectivities, while acetonides afforded poor selectivities.
(18) MacLay, W. D.; Hann, R. M.; Hudson, C. S. *J. Am. Chem. Soc.* **1938**, *60*, 1035.
(19) For past examples, see: (a) Kochetkov, N. K.; Dmitriev, B. A. *Tetrahedron* **1965**, *21*, 803. (b) Brimacombe, J. S.; Hanna, R.; Bennett, F. *Carbohydr. Res.* **1985**, *135*, C17. (c) Brimacombe, J. S.; Kabir, A. K. M. S.; Taylor, I. D. *Carbohydr. Res.* **1985**, *140*, C9.
(20) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651.
(21) Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611.
(22) Hentges, S. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 4263.
(23) A study of double asymmetric induction during osmylation has recently been reported: Annunziata, R.; Cinquini, M.; Cozzi, F.; Raimondi, L. *Tetrahedron* **1988**, *44*, 6897.
(24) Note: Oxidation of dihydroquinidine acetate (*m*-CPBA, CH_2Cl_2) yielded its *N*-oxide, which was found to serve as a stoichiometric oxidant to oxidize olefins in the presence of catalytic osmium tetraoxide, with diastereoselectivities comparable to the NMO conditions.
(25) Jacobsen, E. N.; Markó, I.; Mungall, W. S.; Schröder, G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 1968.
(26) Other chiral ligands for asymmetric osmylation: (a) Yamada, T.; Narasaka, K. *Chem. Lett.* **1986**, 131. (b) Tokles, M.; Snyder, J. K. *Tetrahedron Lett.* **1986**, *27*, 3951. (c) Annunziata, R.; Cinquini, M.; Cozzi, F.; Raimondi, L.; Stefanelli, S. *Tetrahedron Lett.* **1987**, *28*, 3139. (d) Tomioka, K.; Nakajima, M.; Koga, K. *J. Am. Chem. Soc.* **1987**, *109*, 6213. (e) Hirama, M.; Oishi, T.; Itō, S. *J. Chem. Soc., Chem. Commun.* **1989**, 665. (f) Corey, E. J.; Jardine, P. D.; Virgil, S.; Yuen, P.-W.; Connell, R. D. *J. Am. Chem. Soc.* **1989**, *111*, 9243.

Scheme VII[a]



[a] (a) TFA–MeOH, reflux; H_2SO_4–acetone (65%). (b) DIBAL-H, CH_2Cl_2. (c) BzCl (34%, two steps). (d) Tf_2O, Py, CH_2Cl_2. (e) nBu_4NN_3, PhH (81%, two steps).

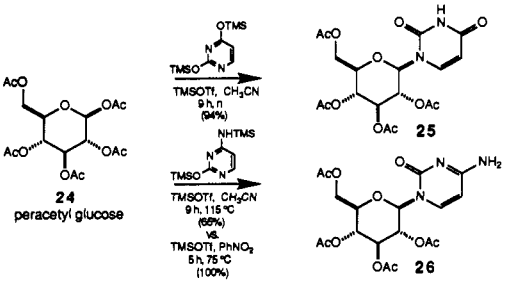
formed on a multigram scale, the undecose chain was constructed with the necessary oxidation level and stereochemistry at each carbon.

2. Formation of the Pyranose Ring and the Introduction of the C4 Amino Group. The pyranose ring of hikosamine was expected to be obtained by carrying out a Fischer-type glycosidation reaction under thermodynamic equilibration conditions on the aldehyde **16f**, which was prepared from **14** by a benzylation/DIBAL-H reduction sequence. Isolation of the C4 hydroxyl group by ketalization of the vicinal hydroxyl groups at C8 and C9 and displacement with azide after activation were anticipated to afford the azido precursor to hikosamine. This scheme was plagued with problems: Benzylation of **14** could not be achieved under a variety of conditions, presumably because of its sensitivity toward elimination and decomposition. This problem was circumvented by adopting an alternate route (Scheme VI). The α,β-unsaturated ester **13b** was reduced down to its allylic alcohol and protected as a TBDPS ether.[28] Catalytic bis-osmylation afforded the tetraol as a separable mixture of diastereomers.[29] Benzylation occurred without incident, and desilylation followed by Swern oxidation furnished the desired aldehyde **16f**.

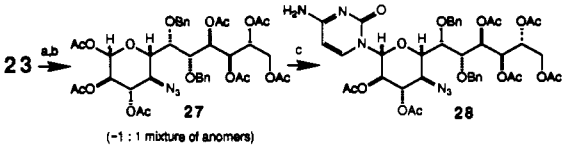
Subjection of **16f** to a variety of glycosidation conditions unexpectedly yielded the furanoside preferentially, and efforts to drive the reaction to the pyranoside isomer by extended heating resulted in gradual decomposition. Similar results were obtained with the allyl-protected aldehyde. The plan was again changed to accommodate this result: with the C4 oxygen protected within the ring, the remaining hydroxyl groups could first be protected. Ring opening would then present the C4 hydroxyl group for substitution with a nitrogen nucleophile. Perbenzylation of the furanoside yielded **17b**, which resisted hydrolysis but was converted to the lactol **19** by treatment with Me_2BBr followed by aqueous workup.[30] Alternatively, the allyl glycoside was prepared and benzylated to give the derivative **18b**, which was deallylated by an isomerization/hydrolysis procedure[31] to afford **19**. Ring opening was readily accomplished by the formation of the dithiolane **20**. Displacement at the C4 position of **20** and related acyclic compounds, however, proved extremely difficult, and the above strategy was abandoned in favor of the strategy described below.[32]

The hydroxy ester **14** was cyclized to its γ-lactone (IR: 1778 cm^{-1}) and selectively ketalized to yield the diastereomerically pure lactone **21**, after purification by flash chromatography (Scheme VII).[33] Reduction of **21** with DIBAL-H and selective benzoylation[34] of the crude lactol afforded the pure alcohol **22**, after purification by preparative HPLC. With the C4 hydroxyl group differentiated, a nitrogen substituent was introduced by formation of the triflate and displacement with tetrabutylammonium azide[35] to afford the azide **23**.[36]

Scheme VIII

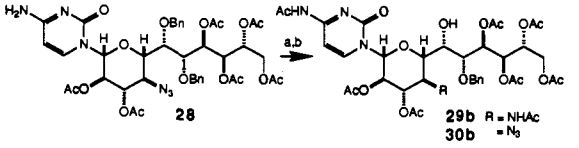


Scheme IX[a]



[a] (a) Amberlyst-15, MeOH, reflux. (b) NaOMe, MeOH; Ac_2O, Py, DMAP, 12 h (83%, three steps). (c) Bis(TMS)cytosine, TMSOTf, $PhNO_2$, 3.5 h, 127 °C (76%).

Scheme X[a,b]



[a] R = NHAc: (a) AcSH, 113 °C, 24 h (73%). (b) DDQ, CH_2Cl_2 buffer (10:1) (52%, 32% starting material). [b] R = N_3: (a) Ac_2O, Py, DMAP (96%). (b) DDQ, CH_2Cl_2–H_2O (74%).

3. Introduction of the Cytosyl Group. Recent advances in the silyl Hilbert–Johnson reaction[37,38] for the creation of pyrimidine glycosides encouraged us to apply it to the synthesis of hikosaminylcytosine. After initial failures, model studies identified several crucial elements necessary for success with this reaction. The use of acetyl protecting groups instead of benzoyl groups about the pyranose ring resulted in increased yields. Subjection of peracetyl glucose **24** to silylated uracil under the Vorbrüggen conditions (TMSOTf, CH_3CN)[39] readily afforded the nucleoside **25**[40] (Scheme VIII). However, the reaction with silylated cytosine to afford **26**[41] was very sluggish and required extensive heating. It was found that the same reaction in nitrobenzene occurred significantly faster than in acetonitrile. Nitromethane also yielded better results than acetonitrile but was inferior to nitrobenzene. In light of these results, the acetylated sugar **27** was prepared as a mixture of anomers by deketalization, debenzoylation, and peracetylation of **23** (Scheme IX). Treatment of **27** with bis-

(27) The amount of diastereomer **14** was increased from 53% to 75% of the total diastereomeric mixture when **15** was used.

(28) The TBDPS protecting group was preferred over the TBDMS protecting group, because with the latter partial silyl group migration to the secondary hydroxyl groups occurred during the subsequent benzylation step.

(29) The major and desired diastereomer was obtained as 58% of the total mixture. The use of the chiral amine catalyst increased this to 68%.

(30) Guindon, Y.; Bernstein, M. A.; Anderson, P. C. *Tetrahedron Lett.* **1987**, *28*, 2225.

(31) Boss, R.; Scheffold, R. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 558.

(32) Intramolecular substitution at the C4 position was successful by conversion of the lactol to its γ-hydroxy-*N*-methoxy amide derivative and cyclization under the Mitsunobu conditions. This approach was not pursued further.

(33) Formation of the γ-lactone instead of the δ-lactone was crucial to the success of this scheme. This enabled the selective protection of the side chain hydroxyl groups, which in turn made possible the selective benzoylation reactions to isolate the C4 hydroxyl group.

(34) See: (a) Reist, E. J.; Spencer, R. R.; Calkins, D. F.; Baker, B. R.; Goodman, L. *J. Org. Chem.* **1965**, *30*, 2312. (b) Reference 11b,c.

(35) See: Danishefsky, S. J.; DeNinno, M. P.; Chen, S.-h. *J. Am. Chem. Soc.* **1988**, *110*, 3929.

(36) The structure was confirmed by conversion to methyl peracetyl-α-hikosaminide by glycosidation, reduction, deprotection, and peracetylation. The ^1H NMR spectrum matched the one reported by Maring (Maring, C. J. Ph.D. Thesis, Yale University, New Haven, CT, 1986).

(37) Iwai, I.; Nishimura, T.; Shimizu, B. *Syn. Proc. Nucleic Acid Chem.* **1968**, *1*, 388.

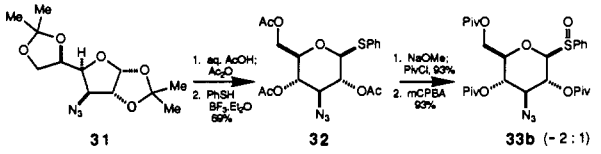
(38) (a) *Chemistry of Nucleotides and Nucleosides*; Townsend, L. B., Ed.; Plenum: New York, 1988. (b) Zorbach, W. W. *Synthesis* **1970**, 329.

(39) (a) Niedballa, U.; Vorbrüggen, H. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 461. (b) Vorbrüggen, H.; Krolikiewicz, K.; Bennua, B. *Chem. Ber.* **1981**, *114*, 1234.

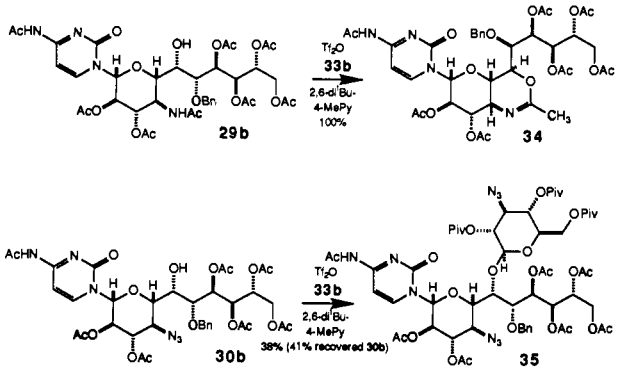
(40) See ref 39b for another synthesis.

(41) Rogers, G. T.; Ulbricht, T. L. V. *J. Chem. Soc. C* **1970**, *8*, 1109.

Scheme XI



Scheme XII

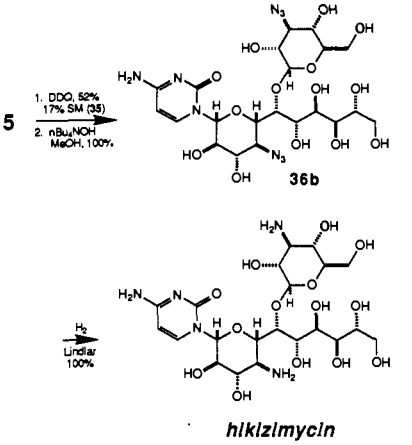


(trimethylsilyl)cytosine and TMSOTf in nitrobenzene (127 °C) yielded the desired nucleoside **28** in 76% yield.

4. Introduction of the Kanosamine Sugar. Before glycosidation could be attempted, the hydroxyl group at the C6 position of hikosaminylcytosine had to be unmasked. This task was made less daunting by the partial differentiation offered by the benzyl and acetyl protecting groups. Reductive debenzylation[42] was attempted initially. The azide **28** was first reduced and N-acetylated on the hikosaminyl and cytosyl amino groups in one step by heating in neat thioacetic acid;[43] the resulting bis(acetamide) was subjected to palladium hydroxide and hydrogen gas. Unfortunately, the cytosine group was found to undergo decomposition when subjected to the latter conditions.[44] Oxidative debenzylation of the bis(acetamide) was next attempted with excess DDQ in dichloromethane–water,[45,46] a condition that is commonly used to remove *p*-methoxybenzyl protecting groups. Surprisingly, a monodebenzylated product was obtained selectively and was assigned as the desired alcohol **29b** on the basis of decoupling experiments (Scheme X). The azido derivative also showed high site selectivity, yielding the desired alcohol **30b** (following an initial N-acetylation of the cytosine ring). The lower rate of oxidative debenzylation at C7, which is flanked by an acetoxy substituent, may reflect in part the decreased electron density at this site relative to C6.[47]

The alcohols **29b** and **30b** were subjected to a number of glycosidation protocols[48,49] without success, possibly because of steric

Scheme XIII



hindrance at the C6 position. Glycosidation was eventually achieved by applying the sulfoxide activation method reported by Kahne.[50] The preparation of the requisite sulfoxide derivative of kanosamine is shown in Scheme XI. The azide **31** was prepared in four steps from D-glucose by a literature procedure.[51] Transformation to the sulfide **32** was achieved by deketalization, acetylation, and thiolation. The acetyl groups of the major β-anomer were removed and replaced by pivaloyl groups; hindered acyl groups (pivaloyl,[52] benzoyl,[53] and 2,4,6-trimethylbenzoyl[54]) at the C2 position have been reported to improve glycosidation, presumably by minimizing orthoester formation. Oxidation of the sulfide with *m*-CPBA afforded a separable mixture of sulfoxides **33b**. Activation of the sulfoxide with triflic anhydride followed by addition of the alcohol **29b** to the mixture at −75 °C and then gradual warming resulted in a new product assigned as **34** on the basis of ^{1}H NMR data (Scheme XII).[55] This rearranged product hydrolyzed on standing to regenerate the original alcohol **29b**. This reaction was repeated with the azido alcohol **30b**, for which such a side reaction is not possible. A coupled product was obtained, and its ^{1}H NMR spectrum was consistent with the β-linked ($J_{1,2}$ = 8 Hz) structure **35**.

Conversion of **35** to hikizimycin required the following transformations: debenzylation of the C7 hydroxyl group, deacylation of the undecose and hexose sugar moieties and the cytosine residue, and reduction of the two azido groups to amino groups. A two-step deacylation/reduction scheme was first pursued. Removal of the sugar acetates and the labile cytosyl *N*-acetate was easily accomplished with sodium methoxide–methanol. Depivaloylation was more challenging but was readily achieved with methanolic tetrabutylammonium hydroxide.[56] Debenzylation under various reducing conditions was unsuccessful, again due to the sensitivity of the cytosyl group.[57] Oxidative debenzylation with DDQ was once again investigated. As anticipated from the earlier DDQ-mediated debenzylation, the reaction was sluggish, and significant

(42) Review on cleavage of ethers: Bhatt, M. V.; Kulkarni, S. U. *Synthesis* **1983**, 249.

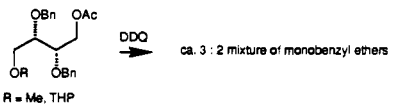
(43) Rosen, T.; Lico, I. M.; Chu, D. T. W. *J. Org. Chem.* **1988**, *53*, 1580.

(44) Degradation studies: Das, B. C.; Defaye, J.; Uchida, K. *Carbohydr. Res.* **1972**, *22*, 293.

(45) Oikawa, Y.; Yoshioka, T.; Yonemitsu, O. *Tetrahedron Lett.* **1982**, *23*, 885.

(46) Few examples of the DDQ-mediated debenzylation of secondary and tertiary benzyl ethers have been reported: (a) Oikawa, Y.; Horita, K.; Yonemitsu, O. *Tetrahedron Lett.* **1985**, *26*, 1541. (b) Tanaka, T.; Oikawa, Y.; Nakajima, N.; Hamada, T.; Yonemitsu, O. *Chem. Pharm. Bull.* **1987**, *35*, 2203. (c) Sviridov, A. F.; Ermolenko, M. S.; Yashunsky, D. V.; Borodkin, V. S.; Kochetkov, N. K. *Tetrahedron Lett.* **1987**, *28*, 3839. (d) Vedejs, E.; Buchanan, R. A.; Watanabe, Y. *J. Am. Chem. Soc.* **1989**, *111*, 8430.

(47) DDQ-mediated debenzylation of the model compounds below showed only marginal selectivities. Thus, there may be other factors accounting for the selectivity observed in the reported system.



(48) Reviews: (a) Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155. (b) Paulsen, H. *Chem. Soc. Rev.* **1984**, *13*, 15. (c) Schmidt, R. R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 212.

(49) (a) Trumtel, M.; Veyrieres, A.; Sinay, P. *Tetrahedron Lett.* **1989**, *30*, 2529. (b) Grundler, G.; Schmidt, R. R. *Carbohydr. Res.* **1985**, *135*, 203. (c) Nicolaou, K. C.; Seitz, S. P.; Papahatjis, D. P. *J. Am. Chem. Soc.* **1983**, *105*, 2430. (d) Koto, S.; Ito, Y.; Umezawa, S. *Bull. Chem. Soc. Jpn.* **1965**, *38*, 1447. (e) Suzuki, K.; Maeta, H.; Matsumoto, T. *Tetrahedron Lett.* **1989**, *30*, 4853.

(50) Kahne, D.; Walker, S.; Cheng, Y.; Van Engen, D. *J. Am. Chem. Soc.* **1989**, *111*, 6881.

(51) See: Richardson, A. C. *Methods Carbohydr. Chem.* **1972**, *6*, 218.

(52) Sato, S.; Nunomura, S.; Nakano, T.; Ito, Y.; Ogawa, T. *Tetrahedron Lett.* **1988**, *29*, 4097.

(53) Garegg, P. J.; Konradsson, P.; Kvarnstrom, I.; Norberg, T.; Svensson, S. C. T.; Wigilius, B. *Acta Chem. Scand. B* **1985**, *39*, 569.

(54) (a) Nunomura, S.; Ogawa, T. *Tetrahedron Lett.* **1988**, *29*, 5681. (b) Nunomura, S.; Mori, M.; Ito, Y.; Ogawa, T. *Tetrahedron Lett.* **1989**, *30*, 5619.

(55) The C5′ proton appears as a simple triplet at δ 3.7. The C4′ proton shifted upfield from δ 4.4 to 3.4 upon cyclization.

(56) (a) Griffin, B. E.; Jarman, M.; Reese, C. B. *Tetrahedron* **1968**, *24*, 639. (b) van Boeckel, C. A. A.; van Boom, J. H. *Tetrahedron Lett.* **1979**, 3561.

(57) Raney nickel and hydrogenation with the Lindlar catalyst appeared promising with model compounds but were unsuccessful with **35**.

decomposition of **35** resulted from the acidic products formed from the hydrolysis of DDQ. To minimize this problem, the reaction was attempted without added water: treatment of **35** with excess DDQ in dry dichloromethane at 58 °C for 2 days resulted in clean debenzylation to afford the desired alcohol (Scheme XIII).[58] Complete deacylation with refluxing methanolic tetrabutylammonium hydroxide readily afforded the polyol **36b**. Finally, hydrogenation with Lindlar's catalyst,[59] which reduced both azido groups, yielded hikizimycin in quantitative yield. The synthetic substance thus produced was found to be identical to natural hikizimycin in all respects.[60,61]

Conclusion

The earlier part of these investigations featured the efficient construction of the undecose segment of hikizimycin by employing the two-directional approach to acyclic chain synthesis. The olefination/osmylation methodology proved highly successful in providing the necessary stereocenters with excellent selectivities. Many challenges arose and were overcome during the course of the synthesis. The cytosinylation of a pyranoside required the development of unusual conditions that may prove valuable for the synthesis of other challenging nucleosides. The sulfoxide activation method for the glycosidation of hindered glycosyl acceptors provided a solution to the difficult problem of hikizimycin disaccharide synthesis. Finally, a critical series of selective deprotection reactions was developed that take advantage of the subtle (and still not fully understood) electronic and conformational nuances of the hikizimycin framework. The identity of the synthetic material hikizimycin served to confirm the structure assignment, which was previously based principally on degradation studies and ^{13}C NMR correlations.

Experimental Section

General Methods. Optical rotations were measured on a Perkin-Elmer 241 polarimeter using a sodium lamp (589 nm, D line). They are reported as follows: $[\alpha]^{temperature}_D$ (concentration (*c*, g/100 mL), solvent). A 1-mL quartz sample cell was used. Proton magnetic resonance spectra (^1H NMR) were recorded on Bruker instruments. The spectra were referenced to $CDCl_3$ (7.27 ppm) and D_2O (4.67 ppm). Data are reported as follows: chemical shift (multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, oct = octet, m = multiplet, br = broadened), coupling constant (hertz), integration, and peak assignment). Carbon magnetic resonance spectra (^{13}C NMR) were recorded on Bruker instruments. Spectra were referenced to $CDCl_3$ (77.00 ppm) and D_2O (66.30 ppm for added dioxane). An exponential multiplication (0.5–2 Hz) was routinely used for data processing. Infrared spectra (IR) were recorded on a Nicolet 5SX or 5PC FT-IR spectrometer. Band frequencies are reported in cm^{-1}. Bands are characterized as follows: s = strong, m = medium, w = weak, or br = broadened. Samples were typically prepared as films by evaporating a sample solution on a salt plate. Melting points were taken with a Mel-Temp apparatus and were not corrected. Low-resolution mass spectra (MS) were measured on a Hewlett-Packard 5985-GC/MS system. High-resolution mass spectra (HRMS) were recorded on a JEOL SX-102 mass spectrometer or on a Kratos MS-80RFA instrument. Significant fragments are reported as follows: *m/z* (relative intensity). Elemental analyses were performed by Atlantic Microlabs, Inc. (Norcross, GA).

Preparative TLC was run on Merck silica gel 60F glass plates (2.0-mm thick). Flash chromatography was performed using E. Merck silica gel 60 (230–400 mesh). High-performance liquid chromatography (HPLC) was performed with a Waters 510 liquid chromatograph equipped with a μPorasil column. Preparative HPLC was done with a Waters Delta Prep 3000 system.

[*R*-(*R,*R**)]-Bis(1-methylethyl) 2,3-Bis(phenylmethoxy)butanedioate (1a).** Sodium hydride (95.87 g, 2.00 mol) was washed twice with THF and suspended in 4 L of THF. The mixture was cooled over an ice bath, and L-(+)-diisopropyl tartrate (200 mL, 0.951 mol) was added over 20 min. After an additional 10 min, tetrabutylammonium iodide (3.51 g, 0.0095 mol) was added followed by benzyl bromide (238 mL, 2.00 mol). The mixture was allowed to warm to room temperature and stir for 7 h. After cooling over an ice bath, the reaction mixture was quenched with 200 mL of water, and the mixture was neutralized with 31 mL of 10% HCl. The mixture was concentrated to about one-fourth volume, diluted with 1 L of water, and extracted with 0.5 L of ethyl acetate. The organic layer was washed with 1 L of saturated NaCl, and the combined aqueous layers were washed twice with 400 mL of dichloromethane. The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated by rotary evaporation. During evaporation, the product crystallized out of solution. Two crops were isolated from the crude mixture and then recrystallized from ethyl acetate and hexane to afford 148.4 g of product in three crops. The original mother liquor was passed through silica gel with ethyl acetate and hexane, the filtrate was concentrated, and the solid was recrystallized to afford 59.9 g of additional product. The total yield was 208.3 g (53%). The monobenzylated product was also isolated after silica gel chromatography (36.6 g, 12%): $[\alpha]^{20}_D$ = +62.3° (*c* 2.0, ethyl acetate); IR (neat) 2986 (w), 1743 (s), 1211 (m), 1104 (m), 737 (m), 699 (m); ^1H NMR ($CDCl_3$, 250 MHz) δ 1.16 (d, *J* = 6.3 Hz, 6 H, CH_3), 1.24 (d, *J* = 6.3 Hz, 6 H, CH_3), 4.40 (s, 2 H, α), 4.47 (d, *J* = 11.7 Hz, 2 H, CH_2Ph), 4.84 (d, *J* = 11.7 Hz, 2 H, CH_2Ph), 5.05 (sept, *J* = 6.3 Hz, 2 H, Me_2CHOR), 7.3 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 21.58, 21.67, 69.08, 73.35, 79.03, 127.85, 128.25, 137.22, 168.84; mp 79.5–80.5 °C; MS (CI, isobutane) 415 (M + 1, 22), 181 (100). Anal. Calcd for $C_{24}H_{30}O_6$: C, 69.54; H, 7.29. Found: C, 69.61; H, 7.30.

[*S*-(*R,*R**)]-Diethyl (2*E*,6*E*)-4,5-Bis(phenylmethoxy)-2,6-octadienedioate (1b).** Triethyl phosphonoacetate (129 mL, 649 mmol) was dissolved in 2.5 L of dichloromethane and cooled to −78 °C. *n*-BuLi (2.5 M in hexane, 259 mL, 649 mmol) was added over 20 min, and after 10 min, the bis-ester **1a** (103.4 g, 249.4 mmol) was added. After 30 min, DIBAL-H (1 M in CH_2Cl_2, 649 mL, 649 mmol) was added over 4 h at −78 °C, and the reaction was allowed to warm to room temperature over 17.5 h. The mixture was heated at reflux for 7 h and then quenched with 0.5 L of potassium sodium tartrate after cooling over an ice bath. The mixture was neutralized with 140 mL of HCl and allowed to stir overnight. Water (0.5 L) was added, and the aqueous layer was extracted twice with 400 mL of dichloromethane. The combined organic layers were dried over anhydrous $MgSO_4$, filtered through sand–Celite–silica gel, concentrated, and then purified by flash chromatography through silica gel with 10–30% ethyl acetate–hexane. The desired (*E*,*E*)-bis-α,β-unsaturated ester **1b** (58.4 g, 53%), as well as the *E*,*Z* isomer (1.4 g, 1.3%) and ethyl (2*E*)-2,3-dideoxy-4,5-bis-*O*-(phenylmethyl)-L-*threo*-hexenoate (16.2 g, 18%), were obtained: $[\alpha]^{22}_D$ = +15.0° (*c* 3.14, $CHCl_3$); IR (neat) 3032 (w), 2870 (w), 1720 (s), 1659 (w), 1434 (w), 1272 (m), 1176 (m), 1110 (m), 983 (w), 737 (w); ^1H NMR ($CDCl_3$, 250 MHz) δ 1.30 (t, *J* = 7.2 Hz, 6 H, CH_3), 4.13 (d, *J* = 4.7 Hz, 2 H, $CHOBn$), 4.21 (q, *J* = 7.2 Hz, 4 H, OCH_2Me), 4.45, 4.64 (d, *J* = 12.0 Hz, 2 H, CH_2Ph), 6.07 (dd, *J* = 15.7, 0.87, 2 H, α-vinylic), 6.89 (dd, *J* = 15.8, 5.6, 2 H, β-vinylic), 7.3 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.16, 60.47, 71.76, 79.18, 124.02, 127.70, 127.82, 128.37, 137.46, 143.58, 165.75; MS (DIP-CI, isobutane) 439 (M + 1, 18), 107 (100). Anal. Calcd for $C_{26}H_{30}O_6$: C, 71.21; H, 6.90. Found: C, 71.18; H, 6.91.

Diethyl 4,5-Bis-*O*-(phenylmethyl)-D-*threo*-L-*galacto*-octarate (2a). *N*-Methylmorpholine *N*-oxide (71.9 g, 613 mmol) and the bis-ester **1b** (89.7 g, 204 mmol) were dissolved in 2 L (8:1) of acetone–water. OsO_4 (0.45 M in acetone, 22.7 mL, 10.2 mmol) was added, and the solution was stirred for 18 h at room temperature. After cooling over an ice bath, the reaction was quenched by the addition of 0.5 L of saturated $NaHSO_3$. Most of the acetone was removed by rotary evaporation, and the aqueous mixture was extracted three times with ethyl acetate (2 L total). The combined organic layers were dried over anhydrous $MgSO_4$, filtered through Celite, and concentrated. Crystals were obtained during concentration. Three crops yielded, after drying overnight under vacuum, the tetraol (73.4 g, 71%): $[\alpha]^{23}_D$ = +4.5° (*c* 2.04, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ 1.30 (t, *J* = 7.1 Hz, 6 H, CH_3), 3.12 (d, *J* = 7.4 Hz, 2 H, β-OH), 3.46 (d, *J* = 6.1 Hz, 2 H, α-OH), 3.95 (d, *J* = 9.0 Hz, 2 H, γ-H), 4.27 (m, 6 H, OCH_2Me + β-H), 4.47 (d, *J* = 6.1 Hz, 2 H, α-H), 4.70 (s, 4 H, CH_2Ph), 7.3 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.05, 62.01, 70.67, 71.88, 74.29, 76.65, 128.15, 128.51, 137.63, 173.79; IR (neat) 3487 (br), 3410 (br), 2979 (m), 1730 (s); mp 113–115 °C; MS (DIP-CI, isobutane) 507 (M + 1, 54), 489 (M − OH, 42), 91 (Trop, 100). Anal. Calcd for $C_{26}H_{34}O_{10}$: C, 61.65; H, 6.76. Found: C, 61.60; H, 6.78.

Diethyl 2,3,6,7-Tetrakis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-4,5-bis-*O*-(phenylmethyl)-D-*threo*-L-*galacto*-octarate (2b). To a solution of the tetraol **2a** (65.7 g, 130 mmol) and 2,6-dimethyllutidine (75.5 mL, 648

(58) Oxidative dehydrogenation of aromatic compounds at the benzylic position under anhydrous conditions has been reported: Naidu, M. V.; Rao, G. S. K. *Synthesis* **1979**, 144.

(59) Corey, E. J.; Nicolaou, K. C.; Balanson, R. D.; Machida, Y. *Synthesis* **1975**, 590.

(60) Comparison of their ^{13}C NMR data showed slight differences in a few of their resonances. However, a 1:1 mixture of the synthetic and natural materials gave only one set of peaks.

(61) The ^1H NMR spectra of the peracetylated derivatives of the two materials were also identical.

mmol) in 1.3 L of dichloromethane was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (125 mL, 545 mmol) over 2.5 h at 0 °C. The mixture was stirred for 14 h at room temperature and quenched by the addition of 0.5 L of saturated $NaHCO_3$. One liter of water was added, and the aqueous layer was extracted twice with 400 mL of dichloromethane. The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated to afford an oil, which was purified by flash chromatography through silica gel with 5% ethyl acetate–hexane. Concentration afforded **2b** (124 g, 100%) as a viscous oil, which solidified on standing: $[\alpha]^{24}_D$ = +14.1° (*c* 2.08, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ −0.02, 0.02, 0.05, 0.08 (s, 6 H, $SiCH_3$), 0.90, 0.92 (s, 18 H, Si^{t}Bu), 1.25 (t, *J* = 7.1 Hz, 6 H, CH_2CH_3), 3.98 (d, *J* = 7.0 Hz, 2 H), 4.15 (m, 4 H, CH_2CH_3), 4.62 (d, *J* = 1.3 Hz, 2 H), 4.66 (dd, *J* = 7.4, 1.3 Hz, 2 H), 4.75, 4.99 (d, 11.9 Hz, 2 H, CH_2Ph), 7.3 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ −4.65, −4.55, −3.97, −3.85, 18.26, 18.44, 26.03, 26.12, 14.02, 60.72, 72.44, 72.85, 73.88, 79.54, 173.26; IR (neat) 2929 (s), 2858 (s), 1759 (s), 1755 (s), 1725 (m), 1256 (s), 1110 (s), 836 (s), 778 (s); mp 54–57 °C; MS (DIP-EI, He) 905 (M − ^{t}Bu, 25), 443 (100). Anal. Calcd for $C_{50}H_{90}O_{10}Si_4$: C, 62.32; H, 9.41. Found: C, 62.22; H, 9.45.

Ethyl 2,3,6,7-Tetrakis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-4,5-bis-*O*-(phenylmethyl)-D-*threo*-L-*galacto*-octonate (3). The bis-ester **2b** (119.5 g, 124 mmol) was dissolved in 2 L of dichloromethane, and DIBAL-H (1 M in CH_2Cl_2, 285 mL, 285 mmol) was added over 3 h at −78 °C. After 1 h at −78 °C, the reaction was quenched by adding 100 mL of acetone and stirred overnight with 0.5 L of potassium sodium tartrate and 0.5 L of water. The aqueous layer was extracted twice with 300 mL of dichloromethane. The combined organic layers were dried over anhydrous $MgSO_4$ and evaporated to give a residue, which was purified by flash chromatography with 5–20% ethyl acetate–hexane. The desired alcohol **3** (93.8 g, 82%) and the diol **4** (11.0 g, 10%), as well as a mixture of **2b** and aldehydes (7.8 g), were isolated: $[\alpha]^{24}_D$ = +15° (*c* 2.4, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ 0.018, 0.114 (s, 6 H, $SiCH_3$), 0.056, 0.060, 0.107, 0.142 (s, 3 H, $SiCH_3$), 0.88, 0.93 (s, 9 H, Si^{t}Bu), 0.92 (s, 18 H, Si^{t}Bu), 1.24 (t, *J* = 7.2 Hz, 3 H, CH_3), 2.58 (t, *J* = 5.9 Hz, 1 H, OH), 3.86 (m, 2 H, CH_2OH), 3.99 (d, *J* = 2.0 Hz, 1 H), 4.02 (d, *J* = 3.1 Hz, 1 H), 4.07 (m, 1 H), 4.13 (m, 2 H, OCH_2Me), 4.26 (dd, *J* = 6.2, 3.4 Hz, 1 H), 4.56 (m, 2 H), 4.93, 4.81 (d, *J* = 11.9 Hz, 2 H, CH_2Ph), 4.96, 4.85 (d, *J* = 11.4 Hz, 2 H, CH_2Ph), 7.3 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ −4.59, −4.30, −4.00, −3.94, −3.87, 14.11, 18.22, 18.36, 18.49, 26.06, 26.16, 60.71, 62.91, 72.09, 72.74, 72.79, 73.97, 74.41, 75.82, 78.51, 79.14, 83.73, 126.92, 126.98, 127.04, 128.04, 139.42, 139.54, 173.02; IR (neat) 3500 (br), 2929 (s), 2857 (s), 1755 (m), 1727 (w), 1472 (m), 1255 (s), 1112 (s), 836 (s), 777 (s); MS (FAB) 943 (M + Na, 8), 73 (100). Anal. Calcd for $C_{48}H_{88}O_9Si_4$: C, 62.56; H, 9.62. Found: C, 62.48; H, 9.66.

Octa-*O*-acetyl-D-*threo*-L-*galacto*-octitol (5). To a solution of diol **4** (1.65 g, 1.88 mmol) in THF (20 mL) was added tetrabutylammonium fluoride (1.0 M in THF, 8.25 mL, 8.25 mmol) at 0 °C, and the solution was allowed to stir for 3.5 h. The mixture was diluted with water and extracted several times with dichloromethane. The aqueous layers were passed through an ion-exchange resin (AG-501 X8 (D)) and concentrated to afford 0.556 g (70%) of crude desilylated product. An aliquot (360 mg) was dissolved in methanol (50 mL) and shaken in a Parr shaker (65 psi of hydrogen gas) with $Pd(OH)_2/C$ (100 mg) for 40 h. The mixture was diluted with water and filtered through Celite. After evaporation of the water, the residue was recrystallized from water and methanol to afford the octitol (185 mg, 90%). An aliquot (102 mg, 0.421 mmol) was heated for 15 min with fused sodium acetate (68 mg, 0.83 mmol) in acetic anhydride (1.0 mL, 1.1 mmol). The mixture was poured into ice water and extracted with ethyl acetate. The organic layers were dried over anhydrous $MgSO_4$, and the residue, after evaporation of the solvent, was purified by flash chromatography with 40–50% ethyl acetate–hexane to afford **5** (234 mg, 79%). The product was recrystallized from 95% ethanol: $[\alpha]^{22}_D$ = +40.4° (*c* 1.26, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ 1.97, 2.02, 2.03, 2.06 (s, 6 H, acetate), 3.77 (dd, *J* = 7.0, 11.7 Hz, 2 H, C1+8H), 4.24 (dd, *J* = 4.7, 11.7 Hz, 2 H, C1+8H), 5.09 (m, 4 H, C2+3+6+7H), 5.38 (d, *J* = 9.2 Hz, 2 H, C4+5H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 20.57, 20.72, 62.21, 66.42, 67.70, 67.77, 169.49, 169.66, 169.86, 170.13; IR (neat) 2983 (w), 1750 (s), 1371 (m), 1212 (s), 1034 (m); mp 138–139 °C. Literature values: $[\alpha]_D$ = +40.4° (*c* 1.2, $CHCl_3$); mp 141 °C (corrected).

2,3,6,7-Tetrakis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-4,5-bis-*O*-(phenylmethyl)-D-*threo*-L-*galacto*-octodialdose (6). To oxalyl chloride (1.66 mL, 19.4 mmol) in dichloromethane (60 mL) was added DMSO (2.58 mL, 38.9 mmol) at −78 °C, and after 10 min, the diol **4** (5.70 g, 6.48 mmol) in 10 mL of dichloromethane was added over 20 min via cannula. After an additional 30 min, triethylamine (8.13 mL, 58.3 mmol) was added, and the mixture was stirred for 30 min at −78 °C. The cooling bath was removed and water was added. Extraction with dichloromethane, drying over anhydrous $MgSO_4$, and flash chromatography with 5–10% ethyl acetate–hexane afforded the bis-aldehyde **6** as crystals (5.43 g, 96%): $[\alpha]^{21}_D$ = +38.4° (*c* 2.26, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 0.03, 0.11, 0.15, 0.16 (s, 6 H, $SiCH_3$), 0.90, 0.94 (s, 18 H, Si^{t}Bu), 4.07 (d, *J* = 4.8 Hz, 2 H), 4.10 (d, *J* = 4.8 Hz, 2 H), 4.15 (s, 2 H), 4.60 (d, *J* = 11.8 Hz, 2 H, CH_2Ph), 4.79 (d, *J* = 11.8 Hz, 2 H, CH_2Ph), 7.19 (m, 10 H, Ph), 9.73 (s, 2 H, CHO); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −5.20, −4.44, −4.30, 17.99, 18.52, 25.89, 26.11, 75.40, 76.66, 80.30, 82.12, 127.03, 127.50, 128.01, 138.76, 199.50; IR (neat) 2953 (s), 2930 (s), 2859 (s), 1734 (s), 1472 (m), 1256 (s), 1157 (m), 1092 (s), 839 (s), 777 (m); mp = 80–85 °C; MS (FAB) 897 (M + Na, 8.5), 92 (100). Anal. Calcd for $C_{46}H_{82}O_8Si_4$: C, 63.11; H, 9.44. Found: C, 63.23; H, 9.48.

1,2,9,10-Tetradeoxy-5,6-bis-*O*-(phenylmethyl)-D-*threo*-L-*galacto*-deca-1,9-dienitol (7). To a solution of bis-aldehyde **6** (2.58 g, 2.95 mmol) and pyridine (0.075 mL) in 3:1 toluene–THF (30 mL) was added the Tebbe reagent (0.51 M in toluene, 17.3 mL, 8.84 mmol) at −78 °C over 3 min. The mixture was allowed to warm to −15 °C over 2 h. The reaction mixture was quenched with 4 mL of 15% NaOH. The mixture was diluted with water and extracted with ethyl acetate. The organic layers were dried over anhydrous $MgSO_4$ and concentrated to yield a residue, which was purified by flash chromatography with 2.5% ethyl acetate–hexane to furnish the tetra(silyl ether) (2.20 g, 86%). An aliquot (1.85 g, 2.12 mmol) in THF (20 mL) was treated with tetrabutylammonium fluoride (1 M in THF, 9.34 mL, 9.34 mmol) for 3.5 h at 0 °C. Saturated NH_4Cl was added, and the mixture was extracted with ethyl acetate. Drying over anhydrous $MgSO_4$ and flash chromatography with 50–100% ethyl acetate–hexane furnished the tetraol **7** (0.73 g, 83%): $[\alpha]^{27}_D$ = +15.0° (*c* 1.76, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 2.34 (d, *J* = 8.1 Hz, 2 H, C3OH), 3.24 (d, *J* = 3.1 Hz, 2 H, C4OH), 3.88 (s, 4 H, C4H+C5H), 4.32 (~t, 2 H, C3H), 4.63 (d, *J* = 11.3 Hz, 2 H, CH_2Ph), 4.68 (d, *J* = 11.3 Hz, 2 H, CH_2Ph), 5.24 (td, *J* = 1.4, 10.5 Hz, 2 H, vinyl), 5.34 (td, *J* = 1.5, 17.3 Hz, 2 H, vinyl), 5.94 (ddd, *J* = 5.0, 10.5, 17.3 Hz, 2 H, vinyl), 7.33 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 71.25, 73.12, 73.93, 76.88, 116.06, 128.35, 128.43, 128.64, 138.19; IR (neat) 3565 (br), 3473 (br), 3018 (m), 2918 (w), 1390 (w), 1067 (s); mp 114–116 °C; MS (FAB) 437 (M + Na, 5), 415 (M + 1, 42), 181 (100).

Deca-*O*-acetyl-D-*manno*-D-*manno*-decitol (8). A mixture of the olefin **7** (463 mg, 1.12 mmol), NMO (392 mg, 3.35 mmol), and dihydroquinine *p*-chlorobenzoate (519 mg, 1.12 mmol) in 10:1 acetone–water (2.1 mL) was stirred for 3 h at 0 °C. The mixture was diluted with aqueous $NaHSO_3$ and extracted with dichloromethane. The aqueous layer was passed through a column of ion-exchange resin (Ag-501 X8 (D)) and, after concentration, was hydrogenated for 1 day in a Parr shaker with $Pd(OH)_2/C$ under 50 psi of hydrogen. The mixture was filtered through Celite, concentrated, and acetylated with acetic anhydride (4 mL) and fused sodium acetate (150 mg). The solution was concentrated under vacuum, and the residue was purified by flash chromatography and HPLC with 40% ethyl acetate–hexane to afford the C_2-symmetric decitol peracetate **8** (183 mg, 23%). The product was crystallized from ethyl acetate–hexane: $[\alpha]^{25}_D$ = +27.8° (*c* 1.57, $CHCl_3$); ^1H NMR ($CHCl_3$, 500 MHz) δ 2.04, 2.06, 2.08, 2.08, 2.09 (s, 6 H, acetate), 4.03 (dd, *J* = 5.8, 12.4 Hz, 2 H, C1+10H), 4.25 (dd, *J* = 3.0, 12.4 Hz, 2 H, C1+10H), 5.04 (m, 2 H), 5.24 (m, 4 H), 5.40 (dd, *J* = 2.3, 7.7 Hz, 2 H); ^{13}C NMR ($CHCl_3$, 125.8 MHz) δ 20.60, 20.63, 20.66, 20.77, 61.73, 67.10, 67.68, 67.81, 68.38, 169.62, 169.74, 169.81, 170.45; IR (film) 3025 (w), 2986 (w), 1750 (s), 1372 (m), 1215 (s), 1036 (m); mp 119–120 °C; MS (FAB) 723 (M + 1, 7), 663 (M − OAc, 100). Anal. Calcd for $C_{30}H_{42}O_{20}$: C, 49.86; H, 5.86. Found: C, 50.01; H, 5.87.

(2*E*,10*E*)-Diethyl 2,3,10,11-Tetradeoxy-4,5,8,9-tetrakis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-6,7-bis-*O*-(phenylmethyl)-D-*threo*-L-*galacto*-dodeca-2,10-dienarate (9). To a solution of triethyl phosphonoacetate (0.778 mL, 3.92 mmol) in THF (13 mL) was added *n*-BuLi (2.5 M in hexane, 1.57 mL, 3.92 mmol) at −78 °C. The solution was stirred for 5 min with the bath removed and then recooled to −78 °C. The bis-aldehyde **6** (1.15 g, 1.31 mmol) was added, and the solution was allowed to warm to room temperature over 3 h. Saturated NH_4Cl was added, and the mixture was extracted with ethyl acetate. Drying over anhydrous $MgSO_4$ and flash chromatography with 5% ethyl acetate–hexane afforded the bis-α,β-unsaturated ester **9** (1.02 g, 76%): $[\alpha]^{22}_D$ = −4.16° (*c* 4.90, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ −0.07, −0.04, 0.04, 0.05 (s, 6 H, $SiCH_3$), 0.80, 0.90 (s, 18 H, Si^{t}Bu), 1.30 (t, *J* = 7.1 Hz, 6 H, CH_2CH_3), 3.81 (d, *J* = 8.5 Hz, 2 H, C6H), 4.12 (dd, *J* = 3.0, 8.5 Hz, 2 H, C5H), 4.19 (m, 4 H, CH_2CH_3), 4.54 (m, 2 H, C4H), 4.71 (d, *J* = 11.9 Hz, 2 H, CH_2Ph), 4.91 (d, *J* = 11.9 Hz, 2 H, CH_2Ph), 6.03 (dd, *J* = 1.6, 15.8 Hz, 2 H, C2H), 7.32 (m, 12 H, Ph+C3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −4.84, −4.46, −4.09, −3.58, 14.24, 18.23, 25.85, 26.03, 60.20, 72.12, 74.77, 75.20, 79.10, 121.72, 126.60, 126.68, 127.95, 139.81, 148.36, 166.12; IR (neat) 2955 (m), 2930 (m), 2859 (m), 1724

(s), 1472 (w), 1260 (m), 1094 (m), 835 (s), 777 (m); MS (FAB) 1037 (M + Na, 12), 387 (60), 115 (100). Anal. Calcd for $C_{54}H_{94}O_{10}Si_4$: C, 63.86; H, 9.33. Found: C, 63.59; H, 9.40.

(2*E*,10*E*)-2,3,10,11-Tetradeoxy-6,7-bis-*O*-(phenylmethyl)-D-*threo*-L-*galacto*-dodeca-2,10-dienitol (10). To a solution of bis-α,β-unsaturated ester **9** (0.670 g, 0.660 mmol) in THF (5 mL) at 0 °C was added LAH (0.050 g, 1.32 mmol). After 30 min, the mixture was warmed to room temperature and allowed to stir for 3 h. The reaction was recooled and quenched by the addition of acetone. The mixture was diluted with dichloromethane and stirred with aqueous potassium sodium tartrate. Extraction with dichloromethane, drying over anhydrous $MgSO_4$, and concentration afforded crude tetrasilyl bis-allyl alcohol. This was dissolved in THF (5 mL) and treated with tetrabutylammonium fluoride (1 M in THF, 2.9 mL, 2.9 mmol) for 3 h at 0 °C and for 7 h at room temperature. Saturated NH_4Cl was added, and the mixture was extracted with dichloromethane. Drying over anhydrous $MgSO_4$ and flash chromatography with 50% ethyl acetate–hexane to 10% methanol–ethyl acetate yielded the hexaol **10** (0.241 g, 77%): $[\alpha]^{22}_D = -18.4°$ (*c* 1.90, THF); ^{1}H NMR (THF-d_8, 500 MHz) δ 3.64 (d, J = 8.0 Hz, 2 H), 3.69 (t, J = 5.7 Hz, 2 H), 3.74 (t, J = 8.6 Hz, 2 H), 3.92 (d, J = 6.2 Hz, 2 H, OH), 4.00 (t, J = 4.8 Hz, 4 H, C1H_2), 4.03 (d, J = 9.0 Hz, 2 H), 4.37 (t, J = 5.6 Hz, 2 H, C4H), 4.74 (d, J = 11.7 Hz, 2 H, CH_2Ph), 4.84 (d, J = 11.7 Hz, 2 H, CH_2Ph), 5.86 (m, 4 H, vinylic), 7.16 (t, 2 H, Ph), 7.24 (t, 4 H, Ph), 7.34 (d, 4 H, Ph); ^{13}C NMR (THF-d_8, 75.5 MHz) δ 63.09, 71.39, 73.83, 74.49, 79.72, 127.55, 127.95, 128.70, 131.98, 132.64, 140.91; IR (neat) 3333 (br), 2865 (w), 1454 (w), 1101 (s), 1069 (s), 970 (m), 735 (m), 694 (m); mp 145–147 °C; MS (FAB) 497 (M + Na, 50), 154 (matrix, 100); HRMS (FAB) *m/z* 497.2177 (calcd 497.2152 for $C_{26}H_{34}O_8$ + Na).

Dodeca-*O*-acetyl-L-*threo*-L-*galacto*-L-*galacto*-dodecitol (11). A mixture of the olefin **10** (101 mg, 0.213 mmol), NMO (125 mg, 1.06 mmol), and dihydroquinine *p*-chlorobenzoate (99 mg, 0.21 mmol) in 10:1 acetone–water (0.4 mL) was stirred for 3 h at 0 °C and 5 h at room temperature. The mixture was diluted with aqueous $NaHSO_3$ and extracted with dichloromethane. The aqueous layer was passed through an ion-exchange resin (Ag-501 X8 (D)) and concentrated to give a residue, which was hydrogenated in a Parr shaker (55 psi of hydrogen) for 1 day with $Pd(OH)_2$/C. The mixture was filtered through Celite and concentrated to a residue, which was acetylated by heating with acetic anhydride (3 mL) and fused sodium acetate (70 mg). The mixture was concentrated under vacuum, and the residue was purified by flash chromatography and HPLC with 50% ethyl acetate–hexane to afford a C_2-symmetric undecitol **11** (26.4 mg, 14%) and a non-C_2-symmetric dodecitol (34 mg, 18%): $[\alpha]^{25}_D = -12.2°$ (*c* 2.49, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.01, 2.05, 2.06, 2.07, 2.09, 2.11 (s, 6 H, acetate), 3.81 (dd, J = 7.1, 11.7 Hz, 2 H, C1+12H), 4.24 (dd, J = 5.0, 11.7 Hz, 2 H, C1+12H), 5.03 (d, J = 6.7 Hz, 2 H, C6+7H), 5.13 (m, 2 H, C2+11H), 5.21 (dd, J = 2.0, 9.5 Hz, 2 H, C3+10H), 5.34 (dd, J = 1.5, 9.6 Hz, 2 H, C4+9H), 5.38 (br d, 2 H, C5+8H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 20.60, 20.71, 20.74, 62.10, 66.72, 67.54, 67.65, 67.86, 169.49, 169.57, 169.93, 169.98, 170.22, 170.43; IR (film) 3024 (w), 2968 (w), 1751 (s), 1374 (m), 1215 (s), 1037 (m), 759 (m); MS (FAB) 867 (M + 1, 5), 807 (M − OAc, 72), 43 (100). Anal. Calcd for $C_{36}H_{50}O_{24}$: C, 49.88; H, 5.81. Found: C, 49.98; H, 5.82.

Ethyl 2,3,6,7-Tetrakis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-4,5-bis-*O*-(phenylmethyl)-D-*threo*-L-*galacto*-octuronate (12a). To oxalyl chloride (9.55 mL, 112 mmol) in 1 L of dichloromethane was added DMSO (14.9 mL, 224 mmol) dropwise at −78 °C. After 15 min, a solution of **3** (93.8 g, 102 mmol) in dichloromethane was added via cannula over 40 min, and the mixture was allowed to stir for 20 min at −78 °C. Triethylamine (56.8 mL, 407 mmol) was added, and the mixture was allowed to stir for 30 min at −78 °C. The bath was removed, 0.5 L of H_2O was added, and the mixture was allowed to warm to room temperature. The aqueous layer was extracted twice with 150 mL of dichloromethane, and the combined organic layers were dried over anhydrous $MgSO_4$. The residue obtained after evaporation of the solvent was purified by flash chromatography through silica gel with 4% ethyl acetate–hexane. The aldehyde (90.5 g, 97%) was obtained as an oil: $[\alpha]^{24}_D = +15.4°$ (*c* 1.58, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.013, 0.103 (s, 6 H, $SiCH_3$), 0.038, 0.053, 0.058, 0.071 (s, 3 H, $SiCH_3$), 0.903 (s, 9 H, Si^{t}Bu), 0.918 (s, 27 H, Si^{t}Bu), 1.21 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 4.06 (m, 2 H, OCH_2Me), 4.00 (m, 2 H), 4.28 (d, J = 3.3 Hz, 1 H), 4.37 (t, 1 H), 4.45 (dd, J = 2.2, 5.4 Hz, 1 H), 4.5 (d, J = 2.1 Hz, 1 H), 4.72, 4.83 (d, J = 11.9 Hz, 1 H, CH_2Ph), 4.80, 4.86 (d, J = 11.7 Hz, 1 H, CH_2Ph), 7.3 (m, 10 H, Ph), 9.80 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ −4.79, −4.59, −4.26, −4.19, −4.12, −4.00, −3.91, 14.08, 18.14, 18.46, 25.99, 26.08, 60.71, 73.00, 73.77, 74.48, 75.41, 79.70, 80.05, 80.91, 126.95, 127.01, 127.17, 127.34, 127.98, 128.07, 139.06, 139.30, 172.88, 202.36; IR (neat) 2953 (s), 2929 (s), 2890 (s), 1753 (m), 1731 (m), 1472 (m), 1256 (m), 1109 (m), 837 (s), 777 (m); MS (FAB) 941 (M + Na, 5), 73 (100). Anal. Calcd for $C_{48}H_{86}O_9Si_4$: C, 62.70; H, 9.43. Found: C, 62.59; H, 9.47.

Ethyl 8,9-Dideoxy-2,3,6,7-tetrakis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-4,5-bis-*O*-(phenylmethyl)-D-*threo*-L-*galacto*-non-8-enonate (12b). The aldehyde **12a** (89.9 g, 97.8 mmol) was dissolved in 1 L (3:1:0.03) of toluene–THF–pyridine and cooled to −78 °C. The Tebbe reagent (0.73 M, 162 mL, 118 mmol) was added via cannula over 20 min, and the mixture was allowed to warm to −10 °C over 5 h, at which point the reaction was quenched by the addition of 30 mL of 15% NaOH. The mixture was allowed to stir for 0.5 h and then warm to room temperature. It was then passed through Celite by washing with 1 L of ethyl acetate. The filtrate was concentrated, and the residue was purified by flash chromatography through silica gel with 3.2% ethyl acetate–hexane to afford the olefin (73.6 g, 82%) as an oil: $[\alpha]^{21}_D = +25.6°$ (*c* 1.97, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 250 MHz) δ −0.05, −0.02, 0.11 (s, 3 H, $SiCH_3$), 0.06 (s, 9 H, $SiCH_3$), 0.08 (s, 6 H, $SiCH_3$), 0.88, 0.90, 0.91, 0.92 (s, 9 H, Si^{t}Bu), 1.22 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 3.99 (t, 2 H), 4.11 (m, 3 H), 4.44 (t, 1 H), 4.59 (s, 1 H), 4.72 (m, 2 H), 4.77 (d, J = 12.3 Hz, 1 H, OCH_2Ph), 4.96 (d, J = 12.3 Hz, 1 H, OCH_2Ph), 4.99 (d, J = 11.7 Hz, 1 H, OCH_2Ph), 5.23 (d, J = 10.5 Hz, 1 H, vinyl), 5.36 (d, J = 17.3 Hz, 1 H, vinyl), 6.18 (m, 1 H, vinyl), 7.3 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ −4.79, −4.75, −4.24, −4.03, −3.95, −3.74, −3.54, 14.02, 18.20, 18.32, 18.40, 25.94, 26.00, 26.17, 60.66, 70.76, 72.29, 72.84, 73.52, 75.62, 76.24, 77.71, 79.15, 115.90, 126.82, 126.90, 127.11, 128.02, 138.33, 139.98, 173.49; IR (neat) 2956 (s), 2930 (s), 2858 (s), 1757 (m), 1471 (m), 1254 (m), 1114 (br), 837 (m), 778 (m). MS (DIP-EI, He) 859 (M − ^{t}Bu, 11), 349 (100). Anal. Calcd for $C_{49}H_{88}O_8Si_4$: C, 64.14; H, 9.67. Found: C, 63.96; H, 9.71.

1,2-Dideoxy-3,4,7,8-tetrakis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-5,6-bis-*O*-(phenylmethyl)-D-*threo*-L-*galacto*-non-1-enitol (12c). To the ester **12b** (71.5 g, 77.9 mmol) dissolved in dichloromethane (0.5 L) was added DIBAL-H (1 M in CH_2Cl_2, 234 mL, 234 mmol) over 4 h at −78 °C. After 40 min longer at −78 °C, the bath was removed, and 200 mL of sodium potassium tartrate and 200 mL of water were added to the reaction mixture. The mixture was allowed to stir overnight, and the aqueous layer was extracted twice with 150 mL of dichloromethane. The combined organic layers were dried over anhydrous $MgSO_4$ and flash chromatographed through silica gel with 4% ethyl acetate–hexane to afford the alcohol (64.6 g, 95%) as an oil. A mixture of starting material and aldehyde (1:1, 3.3 g) was also isolated: $[\alpha]^{21}_D = +14.1°$ (*c* 2.22, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.02, 0.08, 0.13, 0.13, 0.14 (s, 3 H, $SiCH_3$), 0.10 (s, 9 H, $SiCH_3$), 0.92, 0.92, 0.93, 0.95 (s, 9 H, Si^{t}Bu), 3.11 (t, 1 H, OH), 3.82 (m, 1 H), 3.94 (m, 2 H), 4.02 (m, 2 H), 4.10 (m, 2 H), 4.36 (t, J = 4.2 Hz, 1 H), 4.80 (s, 2 H, OCH_2Ph), 4.92 (q, 2 H, OCH_2Ph), 5.26 (d, J = 10.6 Hz, 1 H, vinyl), 5.39 (d, J = 17.3 Hz, 1 H, vinyl), 6.19 (m, 1 H, vinyl), 7.3 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ −4.89, −4.56, −4.50, −4.32, −4.26, −4.13, −4.06, 18.08, 18.23, 18.32, 25.93, 26.08, 62.17, 71.94, 72.44, 75.12, 75.67, 76.26, 77.24, 78.14, 115.67, 126.71, 126.80, 126.94, 128.01, 128.05, 137.93, 139.81; IR (neat) 3446 (br), 2956 (s), 2929 (s), 2856 (s), 1472 (m), 1256 (s), 1088 (br), 845 (m), 776 (m); MS (FAB) 897 (M + Na, 16), 176 (matrix, 100). Anal. Calcd for $C_{47}H_{86}O_7Si_4$: C, 64.48; H, 9.90. Found: C, 64.53; H, 9.95.

8,9-Dideoxy-2,3,6,7-tetrakis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-4,5-bis-*O*-(phenylmethyl)-D-*threo*-L-*galacto*-non-8-enose (12d). Oxalyl chloride (1.62 mL, 19.1 mmol) was dissolved in 70 mL of dichloromethane, and the solution was cooled to −78 °C. DMSO (3.8 mL, 57.2 mmol) was added, and after 20 min a solution of the hydroxy olefin **12c** (5.56 g, 6.4 mmol) in dichloromethane was added over 20 min via cannula. After 1 h at −78 °C, triethylamine (13.3 mL, 95.2 mmol) was added, and the mixture was allowed to stir for 1 h. The reaction was quenched with water, and the aqueous layer was extracted twice with dichloromethane. The combined organic layers were dried over anhydrous $MgSO_4$, and the residue, after evaporation of the solvent, was purified by flash chromatography through silica gel with 4% ethyl acetate–hexane to afford the aldehyde (5.6 g, 100%) as an oil: $[\alpha]^{21}_D = +22.9°$ (*c* 2.70, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.03, 0.05, 0.08, 0.11, 0.12, 0.14 (s, 3 H, $SiCH_3$), 0.09 (s, 6 H, $SiCH_3$), 0.93 (s, 27 H, Si^{t}Bu), 0.95 (s, 9 H, Si^{t}Bu), 4.01 (t, J = 4.0 Hz, 1 H), 4.08 (t, 1 H), 4.14 (t, J = 4.4 Hz, 1 H), 4.22 (d, J = 3.2 Hz, 1 H), 4.36 (t, 2 H), 4.75 (m, 2 H, OCH_2Ph), 4.81 (s, 2 H, OCH_2Ph), 5.24 (d, J = 10.6 Hz, 1 H, vinyl), 5.38 (d, J = 17.3 Hz, 1 H, vinyl), 6.16 (m, 1 H, vinyl), 7.3 (m, 10 H, Ph), 9.78 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ −4.86, −4.59, −4.34, −4.16, −4.10, −3.98, −3.87, 18.21, 18.33, 18.43, 18.48, 26.01, 26.10, 26.22, 72.82, 73.06, 75.89, 77.23, 77.88, 79.28, 80.26, 115.87, 126.76, 126.81, 127.08, 127.13, 127.96, 138.16, 139.48, 139.81, 201.95; IR (neat) 2954 (s), 2930 (s), 2858 (s), 1732 (m), 1472 (m), 1256 (m), 1088 (m), 836 (s), 777 (m); MS (FAB) 895 (M + Na, 6), 73 (100). Anal. Calcd for $C_{47}H_{84}O_7Si_4$: C, 64.62; H, 9.69. Found: C, 64.49; H, 9.70.

(2*E*)-Ethyl 2,3,10,11-Tetradeoxy-4,5,8,9-tetrakis-*O*-[(1,1-dimethylethyl)dimethylsilyl]-6,7-bis-*O*-(phenylmethyl)-D-*threo*-L-*galacto*-undeca-2,10-dienonate (12e). Triethyl phosphonoacetate (17 mL, 85.8 mmol) was dissolved in 0.5 L of THF, and the solution was cooled to −78 °C. After the addition of *n*-BuLi (2.5 M in hexane, 34 mL, 85.8 mmol), the bath was removed and the mixture was allowed to stir for 5 min. The mixture was recooled, and the aldehyde **12d** (50.0 g, 57.2 mmol), as a solution in THF, was added via cannula over 20 min. The mixture was then allowed to warm slowly to room temperature. After 5 h, the reaction was quenched by the addition of 200 mL of saturated NH_4Cl and 200 mL of water. The aqueous layer was separated and extracted twice with 150 mL of ethyl acetate. The combined organic layers were dried over anhydrous $MgSO_4$, and the residue, after evaporation of the solvent, was purified by flash chromatography through silica gel with 4% ethyl acetate–hexane to afford **12e** (52.2 g, 97%) as an oil: $[\alpha]^{20}_D$ = +8.62° (*c* 2.76, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ −0.03, −0.01, 0.01, 0.03, 0.05, 0.08, 0.09, 0.11 (s, 3 H, $SiCH_3$), 0.85, 0.87, 0.91, 0.95 (s, 9 H, Si^{t}Bu), 1.32 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 3.93 (t, 2 H), 4.20 (m, 4 H), 4.40 (m, 1 H), 4.56 (m, 1 H), 4.86 (q, *J* = 12.2 Hz, 2 H, OCH_2Ph), 4.84 (q, *J* = 12.1 Hz, 2 H, OCH_2Ph), 5.20 (d, *J* = 10.5 Hz, 1 H, vinyl), 5.31 (d, *J* = 17.3 Hz, 1 H, vinyl), 6.03 (dd, *J* = 15.8, 1.6 Hz, 1 H, α-olefinic), 6.17 (m, 1 H, vinyl), 7.4 (m, 11 H, Ph+β-olefinic); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ −4.86, −4.59, −4.34, −4.16, −4.10, −3.98, −3.87, 18.21, 18.33, 18.43, 18.48, 26.01, 26.10, 26.22, 72.82, 73.06, 75.89, 77.23, 77.88, 79.28, 80.26, 115.87, 126.76, 126.81, 127.08, 127.13, 127.96, 138.16, 139.48, 139.81, 201.95; IR (neat) 2955 (s), 2929 (s), 2858 (s), 1724 (m), 1472 (m), 1258 (m), 1091 (m), 835 (s), 776 (m); MS (FAB-thioglycerol) 943 (M + 1, 2), 217 (matrix, 100). Anal. Calcd for $C_{51}H_{90}O_8Si_4$: C, 64.92; H, 9.61. Found: C, 64.82; H, 9.67.

(2*E*)-Ethyl 2,3,10,11-Tetradeoxy-6,7-bis-*O*-(phenylmethyl)-D-*threo*-L-*galacto*-undeca-2,10-dienonate (13a). To the solution of the tetra(silyl ether) **12e** (50.9 g, 53.9 mmol) in 0.5 L of THF was added tetrabutylammonium fluoride (1.0 M in THF, 237 mL, 237 mmol) over 30 min at 0 °C. After 3 h, 200 mL of saturated NH_4Cl and 200 mL of water were added, and the aqueous layer was extracted twice with 150 mL of ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. Flash chromatography through silica gel with 50–100% ethyl acetate–hexane yielded the desired product (22.5 g, 86%) as a solid: $[\alpha]^{21}_D$ = +3.46° (*c* 3.24, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ 1.25 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 2.8 (br, 1 H, OH), 3.1 (br, 1 H, OH), 3.3 (br, 1 H, OH), 3.5 (br, 1 H, OH), 3.87 (q, *J* = 8.6 Hz, 2 H), 3.90 (s, 2 H), 4.15 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 4.36 (br, 1 H), 4.50 (br, 1 H), 4.67 (m, 4 H, OCH_2Ph), 5.20 (d, *J* = 10.6 Hz, 1 H, vinyl), 5.32 (d, *J* = 17.2 Hz, 1 H, vinyl), 5.93 (m, 1 H, vinyl), 6.10 (dd, *J* = 15.7, 1.6 Hz, 1 H, α-olefinic), 6.98 (dd, *J* = 15.7, 4.1 Hz, 1 H, β-olefinic), 7.3 (s, 10 H, Ph); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.04, 60.40, 70.15, 71.23, 72.76, 73.12, 73.96, 74.03, 77.18, 116.10, 121.96, 128.21, 128.29, 128.59, 137.39, 137.48, 138.28, 148.23, 166.48; IR (neat) 3933 (br), 2938 (m), 1699 (s), 1658 (m), 1307 (m), 1069 (s), 698 (m); mp 38–42 °C; MS (DIP-CI, isobutane) 487 (M + 1, 11), 91 (100). Anal. Calcd for $C_{27}H_{34}O_8$: C, 66.65; H, 7.04. Found: C, 66.29; H, 7.28.

(2*E*)-Ethyl 2,3,10,11-Tetradeoxy-4,5:8,9-bis-*O*-(1-methylethylidene)-6,7-bis-*O*-(phenylmethyl)-D-*threo*-L-*galacto*-undeca-2,10-dienonate (13b). The tetraol **13a** (13.0 g, 26.7 mmol) was stirred for 18 h at room temperature in a solution of concentrated H_2SO_4 (2.6 mL) in 1 L of acetone. After the mixture was cooled over an ice bath, 350 mL of a saturated $NaHCO_3$ solution was added. Acetone was removed by rotary evaporation, and the aqueous mixture was extracted four times with a total of 600 mL of dichloromethane. The organic layers were dried over anhydrous $MgSO_4$, and the residue, after evaporation of the solvent, was purified by flash chromatography through silica gel with 10–15% ethyl acetate–hexane to afford **13b** (13.3 g, 88%) as an oil: $[\alpha]^{21}_D$ = +16.9° (*c* 2.91, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ 1.18 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 1.32, 1.35, 1.37, 1.38 (s, 3 H, acetonide), 3.77 (m, 2 H), 3.98 (t, *J* = 7.5 Hz, 2 H), 4.08 (q, *J* = 7.1 Hz, 2 H, OCH_2CH_3), 4.33 (m, 2 H), 4.67 (q, *J* = 11.2 Hz, 2 H, OCH_2Ph), 4.63 (q, *J* = 11.1 Hz, 2 H, OCH_2Ph), 5.11 (dt, *J* = 10.6, 1.2 Hz, 1 H, vinyl), 5.30 (dt, *J* = 17.1, 1.3 Hz, 1 H, vinyl), 5.84 (m, 1 H, vinyl), 5.97 (dd, *J* = 15.6, 1.6 Hz, 1 H, α-olefinic), 6.84 (dd, *J* = 15.6, 4.8 Hz, 1 H, β-olefinic), 7.2 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.17, 26.72, 27.01, 27.10, 60.30, 74.64, 78.68, 79.24, 79.35, 80.50, 80.71, 109.78, 117.48, 121.92, 127.66, 127.78, 127.98, 128.13, 128.28, 128.33, 136.16, 137.89, 138.01, 145.03, 165.97; IR (neat) 2986 (m), 1721 (s), 1661 (w), 1370 (m), 1171 (m), 1069 (s), 697 (m); MS (FAB) 567 (M + 1, 3), 181 (100). Anal. Calcd for $C_{33}H_{42}O_8$: C, 69.94; H, 7.47. Found: C, 70.06; H, 7.47.

Ethyl 4,5:8,9-Bis-*O*-(1-methylethylidene)-6,7-bis-*O*-(phenylmethyl)-D-*glycero*-D-*galacto*-D-*galacto*-undeconate (14). To a mixture containing **13b** (13.1 g, 23.2 mmol), dihydroquinine *p*-chlorobenzoate (10.8 g, 23.2 mmol), and *N*-methylmorpholine *N*-oxide (8.14 g, 69.4 mmol) in 10:1 acetone–water (43.4 mL) was added OsO_4 (0.393 M in acetone, 2.9 mL) at 0 °C, and the mixture was allowed to stir for 4 h at 0 °C. After the addition of solid $NaHSO_3$–$Na_2S_2O_5$ (10 g), the mixture was allowed to stir for 1.5 h at room temperature. The black mixture was diluted with 50 mL of dichloromethane, and 10 g of Na_2SO_4 was added. After 30 min of stirring, the mixture was filtered through Celite followed by dichloromethane rinses. The filtrate was concentrated to afford a residue, which was purified by flash chromatography through silica gel with 40–50% ethyl acetate–hexane to afford **14** as a mixture of diastereomers (13.0 g, 88%): $[\alpha]^{22}_D$ = −32.8° (*c* 4.42, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.29 (t, *J* = 7.1 Hz, 3 H, OCH_2CH_3), 1.37, 1.39 (s, 3 H, acetonide), 1.42 (s, 6 H, acetonide), 2.11 (br, 1 H, OH), 2.90 (d, *J* = 7.6 Hz, 1 H, OH), 3.32 (d, *J* = 5.2 Hz, 1 H, OH), 3.33 (br, 1 H, OH), 3.60 (br m, 2 H), 3.70 (br m, 1 H), 3.84 (ddd, *J* = 8.9, 5.1, 1.0 Hz, 1 H), 3.92 (m, 3 H), 4.09 (dd, *J* = 9.0, 6.3 Hz, 1 H), 4.13 (dd, *J* = 8.5, 6.9 Hz, 1 H), 4.26 (m, 3 H), 4.35 (d, *J* = 7.3 Hz, 1 H), 4.67 (d, *J* = 11.1 Hz, 1 H, CH_2Ph), 4.72 (d, *J* = 11.2 Hz, 1 H, CH_2Ph), 4.86 (d, *J* = 11.2 Hz, 1 H, CH_2Ph), 4.90 (d, *J* = 11.1 Hz, 1 H, CH_2Ph), 7.35 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.1, 26.8, 27.0, 27.2, 27.2, 61.7, 63.6, 70.7, 73.0, 74.2, 74.9, 75.0, 78.2, 78.6, 78.7, 80.1, 80.3, 80.6, 109.8, 128.2, 128.3, 128.5, 137.0, 173.1; IR (neat) 3436 (br), 2984 (m), 1739 (m), 1370 (m) 1212 (m), 1068 (s), 699 (m); MS (FAB) 657 (M + Na, 58), 91 (100); HRMS (FAB) *m/z* 657.2864 (calcd 657.2887 for $C_{33}H_{46}O_{12}$ + Na).

(9*E*)-1,2,9,10-Tetradeoxy-3,4:7,8-bis-*O*-(1-methylethylidene)-5,6-bis-*O*-(phenylmethyl)-D-*threo*-L-*galacto*-undeca-1,9-dienitol (16a). To a solution of α,β-unsaturated ester **13b** (0.37 g, 0.65 mmol) in dichloromethane (10 mL) was added DIBAL-H (1 M in CH_2Cl_2, 3.3 mL, 3.3 mmol) at −78 °C, and the solution was allowed to stir at this temperature for 1 h. Acetone was added to quench the excess hydride, and the mixture was diluted with aqueous potassium sodium tartrate and dichloromethane. The organic layers were dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by flash chromatography with 30% ethyl acetate–hexane to yield the alcohol (0.32 g, 92%): $[\alpha]^{20}_D$ = +14.2° (*c* 2.95, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ 1.44 (s, 6 H, CH_3), 1.46 (s, 6 H, CH_3), 1.54 (t, 1 H, OH), 3.87 (m, 2 H), 4.01 (m, 4 H), 4.49 (m, 2 H), 4.69 (dd, 2 H, CH_2Ph), 4.82 (dd, 2 H, CH_2Ph), 5.23 (d, *J* = 10.3 Hz, 1 H, vinyl), 5.41 (d, *J* = 17.1 Hz, 1 H, vinyl), 5.73 (dd, 1 H, olefinic), 5.91 (m, 2 H, vinyl+olefinic), 7.3 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 26.89, 26.97, 62.75, 74.64, 74.79, 79.52, 80.00, 80.39, 109.01, 117.81, 127.58, 127.68, 127.91, 128.26, 129.06, 133.65, 136.16, 138.39, 138.51.

(9*E*)-1,2,9,10-Tetradeoxy-11-*O*-[(1,1-dimethylethyl)diphenylsilyl]-3,4:7,8-bis-*O*-(1-methylethylidene)-5,6-bis-*O*-(phenylmethyl)-D-*threo*-L-*galacto*-undeca-1,9-dienitol (16b). A solution of the allyl alcohol **16a** (1.00 g, 1.81 mmol), imidazole (0.3 g, 4.3 mmol), and TBDPSCl (0.56 mL, 2.17 mmol) in DMF (10 mL) was stirred overnight at room temperature. The mixture was cooled over ice, and water was added. The mixture was extracted with dichloromethane, and the organic layers were dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by flash chromatography with 4–5% ethyl acetate–hexane to yield the silyl ether contaminated with 6% silanol (1.5 g, quant): $[\alpha]^{26}_D$ = +11.2° (*c* 8.08, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ 1.0 (s, 9 H, ^{t}Bu), 1.3–1.4 (4s, 12 H, CH_3), 3.8 (m, 1 H), 3.96 (m, 1 H), 4.03 (d, 1 H), 4.35 (m, 1 H), 4.6 (d, 2 H, CH_2Ph), 4.7 (dd, 2 H, CH_2Ph), 5.8 (m, 2 H), 7.2 (m, Ph), 7.6 (m, Ph); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 19.21, 26.84, 26.99, 27.08, 27.13, 63.68, 74.59, 79.62, 79.72, 79.81, 80.41, 80.52, 108.84, 108.93, 117.46, 127.42, 127.52, 127.63, 127.78, 127.90, 128.17, 129.59, 132.74, 133.62, 135.50, 136.31, 138.37; IR (neat) 2932 (m), 2858 (m), 1113 (s), 1066 (s), 701 (s).

1-*O*-[(1,1-Dimethylethyl)diphenylsilyl]-4,5:8,9-bis-*O*-(1-methylethylidene)-6,7-bis-*O*-(phenylmethyl)-D-*glycero*-D-*galacto*-D-*galacto*-undecitol (16c). The bis-olefin **16b** (94% pure, 0.34 g, 0.44 mmol), dihydroquinine *p*-chlorobenzoate (0.41 g, 0.88 mmol), and *N*-methylmorpholine *N*-oxide (0.154 g, 1.32 mmol) were dissolved in 4 mL (8:1) of acetone–water. OsO_4 (0.39 M in toluene, 0.056 mL, 0.022 mmol) was added, and the solution was stirred overnight at room temperature. After cooling over an ice bath, the reaction was quenched by the addition of saturated $NaHSO_3$. The mixture was diluted with water and extracted with dichloromethane. The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by flash chromatography with 40% ethyl acetate–hexane to afford **16c** as a white foam (0.23 g, 63%): $[\alpha]^{26}_D$ = −17.3° (*c* 4.32, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ 0.96 (s, 9 H, ^{t}Bu), 1.29 (s, 3 H, CH_3), 1.31 (s, 6 H, CH_3), 1.35 (s, 3 H, CH_3), 1.9 (br, 1 H, OH), 2.3 (br, 1 H, OH), 2.5 (d, *J* = 6.7 Hz, OH), 3.18 (d, *J* = 4.4 Hz, 1 H, OH), 3.5 (m), 3.6 (m), 3.8 (m), 4.1 (m), 4.1 (m), 4.8 (dd, 2 H, CH_2Ph), 4.8 (dd, 2 H, CH_2Ph), 7.2 (m, Ph), 7.6 (m, Ph); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 19.16, 26.82, 27.01, 27.23, 27.28, 63.62, 65.18, 70.29, 71.95, 73.03, 74.91, 75.04, 78.16, 80.04, 80.17, 80.48, 109.73, 109.87, 127.65, 128.13, 128.27, 128.49, 129.66,

133.25, 133.30, 135.52, 136.97, 137.16; IR (neat) 3440 (br), 2931 (m), 1381 (m), 1213 (m), 1113 (s), 1070 (s), 702 (m); MS (FAB, thioglycerol) 831 (M + 1, 8); HRMS *m/z* 831.4154 (calcd 831.4141 for $C_{47}H_{62}O_{11}Si$ + H).

2-Propenyl 2,3,6,7,10,11-Hexakis-*O*-(phenylmethyl)-D-*glycero*-D-*galacto*-D-*galacto*-undecofuranoside (18a). The aldehyde **16f** (0.212 g, 0.223 mmol) was heated at reflux for 2 h as a solution in 1.5:1.5:1 water–THF–TFA (4 mL). The mixture was evaporated to dryness, and the residue was dissolved in 2:1 allyl alcohol–TFA (5 mL). The solution was heated at reflux overnight and then evaporated to a residue, which was purified by flash chromatography to afford the two furanosides (α: 0.105 g, 52%; β: 0.029 g, 14%). Resubjection of the intermediates to the above conditions afforded more product (11% α, 3% β). α-Glycoside (C1 and C4 substituents on the ring disposed syn): $[\alpha]^{22}_D = -32.2°$ (*c* 5.25, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ 2.7 (br), 3.56 (m), 3.70 (q), 3.88 (m), 4.00 (m), 4.10 (m), 4.43 (m), 4.61 (m), 5.03 (s), 5.07 (s), 5.13 (s), 5.20 (s), 5.76 (oct), 7.20 (m); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 68.21, 69.50, 69.59, 69.94, 70.65, 71.91, 72.30, 73.18, 73.59, 74.28, 78.32, 78.91, 80.00, 81.26, 82.94, 87.82, 105.76, 117.08, 127.44, 127.52, 127.58, 127.65, 127.72, 127.78, 127.87, 128.04, 128.13, 128.26, 128.38, 134.05, 137.52, 137.93, 138.02, 138.25, 138.46, 138.55; IR (neat) 3450 (br), 2924 (m), 2867 (m), 1496 (m), 1454 (m), 1093 (s), 736 (s), 697 (s); MS (FAB, thioglycerol) 912.5 (M + 1, 0.7); HRMS *m/z* 911.4299 (calcd 911.4372 for $C_{56}H_{62}O_{11}$ + H). β-Glycoside (C1 and C4 substituents on the ring disposed anti): $[\alpha]^{22}_D = +0.55°$ (*c* 1.45, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ 2.8 (br), 3.65 (m), 3.8 (m), 4.1 (m), 4.5 (m), 4.6 (m), 4.9 (d), 5.3 (d), 5.4 (d), 5.9 (oct), 7.3 (m); IR (neat) 3470 (br), 3030 (w), 1454 (m), 1093 (s), 1028 (m), 697 (m).

2-Propenyl 2,3,5,6,7,8,9,10,11-Nonakis-*O*-(phenylmethyl)-D-*glycero*-D-*galacto*-D-*galacto*-α-undecofuranoside (18b). The mixture of the alcohol **18a** (90 mg, 0.099 mmol), sodium hydride (60% oil emulsion, 40 mg, 0.99 mmol), and benzyl bromide (0.117 mL, 0.99 mmol) in DMF was stirred for 4 h at room temperature. Aqueous ammonium chloride was added, and the mixture was extracted with dichloromethane. The organic layers were dried over $MgSO_4$ and concentrated. The residue was purified by flash chromatography with 10–15% ethyl acetate–hexane to afford the perbenzylated product (95 mg, 81%): $[\alpha]^{22}_D = -16.8°$ (*c* 4.73, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ 3.6 (dd), 3.9 (m), 4.1 (m), 4.5 (m), 4.7 (m), 5.11 (s), 5.8 (oct), 7.2 (m); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 69.59, 68.47, 70.35, 71.80, 71.92, 71.97, 73.24, 73.97, 76.23, 78.55, 78.67, 79.24, 79.84, 82.08, 89.17, 105.43, 117.13, 127.12, 127.28, 127.30, 127.64, 127.80, 127.85, 128.00, 128.07, 128.14, 128.26, 133.95, 137.80, 137.92, 138.15, 138.44, 138.71, 138.86, 138.92, 139.01, 139.07, 139.21; IR (neat) 3030 (w), 2666 (w), 1453 (m), 1096 (s), 734 (m), 696 (s).

8,9:10,11-Bis-*O*-(1-methylethylidene)-6,7-bis-*O*-(phenylmethyl)-D-*glycero*-D-*galacto*-D-*galacto*-undeconic Acid γ-Lactone (21). The tetraol **14** (3.46 g, 5.45 mmol) was dissolved in 1:3 TFA–methanol (100 mL) and was allowed to stir for 2.5 days at reflux. The solution was concentrated by rotary evaporation, and the residue was evaporated several times, first with methanol then with THF. The residue was dissolved in 1% TFA–THF and was allowed to reflux for 10 h. The solution was evaporated to dryness and evaporated several times with THF. The residue was then dissolved in acetone (300 mL) that was treated with H_2SO_4 (12 drops), and the solution was allowed to stir for 2 days. The acid was neutralized with triethylamine, and the mixture was evaporated. The residue was purified by flash chromatography with 40–50% ethyl acetate–hexane to afford diastereomerically pure lactone **21** (2.1 g, 65%) as a glassy resin: $[\alpha]^{22}_D = -35.7°$ (*c* 3.34, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.33, 1.36, 1.40, 1.44 (s, 3 H, acetonide), 3.59, 3.76 (br, 1 H, OH), 3.79 (dd, *J* = 9.5, 5.8 Hz, 1 H), 3.93 (m, 2 H), 3.95 (q, 1 H), 4.08 (br, 1 H, OH), 4.11 (m, 2 H), 4.22 (t, *J* = 6.8 Hz, 1 H), 4.28 (d, *J* = 7.3 Hz, 1 H), 4.48 (m, 2 H), 4.54 (d, *J* = 11 Hz, 1 H, C*H*$_2$Ph), 4.78 (s, 2 H, CH_2Ph), 4.78 (d, *J* = 11 Hz, 1 H, CH_2Ph), 7.31 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 25.3, 26.2, 27.2, 27.3, 67.0, 68.7, 73.2, 74.6, 74.8, 75.0, 76.9, 78.2, 78.5, 79.2, 80.0, 80.9, 109.6, 110.1, 127.7, 127.8, 127.9, 128.4, 137.8, 138.0, 174.2; IR (neat) 3420 (br), 2988 (m), 1784 (s), 1378 (m), 1215 (m), 1067 (s), 754 (m); MS (FAB) 611 (M + Na, 59), 91 (100). HRMS (FAB) *m/z* 611.2491 (calcd 611.2469 for $C_{31}H_{40}O_{11}$ + Na).

8,9:10,11-Bis-*O*-(1-methylethylidene)-6,7-bis-*O*-(phenylmethyl)-1,2,3-tri-*O*-benzoyl-D-*glycero*-D-*galacto*-β-D-*galacto*-undecopyranose (22). DIBAL-H (1 M in CH_2Cl_2, 22.5 mL, 22.5 mmol) was added over 14 min to a solution of **21** (2.65 g, 4.50 mmol) in dichloromethane (68 mL) at −90 °C, and the solution was allowed to stir for 2 h at this temperature. Acetone (5 mL) was added; the bath was removed after 15 min, and 100 mL each of saturated potassium sodium tartrate, water, and dichloromethane were added. After stirring overnight, the mixture was diluted with 1 L of water and extracted several times with hot dichloromethane. The organic layers were dried over anhydrous Na_2SO_4 and concentrated to afford 2.22 g of crude product. To the solution of crude polyol in dry dichloromethane (15 mL) was added benzoyl chloride (2.18 mL, 18.8 mL) over 1 h at 0 °C, and the solution was stirred for 1 h at this temperature. The mixture was diluted with 1 L of water and extracted five times with 200 mL of dichloromethane. The organic layers were dried over anhydrous $MgSO_4$, and the residue, after evaporation of the solvent, was purified by flash chromatography with 15–20% ethyl acetate–hexane to furnish 1.77 g of impure alcohol. Preparative HPLC with 21% ethyl acetate–hexane afforded pure alcohol **22** (1.06 g, 29%) as a glassy solid. The yield was increased by resubjecting the isomers as follows: The materials that were separated from **22** by preparative HPLC were deacylated with sodium methoxide–methanol at room temperature, rebenzoylated by the procedure described above, and purified by flash chromatography. The polar compounds, which were separated during flash chromatography of the impure benzoate, were resubjected to the benzoylation condition. The combined products were purified by preparative HPLC to afford additional alcohol (0.21 g, 5%): $[\alpha]^{22}_D = +29.8°$ (*c* 3.02, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.32, 1.37 (s, 3 H, acetonide), 1.38 (s, 6 H, acetonide), 2.5 (br, 1 H, OH), 3.86 (dd, *J* = 8.0, 2.9 Hz, 1 H), 3.89 (t, *J* = 6.9 Hz, 1 H), 3.99 (t, 1 H), 4.04 (t, 1 H), 4.15 (d, *J* = 7.7 Hz, 1 H), 4.2 (m, 3 H), 4.48 (d, *J* = 2.9 Hz, 1 H), 4.77 (d, *J* = 11.6 Hz, 1 H, CH_2Ph), 4.78 (q, 2 H, CH_2Ph), 4.95 (d, *J* = 11.5 Hz, 1 H, CH_2Ph), 5.44 (dd, *J* = 10.1, 2.9 Hz, 1 H), 6.05 (d, *J* = 8.2 Hz, 1 H), 6.12 (dd, *J* = 8, 10 Hz, 1 H), 7.8 (m, 17 H, Ph), 7.55 (m, 2 H, Ph), 7.9, 8.0, 8.1 (d, 2 H, Ph); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 25.30, 26.29, 27.40, 27.56, 65.84, 67.04, 68.83, 73.79, 74.17, 75.00, 75.11, 76.43, 77.67, 77.78, 79.80, 80.18, 93.25, 127.53, 127.74, 128.11, 128.30, 128.35, 128.41, 128.46, 129.67, 129.85, 130.16, 133.16, 133.34, 133.66, 138.16, 138.43, 164.69, 165.37, 165.55; IR (neat) 3488 (br), 2988 (m), 1736 (s), 1452 (m), 1265 (s), 1028 (s), 710 (m); MS (FAB) 925 (M + Na, 12), 91 (100); HRMS (FAB) *m/z* 925.3371 (calcd 925.3408 for $C_{52}H_{54}O_{14}$ + Na).

4-Azido-4-deoxy-8,9:10,11-bis-*O*-(1-methylethylidene)-6,7-bis-*O*-(phenylmethyl)-1,2,3-tri-*O*-benzoyl-D-*glycero*-D-*galacto*-β-D-*gluco*-undecopyranose (23). To a solution of **22** (1.75 g, 1.94 mmol) and pyridine (1.57 mL, 19.4 mmol) in dichloromethane (13 mL) was added triflic anhydride (0.652 mL, 3.88 mmol) at 0 °C. After 10 min at 0 °C, the ice bath was removed, and the solution was stirred for 1 h at room temperature. The solution was recooled and quenched by the addition of saturated $NaHCO_3$. The mixture was extracted three times with dichloromethane, and the combined organic layers were dried over anhydrous $MgSO_4$. The residue, after evaporation of the solvent, was dissolved in benzene (15 mL) and was stirred for 15 min with tetrabutylammonium azide (1.65 g, 5.81 mmol). The reaction mixture was passed through a plug of silica gel with ethyl acetate, and the filtrate was concentrated. The residue was purified by flash chromatography through silica gel with 10–30% ethyl acetate–hexane to afford **23** (1.46 g, 81%) as a foamy solid: $[\alpha]^{22}_D = +54.9°$ (*c* 2.51, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.37, 1.38, 1.40, 1.43 (s, 3 H, acetonide), 4.0–4.3 (m, 9 H), 4.8–4.9 (m, 4 H, CH_2Ph), 5.61 (dd, *J* = 8.2, 9.7 Hz, 1 H, C2H), 5.80 (t, *J* = 9.8 Hz, 1 H, C3H), 6.11 (d, *J* = 8.1 Hz, C1H), 7.3 (m, 17 H, Ph), 7.54 (m, 2 H, Ph), 7.88 (d, 2 H, Ph), 8.0 (d, 4 H, Ph); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 24.97, 26.29, 27.15, 60.32, 67.21, 71.16, 74.06, 75.30, 75.70, 76.05, 77.18, 78.08, 80.02, 80.61, 82.18, 92.47, 127.44, 127.62, 127.76, 128.00, 128.23, 128.30, 128.38, 128.50, 129.80, 129.89, 130.07, 133.37, 133.53, 133.73, 138.50, 138.62, 164.35, 165.26, 165.61; IR (neat) 2987 (w), 2112 (m), 1738 (s), 1262 (s), 1067 (s), 709 (m); mp 55–65 °C; MS (FAB) 950 (M + Na, 32), 133 (100); HRMS (FAB) *m/z* 950.3467 (calcd 950.3473 for $C_{52}H_{53}O_{13}N_3$ + Na).

4-Azido-4-deoxy-6,7-bis-*O*-(phenylmethyl)-1,2,3,8,9,10,11-hepta-*O*-acetyl-D-*glycero*-D-*galacto*-α(and β)-D-*gluco*-undecopyranose (27). The azide **23** (1.06 g, 1.14 mmol) was heated at reflux with Amberlyst-15 in methanol (70 mL). The mixture was filtered through Celite to remove the resin, and the filtrate was concentrated. The incompletely deketalized compounds were separated by flash chromatography and were resubjected to the deketalization conditions (0.47 g resin, 50 mL of methanol, 9.5 h). The combined products were stirred for 4 h with sodium methoxide (100 mg) in methanol (70 mL) at room temperature. After evaporation of the solvent, the residue was dissolved in 1:1 acetic anhydride–pyridine (20 mL) with DMAP (30 mg) and was allowed to stir for 20 h. The solution was evaporated in vacuo, and the remaining residue was purified by flash chromatography through silica gel with 30% ethyl acetate–hexane to afford the product **27** as an ca. 1:1 mixture of diastereomers (788 mg, 83%). An aliquot of the mixture was separated by HPLC on a μ-Porosil column with 33% ethyl acetate–hexane for characterization. α-Anomer: $[\alpha]^{24}_D = +74.5°$ (*c* 1.50, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.94, 2.01, 2.03, 2.05, 2.08, 2.11, 2.16 (s, 3 H, acetyl), 3.9 (m, 4 H, C4-7H), 4.18 (d, 2 H, C11H), 4.50 (d, *J* = 10.8 Hz, 1 H, CH_2Ph), 4.67 (d, *J* = 11.5 Hz, 1 H, CH_2Ph), 4.75 (d, *J* = 10.9 Hz, 1 H, CH_2Ph), 4.84 (d, *J* = 11.4 Hz, 1 H, CH_2Ph), 4.95 (dd, *J* = 3.7,

10.2 Hz, 1 H, C2H), 5.08 (dt, J = 3.7, 8.8 Hz, 1 H, C10H), 5.29 (dd, J = 1.7, 4.6 Hz, 1 H, C8H), 5.45 (t, J = 9.9 Hz, C3H), 5.54 (dd, J = 1.7, 8.8 Hz, 1 H, C9H), 6.27 (d, J = 3.6 Hz, 1 H, C1H), 7.3 (d, 10 H, Ph); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 20.44, 20.62, 20.72, 20.82, 60.04, 61.70, 67.65, 68.65, 69.32, 70.11, 70.69, 72.46, 75.43, 75.68, 79.24, 80.81, 89.18, 127.74, 127.78, 128.09, 128.20, 128.30, 128.36, 137.97, 138.01, 168.78, 169.73, 169.80, 169.82, 169.88, 170.61; IR (neat) 2114 (m), 1752 (s), 1370 (m), 1215 (s), 1073 (m); MS (FAB) 852 (M + Na, 19), 91 (100). Anal. Calcd for $C_{39}H_{47}N_3O_{17}$: C, 56.45; H, 5.71; N, 5.06. Found: C, 56.48; H, 5.76; N, 4.99. β-Anomer: $[\alpha]^{24}_D$ = +47.0° (c 1.12, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.03, 2.04, 2.06, 2.07, 2.08 (s, 3 H, acetyl), 2.11 (s, 6 H, acetyl), 3.58 (d, J = 10.1 Hz, 1 H, C5H), 3.81 (d, J = 8.9 Hz, 1 H, C6H), 3.91 (dd, J = 6.6, 8.9 Hz, 1 H, C7H), 3.98 (t, J = 10.0 Hz, 1 H, C4H), 4.13 (dd, J = 4.9, 12.5 Hz, 1 H, C11H), 4.23 (dd, J = 2.6, 12.5 Hz, 1 H, C11H), 4.44 (d, J = 10.4 Hz, 1 H, CH_2Ph), 4.67 (d, J = 11.4 Hz, 1 H, CH_2Ph), 4.82 (d, J = 10.4 Hz, 1 H, CH_2Ph), 4.87 (d, J = 11.4 Hz, 1 H, CH_2Ph), 4.99 (dd, J = 8.4, 9.5 Hz, 1 H, C2H), 5.06 (m, 1 H, C10H), 5.22 (t, J = 9.8 Hz, 1 H, C3H), 5.32 (dd, J = 1.8, 6.6 Hz, 1 H, C8H), 5.61 (dd, J = 1.8, 8.8 Hz, 1 H, C9H), 5.63 (d, J = 8.3 Hz, 1 H, C1H), 7.3 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 20.53, 20.59, 20.62, 20.70, 20.77, 20.84, 60.10, 61.77, 68.22, 68.31, 70.49, 70.93, 73.86, 75.39, 75.46, 75.80, 77.16, 81.27, 91.37, 127.64, 127.82, 128.29, 128.33, 137.92, 138.02, 168.63, 169.51, 169.87, 169.91, 170.00, 170.21, 170.61; IR (neat) 2112 (m), 1750 (s), 1370 (m), 1215 (s), 1072 (m), 1036 (m); MS (FAB) 852 (M + Na, 13), 91 (100); HRMS (FAB) m/z 852.2761 (calcd 852.2800 for $C_{39}H_{47}O_{17}N_3$ + Na).

1-[2,3,8,9,10,11-Hexa-*O*-acetyl-4-azido-4-deoxy-6,7-bis-*O*-(phenylmethyl)-D-*glycero*-D-*galacto*-β-D-*gluco*-undecopyranosyl]-4-amino-1,2-dihydro-2-oxo-pyrimidine (28). The peracetate **27** (781 mg, 0.941 mmol) and bis(trimethylsilyl)cytosine (721 mg, 2.82 mmol) were dissolved in nitrobenzene (8 mL). Trimethylsilyl trifluoromethanesulfonate (0.60 mL, 3.10 mmol) was added, and the solution was stirred for 3.5 h at 127 °C. The dark solution was cooled and quenched with saturated $NaHCO_3$ after dilution with dichloromethane. The mixture was extracted four times with dichloromethane, and the organic layers were dried over anhydrous Na_2SO_4. Flash chromatography through silica gel with 0–10% methanol–ethyl acetate afforded **28** (628 mg, 76%) as a glassy solid: $[\alpha]^{24}_D$ = +26° (c 1.53, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.91, 2.03, 2.03, 2.05, 2.06, 2.12 (s, 3 H, acetate), 3.60 (d, J = 10.2 Hz, 1 H, C5′H), 3.78 (d, J = 9.5 Hz, 1 H, C6′H), 3.85 (dd, J = 6.5, 9.5 Hz, 1 H, C7′H), 3.98 (t, J = 10.1 Hz, 1 H, C4′H), 4.12 (dd, J = 4.6, 12.5 Hz, 1 H, C11′H), 4.20 (dd, J = 2.6, 12.5 Hz, 1 H, C11′H), 4.46 (d, J = 10.4 Hz, 1 H, CH_2Ph), 4.63 (d, J = 11.8 Hz, 1 H, CH_2Ph), 4.85 (d, J = 10.3 Hz, 1 H, CH_2Ph), 4.90 (d, J = 11.8 Hz, 1 H, CH_2Ph), 4.93 (t, J = 9.5 Hz, 1 H, C2′H), 5.05 (m, 1 H, C10′H), 5.28 (dd, J = 1.5, 6.4 Hz, 1 H, C8′H), 5.35 (t, J = 9.7 Hz, 1 H, C3′H), 5.56 (dd, J = 1.5, 9.0 Hz, 1 H, C9′H), 5.78 (d, J = 7.5 Hz, 1 H, vinylic), 5.95 (d, J = 9.5 Hz, 1 H, C1′H), 7.04 (d, J = 7.6 Hz, 1 H, vinylic), 7.3 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 20.37, 20.56, 20.60, 20.78, 20.85, 60.52, 61.75, 68.04, 68.14, 70.04, 70.98, 73.70, 75.65, 75.77, 77.63, 77.84, 78.05, 80.50, 81.00, 95.85, 127.78, 127.89, 128.00, 128.21, 128.33, 128.44, 137.86, 138.01, 140.66, 154.96, 165.46, 169.51, 169.83, 169.89, 170.03, 170.32, 170.60; IR (neat) 3344 (br), 3114 (w), 2116 (m), 1750 (s), 1665 (m), 1638 (m), 1491 (w), 1372 (m), 1217 (s), 1072 (m); mp 134–136 °C; MS (FAB) 903 (M + Na, 16), 881 (M + 1, 3), 176 (100). Anal. Calcd for $C_{41}H_{48}N_6O_{17}$: C, 54.91; H, 5.39. Found: C, 55.02; H, 5.42.

***N*-[1-[4-(Acetylamino)-2,3,8,9,10,11-hexa-*O*-acetyl-4-deoxy-6,7-bis-*O*-(phenylmethyl)-D-*glycero*-D-*galacto*-β-D-*gluco*-undecopyranosyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]acetamide (29a).** The azide **28** (0.152 g, 0.17 mmol) was dissolved in thioacetic acid (2 mL), and the solution was heated for 15 h at 65 °C. The reagent was evaporated and the residue was purified by flash chromatography with 30% ethyl acetate–hexane to 5% methanol–ethyl acetate to afford the bis-amide (0.106 g, 67%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.8, 1.9, 1.9, 2.1, 2.2 (s, 3 H, CH_3), 2.0 (s, 9 H, CH_3), 3.84 (dd, J = 4.2, 8.1 Hz, 1 H, C7H), 3.97 (m, 2 H, C5,6H), 4.14 (dd, J = 6.4, 12.4 Hz, 1 H, C11H), 4.29 (dd, J = 2.5, 12.3 Hz, 1 H, C11H), 4.43 (q, 1 H, C4H), 4.48 (d, J = 10.9 Hz, 1 H, CH_2Ph), 4.58 (d, J = 12.2 Hz, 1 H, CH_2Ph), 4.67 (d, J = 11.0 Hz, 1 H, CH_2Ph), 4.82 (d, J = 12.1 Hz, 1 H, CH_2Ph), 4.97 (t, J = 9.4 Hz, 1 H, C2H), 5.14 (m, 1 H, C10H), 5.22 (d, J = 2.8 Hz, 1 H, C8H), 5.27 (t, J = 9.8 Hz, 1 H, C3H), 5.56 (dd, J = 1.4, 8.3 Hz, 2 H, C9H+N4H), 6.02 (d, J = 9.7 Hz, 1 H, C1H), 7.3 (m), 7.6 (br, 1 H, olefinic), 8.7 (br, 1 H, NH).

***N*-[1-[4-(Acetylamino)-2,3,8,9,10,11-hexa-*O*-acetyl-4-deoxy-7-*O*-(phenylmethyl)-D-*glycero*-D-*galacto*-β-D-*gluco*-undecopyranosyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]acetamide (29b).** The bis-benzyl ether **29a** (0.062 g, 0.067 mmol) was stirred with DDQ (0.060 g, 0.27 mmol) in a 10:1 dichloromethane pH 7 buffer solution overnight at room temperature. The mixture was diluted with dichloromethane and extracted with saturated $NaHCO_3$. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography with ethyl acetate to 5% methanol–ethyl acetate to afford the alcohol (0.029 g, 52%) and recovered starting material (0.018 g, 30%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.9–2.2 (s, CH_3), 3.2 (br d, 1 H, OH), 3.74 (m, 1 H), 3.84 (m, 2 H), 4.09 (dd, J = 6, 12 Hz, 1 H, C11H), 4.23 (dd, J = 2.7, 12.4 Hz, 1 H, C11H), 4.36 (q, 1 H, C4H), 4.47 (d, J = 10.9 Hz, 1 H, CH_2Ph), 4.60 (d, J = 10.9 Hz, 1 H, CH_2Ph), 5.13 (m, 2 H, C2,10H), 5.27 (m, 2 H, C3,8H), 5.57 (dd, J = 1.9, 8.0 Hz, 1 H, C9H), 5.8 (d, 1 H), 6.01 (d, J = 9.2 Hz, 1 H), 7.32 (m), 7.61 (d, J = 7.6 Hz, 1 H, olefinic).

***N*-[1-[2,3,8,9,10,11-Hexa-*O*-acetyl-4-azido-4-deoxy-6,7-bis-*O*-(phenylmethyl)-D-*glycero*-D-*galacto*-β-D-*gluco*-undecopyranosyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]acetamide (30a).** The nucleoside **28** (347 mg, 0.394 mmol) and DMAP (3.5 mg) were dissolved in acetic anhydride (0.5 mL) and pyridine (0.75 mL), and the solution was stirred for 1 h at room temperature. The mixture was evaporated in vacuo, and the resulting residue was purified by flash chromatography through silica gel with 75–100% ethyl acetate–hexane to afford the N-acetate (351 mg, 96%): $[\alpha]^{24}_D$ = +40° (c 3.31, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.92, 1.98, 2.04, 2.06, 2.07, 2.13, 2.25 (s, 3 H, acetate), 3.61 (d, J = 10.3 Hz, 1 H, C5′H), 3.79 (d, J = 9.6 Hz, 1 H, C6′H), 3.88 (dd, J = 6.4, 9.6 Hz, 1 H, C7′H), 3.99 (t, J = 10.1 Hz, 1 H, C4′H), 4.14 (dd, J = 4.7, 12.5 Hz, 1 H, C11′H), 4.21 (dd, J = 2.5, 12.5 Hz, 1 H, C11′H), 4.49 (d, J = 10.4 Hz, 1 H, CH_2Ph), 4.59 (d, J = 12.0 Hz, 1 H, CH_2Ph), 4.87 (d, J = 10.4 Hz, 1 H, CH_2Ph), 4.87 (t, J = 9.4 Hz, 1 H, C2′H), 4.94 (d, J = 12.0 Hz, 1 H, CH_2Ph), 5.06 (m, 1 H, C10′H), 5.28 (dd, J = 1.4, 6.4 Hz, 1 H, C8′H), 5.37 (t, J = 9.7 Hz, 1 H, C3′H), 5.56 (dd, J = 1.4, 9.0 Hz, 1 H, C9′H), 5.97 (d, J = 9.3 Hz, 1 H, C1′H), 7.2 (d, J = 7.7 Hz, 1 H, vinylic), 7.4 (m, 11 H, vinylic+Ph); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 20.24, 20.40, 20.49, 20.55, 20.73, 20.78, 24.77, 60.18, 61.67, 67.86, 68.08, 70.48, 70.88, 73.35, 75.56, 75.80, 77.61, 78.04, 80.44, 80.73, 97.93, 127.90, 127.97, 128.18, 128.26, 128.32, 128.50, 137.74, 144.08, 154.46, 163.22, 169.30, 169.59, 169.81, 169.95, 170.00, 170.50, 170.85; IR (neat) 2114 (m), 1752 (s), 1680 (m), 1493 (m), 1372 (m), 1223 (s), 1071 (m); MS (FAB) 945 (M + Na, 33), 897 (13), 75 (100). Anal. Calcd for $C_{43}H_{50}N_6O_{18}$: C, 55.01; H, 5.37; N, 8.95. Found: C, 55.11; H, 5.38; N, 9.00.

***N*-[1-[2,3,8,9,10,11-Hexa-*O*-acetyl-4-azido-4-deoxy-7-*O*-(phenylmethyl)-D-*glycero*-D-*galacto*-β-D-*gluco*-undecopyranosyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]acetamide (30b).** The bis-benzyl ether **30a** (83 mg, 0.090 mmol) was stirred for 1 day at room temperature with DDQ (102 mg, 0.45 mmol) in 10:1 CH_2Cl_2–H_2O (1.3 mL). The mixture was diluted with dichloromethane, extracted with saturated $NaHCO_3$ and $NaHSO_3$, and dried over anhydrous Na_2SO_4. The solvent was evaporated, and the residue was purified by flash chromatography with 75–100% ethyl acetate–hexane to yield **30b** (55 mg, 74%): $[\alpha]^{23}_D$ = +48.3° (c 2.61, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.94, 1.99, 2.02, 2.06, 2.10, 2.12, 2.22 (s, 3 H, acetyl), 3.2 (br, 1 H, OH), 3.62 (dd, J = 5.0, 10.0 Hz, 1 H, C5′H), 3.79 (m, 3 H, C4′+6′+7′H), 4.10 (dd, J = 5.4, 12.5 Hz, 1 H, C11′H), 4.22 (dd, J = 2.7, 12.5 Hz, 1 H, C11′H), 4.54 (d, J = 10.9 Hz, 1 H, CH_2Ph), 4.65 (d, J = 10.9 Hz, 1 H, CH_2Ph), 5.10 (m, 2 H, C2′+10′H), 5.28 (dd, J = 2.4, 15.2 Hz, 1 H, C8′H), 5.32 (t, J = 9.5 Hz, 1 H, C3′H), 5.58 (dd, J = 2.4, 8.0 Hz, 1 H, C9′H), 5.94 (d, J = 9.6 Hz, 1 H, C1′H), 7.33 (m, 6 H, Ph+vinylic), 7.66 (d, J = 7.5 Hz, 1 H, vinylic), 9.5 (br, 1 H, NH); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 20.31, 20.56, 20.60, 20.71, 20.78, 24.89, 61.61, 61.70, 68.60, 68.77, 70.05, 70.24, 72.24, 73.57, 74.75, 76.61, 76.88, 81.20, 97.54, 128.04, 128.22, 128.34, 128.37, 128.37, 128.56, 128.63, 136.93, 137.68, 144.32, 162.83, 169.39, 169.74, 169.92, 170.18, 170.55; IR (film) 3478 (br), 3307 (br), 3028 (w), 2115 (m), 1750 (s), 1677 (m), 1630 (w), 1560 (w), 1491 (m), 1372 (m), 1226 (s), 1049 (m), 756 (m); MS (FAB) 855 (M + Na, 100); HRMS (FAB) m/z 855.2667 (calcd 855.2661 for $C_{36}H_{44}N_6O_{17}$ + Na).

3-Azido-1,3-dideoxy-1-(phenylsulfenyl)-2,4,6-tri-*O*-acetyl-β-D-glucopyranose (32). To a solution of 3-azido-3-deoxy-1,2,4,6-tetra-*O*-acetyl-D-glucopyranose (1.0 g, 2.7 mmol) and thiophenol (2.78 mL, 2.7 mmol) in 1,2-dichloroethane (9 mL) was added BF_3·Et_2O (1.0 mL, 8.1 mmol). The solution was stirred for 12 h at 48 °C. After dilution with dichloromethane and saturated $NaHCO_3$, the mixture was stirred for 20 min. The mixture was extracted with dichloromethane, and the organic layers were dried over anhydrous $MgSO_4$. Flash chromatography through silica gel with 10–30% ethyl acetate–hexane afforded pure α-sulfide (165 mg, 15%) and β-sulfide **32** (760 mg, 69%). α-Sulfide: $[\alpha]^{24}_D$ = +236° (c 2.06, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.02, 2.15, 2.18 (s, 3 H, acetyl), 3.95 (t, J = 10.3 Hz, 1 H, C3H), 4.02 (dd, J = 2.4, 12.4 Hz, 1 H, C6H), 4.22 (d, J = 5.3, 12.4 Hz, 1 H, C6H), 4.49 (m, 1 H, C5H), 4.95 (t, J = 10.0 Hz, 1 H, C4H), 4.97 (dd, J = 5.6, 10.6 Hz, 1 H, C2H), 5.89 (d, J = 5.6 Hz, 1 H, C1H), 7.30 (m, 3 H, Ph), 7.43 (m, 2 H, Ph); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 20.54, 20.62, 62.02, 68.52, 68.64, 71.80, 85.03, 127.90, 129.17, 132.02, 132.26, 169.17,

169.42, 170.37; IR (neat) 2112 (s), 1750 (s), 1372 (w), 1249 (s), 1040 (m); mp 116.5–118 °C; MS (FAB) 446 (M + Na, 100). Anal. Calcd for $C_{18}H_{21}N_3O_7S$: C, 51.06; H, 5.00. Found: C, 51.12; H, 5.03. β-Sulfide: $[\alpha]^{24}_D = -20°$ (*c* 1.66, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 2.04, 2.08, 2.14 (s, 3 H, acetyl), 3.65 (m, 2 H, C3+5H), 4.14 (m, 2 H, C6H), 4.64 (d, *J* = 10.0 Hz, 1 H, C1H), 4.9 (m, 2 H, C2+4H), 7.29 (m, 3 H, Ph), 7.46 (m, 2 H, Ph); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 20.48, 20.56, 20.66, 62.27, 65.90, 68.52, 70.22, 76.52, 86.34, 128.29, 128.88, 131.99, 132.95, 168.89, 169.03, 170.37; IR (neat) 2110 (s), 1750 (s), 1373 (m), 1221 (s), 1044 (m), 747 (w); mp 134.5–135.5 °C; MS (FAB) 446 (M + Na, 100). Anal. Calcd for $C_{18}H_{21}N_3O_7S$: C, 51.06; H, 5.00. Found: C, 51.18; H, 5.06.

3-Azido-1,3-dideoxy-1-(phenylsulfenyl)-2,4,6-tri-*O*-(2,2-dimethylpropanoyl)-β-D-glucopyranose (33a). The β-sulfide **32** (676 mg, 1.66 mmol) was stirred for 5.5 h with sodium methoxide (200 mg) in methanol (40 mL) at room temperature. The mixture was concentrated, redissolved in 30% methanol–ethyl acetate, and passed through silica gel. The residue after evaporation was stirred with pivaloyl chloride (2.04 mL, 16.6 mmol) and DMAP (25 mg) in pyridine (5 mL) for 18 h at 68 °C. The reaction mixture was diluted with dichloromethane and saturated $NaHCO_3$, and the mixture was extracted with dichloromethane. The organic layers were dried over anhydrous $MgSO_4$ and evaporated. Flash chromatography through silica gel with 5–20% ethyl acetate–hexane furnished the pivalate (748 mg, 82%) as well as the mixed ester (122 mg), which was resubjected to the deacylation-pivalation conditions to afford more of the desired product (104 mg, 11%): $[\alpha]^{22}_D = -7.9$ (*c* 1.86, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.20, 1.23, 1.29 (s, 9 H, pivalate), 3.69 (t, *J* = 9.9 Hz, 1 H, C3H), 3.71 (m, 1 H, C5H), 4.03 (dd, *J* = 6.2, 12.3 Hz, 1 H, C6H), 4.23 (dd, *J* = 1.7, 12.3 Hz, 1 H, C6H), 4.70 (d, *J* = 10.0 Hz, 1 H, C1H), 4.89 (t, *J* = 10.0 Hz, 1 H, C4H), 4.89 (t, *J* = 9.8 Hz, 1 H, C2H), 7.30 (m, 3 H, Ph), 7.50 (m, 2 H, Ph); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 26.94, 27.03, 27.06, 38.79, 38.82, 38.88, 62.21, 66.61, 67.76, 69.77, 76.88, 86.75, 128.24, 128.94, 132.27, 132.69, 176.29, 176.46, 178.01; IR (neat) 2979 (m), 2110 (s), 1738 (s), 1480 (m), 1279 (m), 1130 (s), 1038 (m); mp 139.5–141 °C; MS (FAB) 572 (M + Na, 100). Anal. Calcd for $C_{27}H_{39}N_3O_7S$: C, 59.00; H, 7.15. Found: C, 59.05; H, 7.16.

3-Azido-1,3-dideoxy-1-(phenylsulfinyl)-2,4,6-tri-*O*-(2,2-dimethylpropanoyl)-β-D-glucopyranose (33b). The sulfide **33a** (441 mg, 0.798 mmol) was dissolved in dichloromethane (3.5 mL) and cooled to −75 °C. *m*-CPBA in 1.5 mL of dichloromethane was added via cannula, and the reaction mixture was allowed to warm to room temperature over 40 min before quenching with a saturated solution of $NaHSO_3$ and $NaHCO_3$. The mixture was extracted with dichloromethane, and the organic layers were dried over anhydrous $MgSO_4$. Flash chromatography through silica gel with 10–30% ethyl acetate–hexane afforded the two sulfoxides (141 mg, 31%; 283 mg, 62%). They were each recrystallized from ethyl acetate and hexane. Minor, less polar sulfoxide: $[\alpha]^{17}_D = -92°$ (*c* 1.45, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.06, 1.22, 1.32 (s, 9 H, pivalate), 3.57 (m, 1 H, C5H), 3.75 (t, *J* = 9.9 Hz, 1 H, C3H), 3.90 (dd, *J* = 6.5, 12.4 Hz, 1 H, C6H), 4.16 (dd, *J* = 1.5, 12.4 Hz, 1 H, C6H), 4.24 (d, *J* = 9.9 Hz, 1 H, C1H), 4.86 (t, *J* = 10.0 Hz, 1 H, C4H), 5.26 (t, *J* = 9.8 Hz, 1 H, C2H), 7.53 (m, 3 H, Ph), 7.61 (m, 2 H, Ph); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 26.89, 26.92, 26.99, 38.64, 38.86, 38.98, 61.68, 66.16, 67.35, 77.75, 90.38, 125.37, 128.98, 131.56, 138.63, 176.04, 176.44, 177.86; IR (neat) 2974 (w), 2114 (m), 1733 (s), 1479 (w), 1145 (m), 1054 (w), 746 (w); mp 173.5–174.5 °C; MS (FAB) 588 (M + Na, 100). Anal. Calcd for $C_{27}H_{39}N_3O_8S$: C, 57.33; H, 6.95; N, 7.43. Found: C, 57.26; H, 6.94; N, 7.38. Major, more polar sulfoxide: $[\alpha]^{17}_D = -37°$ (*c* 1.55, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.08, 1.19, 1.32 (s, 9 H, pivalate), 3.68 (m, 1 H, C5H), 3.73 (t, *J* = 9.7 Hz, 1 H, C3H), 3.99 (dd, *J* = 4.2, 12.6 Hz, 1 H, C6H), 4.10 (dd, *J* = 1.7, 12.6 Hz, 1 H, C6H), 4.46 (d, *J* = 10.3 Hz, 1 H, C1H), 4.71 (t, *J* = 10.0 Hz, 1 H, C4H), 4.86 (t, *J* = 9.8 Hz, 1 H, C2H), 7.53 (m, 3 H, Ph), 7.75 (m, 2 H, Ph); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 26.91, 26.96, 38.77, 38.86, 39.02, 60.94, 66.53, 67.05, 68.42, 93.10, 126.58, 128.73, 131.92, 138.18, 176.6, 177.60; IR (neat) 2979 (m), 2110 (s), 1742 (s), 1480 (w), 1280 (m), 1132 (s); mp 153–155 °C; MS (FAB) 588 (M + Na, 95), 57 (^{t}Bu, 100). Anal. Calcd for $C_{27}H_{39}N_3O_8S$: C, 57.33; H, 6.95; N, 7.43. Found: C, 57.23; H, 6.99; N, 7.38.

[4*S*-[4α(*S),4aα,6β,7α,8β,8aβ]]-1-*C*-[6-[4-(Acetylamino)-2-oxo-1-(2*H*)-pyrimidinyl]-7,8-bis(acetyloxy)-4,4a,6,7,8,8a-hexahydro-2-methylpyrano[3,2-*d*][1,3]oxazin-4-yl]-1-*O*-(phenylmethyl)-2,3,4,5-tetra-*O*-acetyl-D-arabinitol (34).** To a mixture of the sulfoxide **33b** (9.7 mg, 0.017 mmol), 2,6-di-*tert*-butyl-4-methylpyridine (3.2 mg, 0.016 mmol), and triflic anhydride (0.0029 mL, 0.017 mmol) in dichloromethane (0.1 mL) was added a solution of the alcohol **29b** (5.8 mg, 0.0068 mmol) in dichloromethane (0.1 mL) at −75 °C. The mixture was allowed to warm to 0 °C over 30 min, and aqueous $NaHCO_3$ was added to stop the reaction. The mixture was extracted with dichloromethane, and the organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography with 50% ethyl acetate–hexane to 20% methanol–ethyl acetate to afford the product (5.8 mg, quant): ^1H NMR ($CDCl_3$, 500 MHz) δ 1.9–2.3 (8s, CH_3), 3.4 (t, 1 H, C4H), 3.7 (t, 1 H, C5H), 3.8 (d, 1 H, C7H), 4.1 (dd, 1 H, C11H), 4.2 (dd, 1 H, C6H), 4.3 (dd, 1 H, C11H), 4.5 (d, 1 H, CH_2Ph), 4.6 (d, 1 H, CH_2Ph), 5.1 (m, 1 H, C10H), 5.1 (t, 1 H, C3H), 5.2 (t, 1 H, C2H), 5.4 (dd, 1 H, C8H), 5.6 (dd, 1 H, C9H), 6.1 (d, 1 H, C1H), 7.4 (m), 7.7 (d, 1 H, olefinic); IR (neat) 2931 (w), 1750 (s), 1487 (m), 1372 (m), 1219 (s), 1047 (m).

***N*-[1-[2,3,8,9,10,11-Hexa-*O*-acetyl-4-azido-6-*O*-[3-azido-3-deoxy-2,4,6-tris-*O*-(2,2-dimethyl-1-oxopropyl)-β-D-glucopyranosyl]-4-deoxy-7-*O*-(phenylmethyl)-D-*glycero*-D-*galacto*-β-D-*gluco*-undecopyranosyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]acetamide (35).** To a solution of the sulfoxide **33b** (26 mg, 0.045 mmol) and 4-methyl-2,6-di-*tert*-butylpyridine (9.2 mg, 0.045 mmol) in toluene (0.2 mL) was added triflic anhydride (0.0076 mL, 0.045 mmol) at −50 °C. The mixture was allowed to warm to 0 °C. The alcohol **30b** (12 mg, 0.015 mmol) in dichloromethane (0.2 mL) was added over 2 min, and the mixture was then allowed to stir for 30 min at 0 °C. The reaction mixture was quenched with saturated $NaHCO_3$ and diluted with dichloromethane. The organic layers, from extraction with dichloromethane, were dried over anhydrous Na_2SO_4 and evaporated. The residue was purified by preparative TLC, developing twice with 85% ethyl acetate–hexane, to afford the glycoside **35** (6.9 mg, 38%) and recovered impure alcohol **30b** (4.9 mg, 41%): $[\alpha]^{20}_D = +19.8°$ (*c* 1.23, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.16, 1.22, 1.26 (s, 9 H, pivalate), 1.95, 2.00, 2.07, 2.12, 2.22 (s, 3 H, acetate), 2.00 (s, 6 H, acetate), 3.49 (t, *J* = 9.7 Hz, 1 H, C3″H), 3.73 (m, 2 H, C5′+5″H), 3.81 (dd, *J* = 5.7, 7.2 Hz, 1 H, C7′H), 3.38 (t, *J* = 10.0 Hz, 1 H, C4′H), 4.00 (dd, *J* = 4.4 Hz, 1 H, C6″H), 4.03 (dd, *J* = 5.5 Hz, 1 H, C11′H), 4.16 (m, 2 H, C6′+11′H), 4.42 (d, *J* = 12.0 Hz, 1 H, C6″H), 4.46 (d, *J* = 11.2 Hz, 1 H, CH_2Ph), 4.69 (d, *J* = 11.2 Hz, 1 H, CH_2Ph), 4.93 (d, *J* = 8 Hz, 1 H, C1″H), 4.96 (t, *J* = 8 Hz, 1 H, C2″H), 5.07 (~t, 2 H, C4″+10′H), 5.18 (m, 2 H, C2′+8′H), 5.38 (t, *J* = 9.6 Hz, 1 H, C3′H), 5.40 (dd, 1 H, C9′H), 6.00 (d, *J* = 9.3 Hz, 1 H, C1′H), 7.27 (m, 6 H, Ph+vinylic), 7.88 (d, *J* = 7.8 Hz, 1 H, vinylic), 8.59 (br s, 1 H, NH); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 20.34, 20.58, 20.62, 20.84, 24.98, 26.82, 27.03, 38.85, 38.91, 60.46, 61.36, 61.89, 65.62, 67.77, 67.86, 68.04, 68.34, 69.72, 70.28, 71.21, 73.50, 73.69, 74.97, 76.41, 78.53, 81.32, 97.38, 100.46, 128.01, 128.06, 128.46, 137.44, 144.87, 154.55, 162.52, 169.32, 169.67, 169.89, 170.15, 170.54, 176.41, 176.50, 178.02; IR (film) 2974 (w), 2110 (m), 1748 (s), 1683 (w), 1484 (w), 1370 (w), 1223 (s), 1131 (w); MS (FAB) 1294 (M + Na, 25), 91 (trop, 75), 57 (^{t}Bu, 100); HRMS (FAB) *m/z* 1294.4980 (calcd 1294.4980 for $C_{57}H_{77}N_9O_{24}$ + Na).

***N*-[1-[2,3,8,9,10,11-Hexa-*O*-acetyl-4-azido-6-*O*-[3-azido-3-deoxy-2,4,6-tris-*O*-(2,2-dimethyl-1-oxopropyl)-β-D-glucopyranosyl]-4-deoxy-D-*glycero*-D-*galacto*-β-D-*gluco*-undecopyranosyl]-1,2-dihydro-2-oxo-4-pyrimidinyl]acetamide (36a).** The benzyl ether **35** (12.3 mg, 0.0097 mmol) was stirred in dichloromethane (0.7 mL) with DDQ (22 mg, 0.097 mmol) for 43 h at 58 °C in a sealed flask. The mixture was diluted with dichloromethane and extracted with saturated $NaHCO_3$. The organic layer was dried over anhydrous Na_2SO_4, and the residue, after evaporation, was purified by preparative TLC, developing twice with 85% ethyl acetate–hexane to afford the alcohol **36a** (5.9 mg, 52%) and recovered benzyl ether **35** (2.1 mg, 17%): $[\alpha]^{23}_D = +27.7°$ (*c* 1.07, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.26, 1.28, 1.29 (s, 9 H, pivalate), 2.04, 2.08, 2.08, 2.10, 2.16, 2.24 (s, 3 H, acetate), 2.88 (br, 1 H, OH), 3.61 (t, *J* = 9.7 Hz, 1 H, C3″H), 3.64 (s, 1 H, C5′H), 3.67 (dd, *J* = 4.2, 9.9 Hz, 1 H, C5″H), 3.72 (~t, 2 H, C4′+7′H), 3.80 (dd, *J* = 2.7, 10.3 Hz, 1 H, C6′H), 3.92 (dd, *J* = 4.4, 12.5 Hz, 1 H, C6″H), 4.02 (dd, *J* = 5.3, 12.5 Hz, 1 H, C11′H), 4.24 (dd, *J* = 2.2, 12.5 Hz, 1 H, C11′H), 4.55 (d, *J* = 12.4 Hz, 1 H, C6″H), 4.88 (d, *J* = 7.9 Hz, 1 H, C1″H), 4.90 (dd, *J* = 7.9, 8.5 Hz, 1 H, C2″H), 5.04 (t, *J* = 10.0 Hz, 1 H, C4″H), 5.08 (m, 1 H, C10′H), 5.13 (d, *J* = 9.0 Hz, 1 H, C8′H), 5.23 (t, *J* = 9.3 Hz, 1 H, C2′H), 5.39 (t, *J* = 9.5 Hz, 1 H, C3′H), 5.52 (dd, *J* = 1.8, 9.4 Hz, 1 H, C9′H), 5.99 (d, *J* = 9.3 Hz, 1 H, C1′H), 7.44 (d, *J* = 7.4 Hz, 1 H, vinylic), 7.83 (d, *J* = 7.5 Hz, 1 H, vinylic), 8.92 (s, 1 H, NH); ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 20.35, 20.53, 20.64, 20.85, 20.92, 26.99, 27.03, 27.20, 38.94, 60.84, 60.95, 62.06, 65.19, 67.53, 68.04, 68.35, 68.93, 70.03, 70.31, 71.34, 73.74, 78.22, 81.64, 97.51, 101.30, 144.65, 169.23, 169.79, 170.53, 171.00, 176.34, 176.59, 178.02, 179.30; IR (film) 3322 (wb), 2975 (w), 2110 (m), 1748 (s), 1684 (w), 1487 (w), 1372 (w), 1223 (s), 1130 (m), 1057 (w); MS (FAB) 1204 (M + Na, 58), 323 (100); HRMS (FAB) *m/z* 1204.4580 (calcd 1204.4510 for $C_{50}H_{71}N_9O_{24}$ + Na).

Hikizimycin. The alcohol **36a** (10.7 mg, 0.009 05 mmol) was heated at reflux for 2 h in methanol (2 mL) with tetrabutylammonium hydroxide (0.18 mL). The mixture was passed through a weakly acidic ion-exchange resin (Amberlite CG-50) to remove the base, and the solvent was

evaporated to afford **36b**. The residue was dissolved in water (2 mL) and stirred for 30 min under a hydrogen atmosphere (1 atm) with Lindlar catalyst (50 mg). The mixture was filtered through Celite and concentrated to afford hikizimycin (5.4 mg, quant): $[\alpha]^{23}_D = -13°$ (*c* 0.53, H_2O); ^1H NMR (D_2O, 500 MHz) δ 2.65 (t, J = 9.8 Hz, 1 H, C3″H), 2.90 (t, J = 9.8 Hz, 1 H, C4′H), 3.12 (dd, J = 7.8, 10.0 Hz, 1 H, C2″H), 3.16 (t, J = 9.7 Hz, 1 H, C4″H), 3.33 (m, 1 H, C5″H), 3.40 (t, J = 9.3 Hz, 1 H, C3′H), 3.52 (dd, J = 6.2, 11.7 Hz, 1 H, C11′H), 3.61 (m, 4 H), 3.71 (dd, J = 2.6, 11.7 Hz, 1 H, C11′H), 3.77 (~d, 2 H, C5′+7′H), 3.86 (d, J = 9.8 Hz, 1 H), 4.19 (d, J = 4.4 Hz, 1 H), 4.49 (d, J = 7.8 Hz, 1 H, C1″H), 5.43 (d, J = 9.4 Hz, 1 H, C1′H), 5.94 (d, J = 7.5 Hz, 1 H, vinylic), 7.56 (d, J = 7.6 Hz, 1 H, vinylic); ^{13}C NMR (D_2O, 100.6 MHz) δ 53.14, 57.14, 60.60, 63.02, 67.59, 68.61, 68.67, 69.09, 70.60, 71.02, 72.99, 76.49, 76.90, 78.21, 79.41, 83.59, 96.62, 103.84, 141.70, 157.66, 165.73; IR (film) 2246 (br), 2925 (m), 2854 (w), 1654 (s), 1604 (m), 1497 (m), 1379 (w), 1291 (w), 1212 (w), 1074 (s), 784 (w); MS (FAB) 584 (M + 1, 5.2), 606 (M + Na, 5.8), 185 (100); HRMS (FAB) m/z 584.2432 (calcd 584.2416 for $C_{21}H_{37}N_5O_{14}$ + H).

Peracetylhikizimycin. Natural hikizimycin (0.043 g, 0.074 mmol) was stirred in acetic anhydride (0.7 mL) and pyridine (0.6 mL) containing DMAP (cat.). The mixture was allowed to stir for 6 days with occasional sonication. The mixture was evaporated, and the residue was purified by flash chromatography with ethyl acetate to 10–20% methanol–ethyl acetate to afford the peracetate (0.064 g, 77%). Synthetic hikizimycin was acetylated in a similar manner: ^1H NMR ($CDCl_3$, 250 MHz) δ 1.8–2.3 (s, CH_3), 3.7 (d, 1 H), 4.0 (m, 4 H), 4.2 (d, 1 H), 4.3 (m, 2 H), 4.7 (br, 1 H), 4.8 (t, 1 H), 4.9 (t, 1 H), 5.1 (m, 3 H), 5.3 (m, 4 H), 6.0 (d, 2 H), 6.9 (br, 1 H), 7.5 (d, 1 H), 7.9 (d, 1 H), 9.0 (br, 1 H), peak positions were variable; ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 20.12, 20.50, 20.77, 20.85, 20.94, 21.11, 22.73, 22.90, 24.76, 50.17, 53.44, 61.72, 62.10, 67.50, 67.90, 68.13, 68.40, 68.96, 70.00, 71.76, 73.01, 73.89, 74.21, 81.13, 81.31, 97.30, 101.85, 145.78, 155.01, 162.91, 169.27, 169.54, 169.86, 170.00, 170.08, 170.16, 170.36, 170.46, 171.16, 171.24; IR (neat) 3316 (br), 2986 (w), 1750 (s), 1684 (m), 1489 (m), 1372 (m), 1223 (s), 1044 (m).

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Supplementary Material Available: Spectral data of the natural and synthetic hikizimycins as well as their peracetates (5 pages). Ordering information is given on any current masthead page.

Dynamics of the Reactions of [*meso*-Tetrakis(2,6-dimethyl-3-sulfonatophenyl)porphinato]-manganese(III) Hydrate with Various Alkyl Hydroperoxides in Aqueous Solution. Product Studies and Comparison of Kinetic Parameters

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Abstract: The second-order rate constants (k_{1y}) for reactions of [*meso*-tetrakis(2,6-dimethyl-3-sulfonatophenyl)porphinato]manganese(III) hydrate [(**1**)$Mn^{III}(X)_2$, X = H_2O or HO^-] with *t*-BuOOH and (Ph)(Me)$_2$COOH have been determined in aqueous solution in the pH range 7.3–12.6. The pH dependencies of k_{1y} were fitted to a kinetic expression (eq 2) that was similar to that shown previously to describe the pH dependence of the reaction of (**1**)$Mn^{III}(X)_2$ with (Ph)$_2$(MeOCO)COOH. Comparison of the very similar pH–rate profiles for *t*-BuOOH, (Ph)(Me)$_2$COOH, and (Ph)$_2$(MeOCO)COOH (ROOH) showed that the log of the second-order rate constants exhibits only a modest dependency on the acidity of the ROH leaving group (–0.32 for the pH 7.3–10.0 range) as would be expected of a homolytic reaction. Product analysis on the reactions with *t*-BuOOH in the absence of the ABTS trapping agent provided (Me)$_2$CO (60–70%) as the major product with the remainder of the oxidant recovered as *t*-BuOH (12%), *t*-BuOOMe, (*t*-BuO)$_2$, MeOH, and HCHO. The product distributions showed no significant dependence on the pH of the reaction solutions. In the presence of ABTS (Me)$_2$CO is formed in 5% yield, and the main product is *t*-BuOH (89%). These findings are consistent with a mechanism involving the homolytic (but not heterolytic) cleavage of the O–O bond of manganese(III)-coordinated alkyl hydroperoxide. Addition of imidazole to the reaction of (**1**)$Mn^{III}(X)_2$ with *t*-BuOOH resulted in a ~4–10-fold enhancement in the rate of reaction. The pH dependence of log k_{1m} for the reaction in the presence of imidazole, from pH 5.3 to 12.6, was found to be in accord with that determined previously for (Ph)$_2$-(MeOCO)COOH. The product distribution for the reactions in the presence of imidazole showed significant dependence on the pH of the reaction mixtures. At pH 7.8 and 10.0 the product profiles were only consistent with a homolytic mechanism for the O–O bond cleavage where the major product was (Me)$_2$CO (63–67%), with the remainder being *t*-BuOH (19%), *t*-BuOOMe (13–16%), (*t*-BuO)$_2$, MeOH, and HCHO. At pH 12.6, the yield of *t*-BuOH (63%) increased dramatically with concomitant decreases in the yields of (Me)$_2$CO (34%), *t*-BuOOMe (4%), (*t*-BuO)$_2$, MeOH, and HCHO. The latter product distribution finds explanation in a change in mechanism of the O–O bond cleavage from homolysis to heterolysis as a result of the proton dissociation of the manganese(III)-coordinated ImH (i.e., (**1**)Mn^{III}(OOR)(ImH) → [(**1**)Mn^{III}(OOR)(Im)]$^-$). The acidity dependences of the 1e$^-$ oxidation and reduction potentials of (**1**)Mn^{III}(X)(ImH) have been used to determine the acid ionization constants for the mono-imidazole-ligated (**1**)$Mn^{II}(H_2O)$(ImH), (**1**)$Mn^{III}(H_2O)$(ImH), and (**1**)$Mn^{IV}(H_2O)$(ImH) species. The change in 1e$^-$ oxidation potentials with pH has also been compared to the change in rate constants with pH for reactions occurring in the presence and absence of imidazole.

Introduction

Redox reactions involving manganese are of significance in a number of biochemical systems. Manganese is known to participate in the oxidation of water to molecular oxygen in photosystem II of green plant photosynthesis[1] as well as in certain catalases,[2] peroxidases,[3] and superoxide dismutase enzymes.[4] Low molecular weight complexes of manganese have also been shown

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