Synthesis of 12 Stereochemically and Structurally Diverse C-Trisaccharides

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Cell surface carbohydrates and their analogs may be used to study the cellular interactions responsible for adhesion to pathogenic bacteria, viruses, and other cells and may represent leads for drug discovery. We have generated 12 C-trisaccharides (**7**−**18**) as potential inhibitors for the cell surface proteins of the bacterium *Helicobactor pylori*. The strategy used has resulted in the generation of C-trisaccharides structures that are represented by the formula Fuc-α(1-2)-hexose-(1-3)-GlcNAc where each of the 12 compounds possesses a central sugar that has been systematically replaced with stereochemically diverse structures, including D and L sugars, through *de novo* synthesis. This approach relies upon an organometallic coupling of terminal monosaccharides **19** and **20** to prepare a "disaccharide" in a convergent manner. This intermediate is then divergently derivatized to form a variety of structural analogs about the central hexose. For the separable compounds, the assignment of stereochemistry was done using standard NMR techniques. In cases where inseparable diastereomeric mixtures were generated, we have described a novel recursive *stereochemical* deconvolution strategy. This recursive strategy is demonstrated in the diastereoselective synthesis of trisaccharides **14**, subsequent to its initial rapid synthesis as a component of a diastereomeric mixture. Biological assays of these compounds should provide an insight into the binding requirements of carbohydrate receptors.

Introduction

Oligosaccharides on the surface of cells are responsible for many cell−cell recognition events in biological systems. These oligosaccharides are bound by receptor proteins found on the surface of various other cells, leading to adhesion.[1] The biological consequences of these events can be beneficial as in fertilization or detrimental as in bacterial[2] or viral adhesion,[3] metastasis,[4] and inflammation.[5] The development of compounds that can interrupt this process by preferentially binding to the receptors of specific carbohydrates or that can be used as molecular probes of these receptors has clear therapeutic value and has been the impetus behind the recent increase in activity in this field of research.

Our desire has been to develop synthetic strategies that will yield structurally diverse glycomimetics which may be used to examine the carbohydrate−protein interactions at the molecular level. To this end, we have demonstrated a combinatorial approach to C-glycopeptide ligands on solid support using the Ugi four-component condensation[6] as well as a synthesis of stereochemically diverse C-disaccharides[7] and C-trisaccharides[8] through solution phase chemistry, thereby generating these sugars partially *de novo*, i.e., from non-carbohydrate starting materials. In this paper we wish to elaborate on the approach we developed for the synthesis of 12 C-trisaccharide glycomimetics of the H type I blood group determinant **1** having a general stucture **2** which possesses a diverse core hexose (Figure 1). We also describe the rationale behind the development of chemical steps which alow for the identification of unknown structures through a recursive *stereochemical* deconvolution.

Background

There has been interest in translating the successes of combinatorial chemistry[9] onto carbohydrates. However, addressing the issues of carbohydrate diversity is a daunting task. Oligosaccharides derive their diversity from connectivity and stereochemistry. When these two factors are considered in a calculation of possible diastereomers of a hexose disaccharide, one arrives at over 5000 possible structures, as compared to the 8 possible diastereomers of a peptide dimer.[10] This, along with the lack of efficient, stereoselective coupling strategies, the high cost of uncommon hexoses (i.e., idose and altrose), and the need for selectively protected alcohols has limited the ability to treat sugars in a manner similar to that of peptides. As a consequence, the application of small

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(10) While only a fraction of the 5000 possible disaccharides occur in nature, the diversity pool nonetheless is of great interest.

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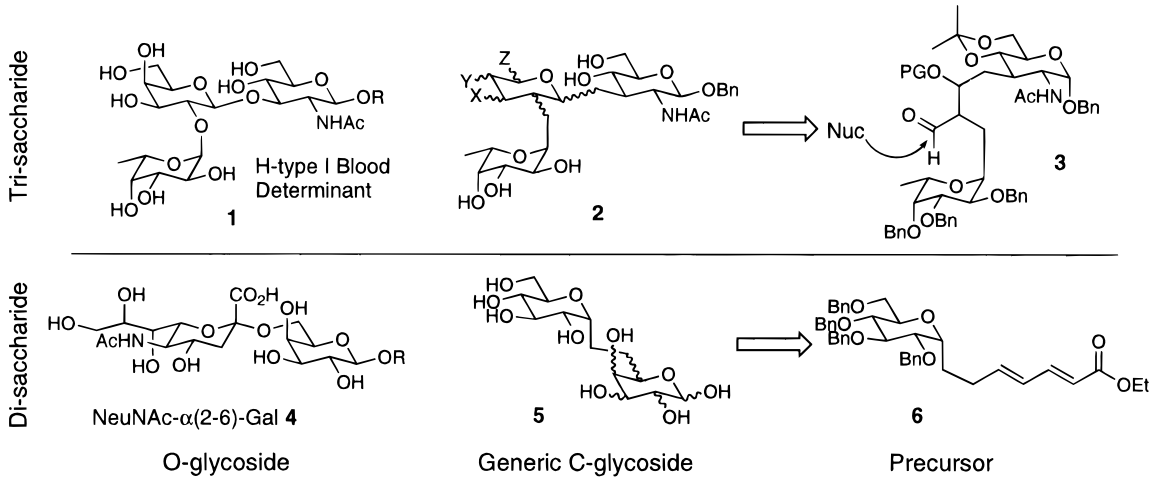

Figure 1. Retrosynthetic analysis of C-glycoside mimetics.

molecule combinatorial chemistry approaches[11] may be better suited to tackling many of the challenges that are presented by this ubiquitous class of molecules.[12]

A variety of approaches to carbohydrate diversity in drug discovery has been reported in recent years, mostly incorporating commercially available sugars as known essential recognition elements. The *de novo* synthesis of carbohydrates is another option being explored for preparing diverse carbohydrate structures which may show preferential binding over available hexoses. To put our study in perspective, the following three paragraphs serve as a brief review of the advances in the carbohydrate field which have the potential to access the immense diversity available to these biopolymers.

Using the benefits of solid phase synthesis, researchers have been successful in performing glycosylations with various sugar donors such as glycosyl halides,[13] trichloroacetimidates,[14] glycosyl sulfoxides,[15] and glycosyl sulfides[16] or through enzymatic coupling with polymer bound substrates.[17] Other methods rely on the inclusion of preformed glycosylated amino acids into automated peptide synthesis[18] and the formation of N-linked glycopeptides toward the end of the peptide synthesis using the β-glycosyl amines and activated aspartic acids.[19] Danishefsky has formed O-glycosides on solid support using the glycal technology,[20] a method which may prove to be well suited for library generation. Conceptually, this method differs from the others in that the sugars are extended at the reducing end rather than through glycosylations onto polymer bound carbohydrates. These types of methods have thus far yielded the largest numbers of compounds.[21]

Solution and solid phase synthesis has been used to generate glycomimetics of cell surface carbohydrates, the most popular target being sialyl Lewis x.[6,22] These strategies have focused on using non-carbohydrate scaffolds in conjunction with commercially available hexoses to present varied functionality not usually available from sugars. The compounds have been pursued to limit the complexity of the oligosaccharide, increase the favorable protein−ligand interaction, and increase bioavailability. While not all are combinatorial approaches, many of these examples have core structures and flexible synthe-

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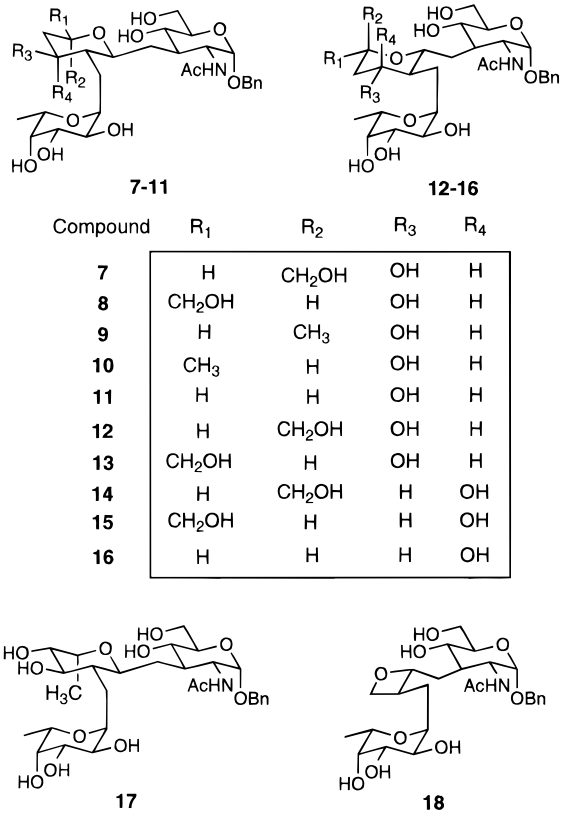
sis well-suited for combinatorial library generation. Another conceptual approach, shown by Hindsgaul, addresses the possibility of a random glycosylation on an unprotected glycoside, resulting in a statistical mix of oligosaccharides in ratios proportional to the reactivity of each available hydroxyl.[23]

Preparing diverse carbohydrates *de novo* from achiral precursors via solution or enzymatic synthesis is an attractive alternative to the above approaches.[24] These methods can allow for radically different hexose structures which may be important for protein−carbohydrate binding. As examples, the unnatural O-glycosides prepared by Lemieux[25] and Hindsgaul[26] and C-glycosides prepared by Kishi[27] show that slight modifications in structure, such as heteroatom deletion or substitution, can have large effects on binding affinities, providing valuble information about the active site of receptors and glycosyltranferases. Glucosidase inhibition by azasugars also demonstrates the necessity of introducing functionality beyond the native structure of a sugar to achieve enhanced binding affinities.[28] Most of the research in the *de novo* area has focused on monosaccharides, benefitting greatly from the increased knowledge and successes of stereoselective synthesis as well as increased understanding of enzyme systems. Wong has contributed to this area by preparing many non-natural monosaccharides with diverse functionality through an elegant combination of chemoenzymatic synthesis.[29] These approaches have yet to be applied to the generation of large numbers of compounds in a combinatorial fashion.

We have been interested in the synthesis of C-di- and C-trisaccharides in which a particular monomer of interest could be substituted with a diverse set of carbohydrates. We feel that the most efficient way to prepare these sugars with all the possible diastereomeric relationships of hydroxyl groups as well as other non-natural functional groups would be through *de novo* design. This type of approach has resulted in the synthesis of four disaccharides, Glucose-α(1-6)-D and L)-galactose and -idose, in an early report based on the general structure **5** (Figure 1). This common motif (*x*-6-linked disaccharide) exemplified in NeuNAc-α(2-6)Gal (**4**) was generated from the acyclic α,*β*-*δ*,*γ* unsaturated ester **6** via a dihydroxylation and reduction procedure. Treatment of the remaining olefin stereoisomers of **6** with the same reaction conditions would supply the remaining diastereomers.

Chart 1



Compound	R_1	R_2	R_3	R_4
7	H	CH_2OH	OH	H
8	CH_2OH	H	OH	H
9	H	CH_3	OH	H
10	CH_3	H	OH	H
11	H	H	OH	H
12	H	CH_2OH	OH	H
13	CH_2OH	H	OH	H
14	H	CH_2OH	H	OH
15	CH_2OH	H	H	OH
16	H	H	H	OH

This paper describes the generation of 11 C-trisaccharides **7**−**17** (Chart 1) having the formula Fuc-C-(1-2)-hexose-C-(1-*x*)-GlcNAc (**2**), that of the Lewis type I blood group determinant **1**, six of which were presented in a recent communication,[8] and an additional C-saccharide (**18**) containing an oxetane as a replacement for the central sugar. It was necessary that the syntheses of the compounds have as few steps as possible, be flexible in allowing different reaction conditions, and be predictable with respect to the structures' final stereochemistries.

Interest in the Lewis type I blood group determinant **1** as a recognition point for the cellular adhesion of *Helicobactor pylori* to epithelial cells in the gut of some individuals focused our synthesis of C-trisaccharides on this structure type. Our synthetic strategy is based on the C-trisaccharide **2**, a mimic of blood group determinant **1**. A vast number of candidates that would effectively model hydroxyl deletions, substitutions, and/or stereochemical inversions was considered for synthesis. Our goal was to find a lead series of compounds with biological activity rather than to prepare specific trisaccharides. We are also interested in the possibility of finding active library components which have truly novel characteristics, such as a mixed D-L-D trisaccharide. Due to an individual trisaccharide's limited probability of success in a screen, the extremely difficult synthesis required to make these complex compounds hardly justifies the effort. As a solution to this dilemma, a strategy was developed which could rapidly access C-trisaccharides in a series such as Fuc-hexose-NAcGlc through a divergent

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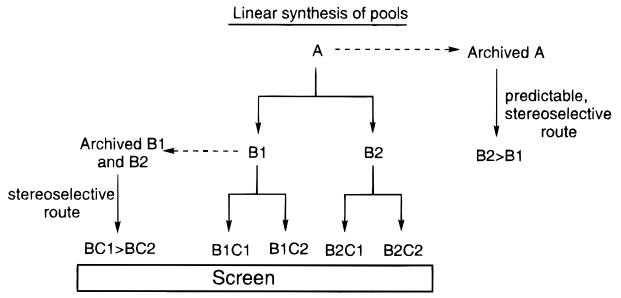

Figure 2. Schematic of the recursive strereochemical deconvolution process.

route. We planned to test compounds as diastereomeric mixtures that could later be deconvoluted to their stereochemical identity. The groundwork for this approach is presented herein, demonstrated with the use of a recursive *stereochemical* deconvolution (RSD)[30] that may be applied to the synthesis of many of these trisaccharides and possibly other natural products and their derivatives if a similar strategy is employed.[31]

This synthetic approach to C-trisaccharides coupled with a novel deconvolution strategy represents a practical method to rapidly prepare and sort unnatural C-trisaccharides via biological evaluation of diastereomeric mixtures. This strategy differs from recursive deconvolution in that the researcher is deconvoluting stereochemistry, performed through stereoselective synthesis, rather than deconvoluting structure by identifying library inputs. The absolute structure of a compound of interest can be determined via a recursive treatment of an active pool of diastereomeric mixtures through further elaboration of archived intermediates and subsequent retesting. Ideally, each transformation can be performed in a nonselective as well as a stereoselective fashion (Figure 2). In the first pass, a rapid protocol that would elicit limited selectivity would be used, creating a mixture of diastereomers. Prior to each stereogenic step, material would be archived for later use. If a pool of end product compounds is identified from a biological assay as active, then an elucidation of the absolute stereochemistry could be attempted using conventional methods (i.e., X-ray, NMR). Alternatively, previously archived material would be used to perform the second set of reliable, previously investigated stereoselective chemical steps that has an influence on the end product ratios. Comparison of the activity in the original compound pool with that of the newly synthesized, stereochemically biased compound pools would identify the absolute structure of the compound of interest. This process of rapid synthesis of compounds in diastereomer pools goes against the established paradigm of syntheses employing a high degree of stereocontrol. However, given the stereochemical complexity of these and other products, along with the particular strengths of combinatorial chemistry, this type of approach to novel therapeutics is attractive. For instance, a recent publication by Sinha and Keinan describes the synthesis of eight bis-THF acetogenin diastereomers through an approach which could be coupled with a RSD strategy to potentially reduce the number of synthetic steps.[32]

For example, reactions performed on A to generate B and then BC compounds could give results ranging from one pool of all four compounds to four separate pools with pure compounds in each pool. In the event that a pool containing B1C1 and B1C2 compounds was found to elicit interesting activity worthy of a structural determination, an archived amount of B1 could be submitted to a predictable stereoselective route that would significantly favor the formation of C1 over C2. If the stereochemically biased pool was found by a screen to be more active than the original pool, the B1C1 compound would be identified as the active component.

To apply this approach to C-trisaccharides **2**, two fixed pendant sugars were positioned at each terminus of the trisaccharide and the central core hexose was created *de novo*. Strategically, the pendant sugars identity and connectivity could be easily changed, making this a convergent approach, general for any trisaccharide of interest with C-1 and C-2 linkages. In addition, permutational alterations of the central hexose should have the most effect on the overall three-dimensional conformation of the trisaccharide. C-Glycosides were also an essential part of our overall scheme due to their resistance to both chemical and enzymatic hydrolysis.[33] In most cases this carbon for oxygen substitution has little effect on the compounds' solution conformation or binding affinity to natural ligands compared to their O-glycosidic counterparts and can be used for therapeutic applications.[27c,34]

Retrosynthetic analysis of **2** affords the complex "C-disaccharide" **3**, possessing both pendant sugars, which can be modified by the addition of a variety of nucleophiles and then converted synthetically to **2** via an intramolecular cyclization. Synthesis of compounds resembling the protected β-hydroxy aldehyde **3** required a coupling of two advanced carbohydrate intermediates, both derived from natural sugar precursors. This strategy has thus far yielded 12 trisaccharides through a rapid, convergent approach that can be applied to a variety of cell surface sugars. It is also important to note that both the central D and L sugars are synthesized with no extra synthetic effort, providing a permutation that would otherwise be financially prohibitive if natural sugar precursors were used as starting materials. First, the synthesis of six 2,4-dideoxy C-trisaccharides will be presented, and second, a variety of other C-trisaccarides will be described to highlight the flexibility of the route.

Results and Discussion

A convergent approach to the disaccharide was sought that would function as the starting point for further

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(34) (a) Nagy, J. O.; Wang, P.; Gilbert, J. H.; Schaefer, M. E.; Hill, T. G.; Callstrom, M. R.; Bednarski, M. D. *J. Med. Chem.* **1992**, *35*, 4501. (b) Bertozzi, C. R.; Cook, D. G.; Kobertz, W. R.; Gonzalez-Scarano, F.; Bednarski, M. D. *J. Am. Chem. Soc.* **1992**, *114*, 10639. (c) Bertozzi, C. R.; Bednarski, M. D. *J. Am. Chem. Soc.* **1992**, *114*, 5543. (d) Mortell, K. H.; Weatherman, R. V.; Kiessling, L. L. *J. Am. Chem. Soc.* **1996**, *118*, 2297. For exceptions, see: (e) Espinosa, J.-F.; Canada, F. J.; Asensio, J. L.; Dietrich, H.; Martin-Lomas, M.; Schmidt, R. R.; Jimenez-Barbero, J. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 303. (f) O'Leary, D. J.; Kishi, Y. *J. Org. Chem.* **1994**, *59*, 6629.

Scheme 1[a]

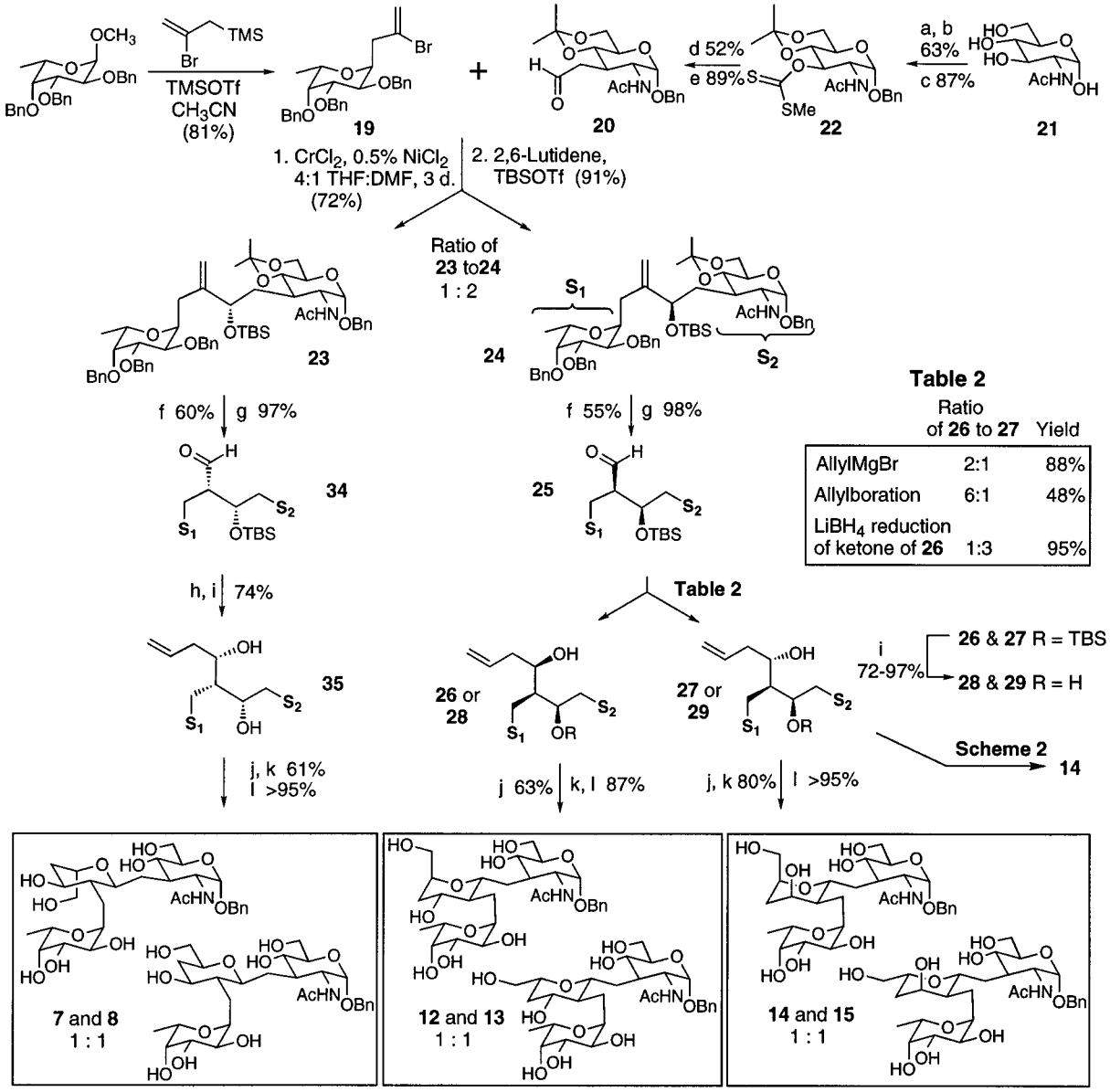


Table 2

	Ratio of **26** to **27**	Yield
AllylMgBr	2:1	88%
Allylboration	6:1	48%
$LiBH_4$ reduction of ketone of **26**	1:3	95%

[a] Reagents and conditions: (a) BnOH, AcCl; (b) 2,2-dimethoxypropane, PTSA; (c) KH, CS_2, MeI, THF; (d) allyltributyltin, AIBN, THF, 65 °C; (e) O_3, PBu_3, CH_2Cl_2, −78 °C; (f) 9-BBN, THF, 0 °C; (g) Dess−Martin periodinane, CH_2Cl_2; (h) allylmagnesium bromide, THF, −78 °C; (i) TBAF, THF, or Et_2O; (j) MCPBA, CH_2Cl_2; (k) catalytic CSA, CH_2Cl_2; (l) H_2, $Pd(OH)_2/C$, MeOH.

manipulations, eventually forming the center hexose (Scheme 1). After attempting three alternative methods for the synthesis of structure **3,** we decided to rely on the $CrCl_2/NiCl_2$ coupling[35] due to its compatibility with a large number of protecting groups, a strategy effective for Kishi in the synthesis of C-sucrose.[36] This coupling required the vinyl bromide C-fucose (Fuc) **19**[37] and the C-3-homologated acetaldehyde of *N*-acetylglucose (GlcNAc) **20**. Fucose derivative **19** was analogous to a C-glucose vinyl bromide used by Kishi in the previously mentioned report and was prepared in the same manner. GlcNAc was selectivly protected by first forming the benzyl glycoside followed by the formation of a six-membered acetonide between the C-6 and C-4 hydroxyls. This protection scheme made available the C-3 hydroxyl which could be converted smoothly to the methyl xanthate **22**. The AIBN-initiated radical allylation between the xanthate and allyltributyltin effected the essential oxygen to carbon replacement, resulting in the equatorial product exclusively. Attempts to replace the acetonide with benzyl groups in a deprotection/protection strategy to provide protecting groups identical to those used on the fucose moiety failed due to the inaccessibility of the C-4 hydroxyl under NaH/BnBr benzylation conditions. Ozonolysis of the olefin followed by reduction of the ozonide with tributylphosphine afforded the desired aldehyde **20**.

With the two modified monosaccharides in hand, we then began to investigate the organometallic coupling and subsequent conversions that would lead to aldehydes like **3**. The vinyl bromide **19** was sufficiently active in the chromium coupling, and although the reaction was slow, the excess vinyl bromide starting material was

(35) (a) Takai, K.; Kimura, K.; Kuroda, T.; Hiyama, T.; Nozaki, H. *Tetrahedron Lett.* **1983**, *24*, 5281. (b) Cintas P. *Synthesis* **1992**, 248. (c) Hashmi, A. S. K. *J. Prakt. Chem.* **1996**, *338*, 491.

(36) (a) Dyer, U. C.; Kishi, Y. *J. Org. Chem.* **1988**, *53*, 3383−3384. (b) Kishi Y. *Pure Appl. Chem.* **1992**, *64*, 343−350.

(37) Hosomi, A.; Sakata, Y.; Sakurai, H. *Tetrahedron Lett.* **1984**, *25*, 2383.

reisolated intact with little reduction of the carbon−halogen bond. This allowed an increase of the nickel chloride concentration to 0.5%, thus facilitating an efficient coupling in a diastereomeric ratio of 1:2 as determined by protection with TBSOTf, followed by separation of the corresponding silyl ether derivatives **23** and **24**. The relative and absolute stereochemistry of **23** was assigned via X-ray crystallography,[58] therefore assigning **24** by corollary (*vide infra*). We next turned our attention to the stereoselective hydroboration of the allylic TBS ethers. Our substrates were incompatible with the catecholborane or catecholborane/Wilkinson's catalyst method.[38] This prompted the use of 9-BBN to effect the stereoselective hydroboration which formed the chiral primary alcohols,[39] a strategy used by Evans in his synthesis of lonomycin A.[40] Although hydroborations on the unprotected allylic alcohols with BH_3 were successful, attempts with the TBS-protected allylic alcohol were discouraging. Oxidation of the primary alcohols following Swern conditions resulted in β-elimination whereas the Dess−Martin periodinane (DMP)[41] oxidized the alcohols smoothly in near quantitative yield, giving aldehydes **25** and **34**.

At this point we examined the nucleophilic additions necessary to complete the carbon skeleton and form the hexose core structure. Aldehyde **25** was homologated by the addition of allylmagnesium bromide to yield separable homoallylic alcohols **26** and **27** in a 2:1 ratio, respectively. The major diastereomer **26** resulted from a Felkin−Ahn addition of the nucleophile to the aldehyde. Next, routes that favor either diastereomer were investigated. This was essential to our future goal of determining an unknown structure from active compound pools via a recursive stereochemical deconvolution. Chiral allylboration[42] using the (+)-Ipc_2BOMe ligand gave the homoallylic alcohols in a 6:1 ratio, as predicted, in a 48% yield.[43] The (−)-Ipc_2BOMe ligand was unable to override the Felkin−Ahn induction. As a viable alternative, the other diastereomer could be favored by oxidizing the alcohol to the β,δ-unsaturated ketone with DMP and subsequently reducing the crude ketone with $LiBH_4$, giving a 1:3 ratio of diastereomers in 95% yield.[44] Compounds **26** and **27** were then separately desilylated with TBAF to give diols **28** and **29**, respectively. The olefin in diol **28** was oxidized with MCPBA to yield a 1:1 mixture of epoxides which was subsequently treated with CSA, resulting in six-membered ring cyclization and removal of the isopropylidene protecting group from the *N*-acetylglucosamine. Oxidation with methyl(trifluoromethyl)dioxirane also provided the epoxides in good yields.[45] Hydrogenation using H_2 with Pearlman's catalyst removed all but the anomeric benzyl group, limiting the diastereomers formed to the two C-trisaccharides **12** and **13**[46] containing the center sugar 2,4-dideoxy-L-galactose for **13** and 2,4-dideoxy-D-altrose for **12**. These sugars may alternatively be referred to as 2,4-dideoxy-L-glucose for **13** and 2,4-dideoxy-D-idose for **12** due to the lack of the hydroxyl on C-4 found in the natural hexoses. Fortunately, due to its slower rate of hydrogenation, the anomeric benzyl group was retained, simplyfing the proton NMR spectra of the end products.

Trisaccharides **14** and **15** were generated from diol **29** in a similar manner combining the epoxidation, cyclization, and deprotection in one step by adding CSA directly to the flask containing MCPBA after 16 h had elapsed. Selective deprotection of the benzyl groups on the fucose gave two trisaccharides **14** and **15** that could be separated by normal flash silica gel chromatography.[47] These two compounds have the center sugars 2,4-dideoxy-L-allose in **15** and 2,4-dideoxy-D-mannose in **14**.[48]

Aldehyde **34** was allylated, and the crude reaction mixture was treated with TBAF to remove the TBS ether, providing compound **35** as expected from Felkin−Ahn addition of the nucleophile, exclusively. The allylated precursor to **35** could be treated with the oxidation (DMP)/reduction ($LiBH_4$) procedure to obtain a 1:1 mixture of alcohol diastereomers when benzene was used as the solvent. Interestingly, the $LiBH_4$ reduction of the ketone in THF still afforded the Felkin−Ahn product as the major diastereomer, contrary to what was observed when these same procedures were performed on compounds **26** and **27**. Other reduction conditions using L-Selectride, LAH, and DIBAL-H were unsuccessful. It was not until the reduction was performed in a nonpolar solvent that the 1:1 ratio of diastereomers was obtained. Satisfied with this result, chiral allylborations were not attempted. Compound **35** was treated with the one-pot epoxidation/cyclization procedure to give two separable trisaccharides. Both compounds were selectively hydrogenated and separated to give pure C-trisaccharides **8** with 2,4-dideoxy-D-galactose as the central sugar and **7** with 2,4-dideoxy-L-altrose as the central sugar.[49,50]

(38) (a) Evans, D. A.; Fu, G. C.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1988**, *110*, 6917. (b) Evans, D. A.; Fu, G. C. *J. Org. Chem.* **1990**, *55*, 2280. (c) Burgess, K.; Donk, W. A. van der; Westcott, S. A.; Marder, T. B.; Baker, R. T.; Calabrese, J. C. *J. Am. Chem. Soc.* **1992**, *114*, 9350. (d) Burgess, K.; Ohlmeyer, M. J. *Chem. Rev.* **1991**, *91*, 1179.

(39) Since these alcohols were isolated as single diastereomers, presumably in 95% or greater de, we were inclined to assign their stereochemistry on the basis of examples at this preliminary stage. The assignment of these centers was later confirmed through proton NMR experiments performed on cyclic intermediates.

(40) Evans, D. A.; Ratz, A. M.; Huff, B. E.; Sheppard, G. S. *J. Am. Chem. Soc.* **1995**, *117*, 3448−3467.

(41) (a) Dess, D. B.; Martin, J. C. *J Org. Chem.* **1983**, *48*, 4156. (b) Ireland, R. E.; Liu, L. *J Org. Chem.* **1993**, *58*, 2899. (c) For preparation, follow Meyer, S. D.; Schreiber, S. L. *J Org. Chem.* **1994**, *59*, 7549.

(42) (a) Brown, H. C.; Jadhau, P. K. *J. Am. Chem. Soc.* **1983**, *105*, 2092. (b) Brown, H. C.; Jadhau, P. K.; Bhat, K. S. *J. Am. Chem. Soc.* **1988**, *110*, 1535. (c) Brown, H. C.; Ramachandran, P. V. *J. Organomet. Chem.* **1995**, *500*, 1.

(43) This assignment was further confirmed by NMR analysis of the tetrabenzylated **15**.

(44) Scarlato, G. R.; DeMattei, J. A.; Chong, L. S.; Ogawa, A. K.; Lin, M. R.; Armsrtong, R. W. *J. Org. Chem.* **1996**, *61*, 6139.

(45) Yang, D.; Wong, M.-K.; Yip, Y.-C. *J. Org. Chem.* **1995**, *60*, 3887.

(46) Compounds **8** and **9** could be separated via chromatography following an acetylation step.

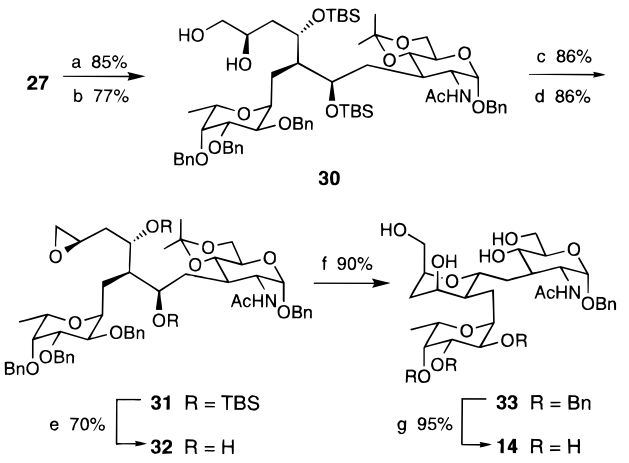
(47) Two fractions were obtained, one with 10% contamination by the other diastereomer and the other with a 15% contamination of the previous diastereomer.

(48) Or 2,4-dideoxy-L-gulose for **15** and 2,4-dideoxy-D-talose for **14**.

(49) Or 2,4-dideoxy-D-glucose for **8** and 2,4-dideoxy-L-idose for **7**.

(50) The tetrabenzylated precursors to **7** and **8** were individually analyzed via 2D COSY, 2D ROESY, and 2D HMQC to establish proton connectivity and then selectively decoupled to determine *J* values of individual resonances. This analysis resulted in the stereochemical assignment of these compounds. It was also at this point that the stereochemical outcomes of hydroboration and Felkin−Ahn addition for this series were confirmed. The stereochemistry of C-1 carbon (of the center sugar) in the precursor to **8** was known from X-ray crystallography and its proton was coupled to the C-2 proton with a large *J* value of 9.8 Hz, indicative of a trans−trans diaxial relationship. The C-3 proton was likewise coupled to C-2 with a 10.4 Hz coupling in addition to couplings with the C-4 axial proton (10.4 Hz) and to the C-4 equatorial proton (4.2 Hz). The C-4 equatorial proton, in addition to a geminal coupling to the C-4 axial proton (12.0 Hz), is weakly coupled to C-5, a pattern similar to the C-4 proton of galactose found in a previously synthesized C-1, C-2 branched C-trisaccharide (see ref 26a). The benzylated precursor to **7** was analyzed in a similar manner but was thought not to exist as a chair due to the combination of the unfavorable A 1,2 strain in the C-1 and C-2 branch points of the center sugar and the 1,3-diaxial interactions caused by C-6. This resulted in a more complicated spectrum with many small couplings between the ring protons, causing broader lines.

Scheme 2[a]

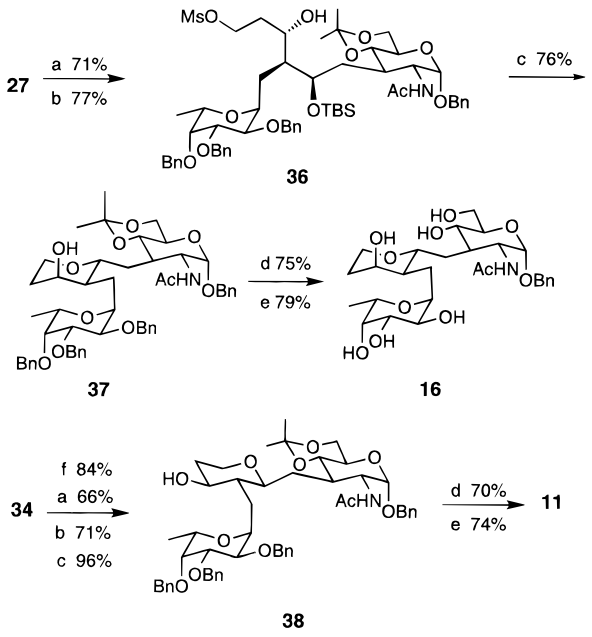


[a] Reagents and conditions: (a) 2,6-lutidene, TBSOTf; (b) OsO_4, $DHQD_2$·pyr, *t*-BuOH/H_2O, 0 °C, 5:1 diastereomers; (c) Et_3N, MsCl, CH_2Cl_2; (d) NaH, Et_2O; (e) TBAF, THF, or Et_2O; (f) catalytic CSA, CH_2Cl_2; (g) H_2, $Pd(OH)_2$/C, MeOH.

Deconvolution of the C-5 stereocenter was addressed by generating a stereochemically pure epoxide starting from the anti Felkin−Ahn product, minor diastereomer **27** (Scheme 2). After TBS protection, the disilane was submitted to Sharpless asymmetric dihydroxylation conditions,[51] generating the desired chiral diol **30**. Dihydroxylation with the DHQD ligand proceeded in good yield, providing a 5:1 ratio of separable diastereomers. The alternative DHQ ligand gave the diols in an opposite 1:2 ratio. Careful addition of 1 equiv of MsCl with excess TEA gave the primary mesylate. Base-mediated ring closure of the mesylate formed the epoxide **31**.[52] Deprotection of both TBS protecting groups gave stereochemically pure dihydroxy epoxide **32** that converged on the nonstereoselective route, using MCPBA to epoxidize compound **29**. As expected, when this diol was treated with the previous conditions of acid-catalyzed cyclization and then hydrogenation, C-trisaccharide **14** was generated as a single compound and compared spectroscopically to the two trisaccharides obtained from the previous nonstereoselective epoxidation. Only then were we able to assign the absolute stereochemistry of both separated compounds **14** and **15**. As a side note, we initially attempted this route using a benzyl-protected C-3 hydroxyl rather than the TBS used in **26**. This protection was necessary to prevent five-membered ring cyclization by this hydroxyl with the primary mesylate under the conditions of epoxide formation. All chemical steps identical to those used to prepare **32** proceeded smoothly upto the CSA cyclization step, resulting only in isolation of starting material. The cyclization of this compound was presumably hindered by the sterics of the benzyl ether protecting group, requiring the switch to the orthogonal and removable TBS protecting group.

We believe that this research can now be applied to the generation of large numbers of sugars with a central carbohydrate that is equatorially branched at C-1 and C-2 and deoxygenated at C-4 simply by incorporating pendant sugars other than Fuc and GlcNAc. A structure generated in this manner that elicits a biological response could be determined via the comparative testing of diastereomerically enriched pools of compounds, archived at each prochiral stage (i.e., **24**, **25**, and **29**). The synthesis is both convergent with respect to the pendant sugars and divergent so that modifications of steps in the later portions of the route can be used to generate a variety of alternative structures.

Scheme 3[a]



[a] Reagents and conditions: (a) O_3, $NaBH_4$, MeOH; (b) Et_3N, MsCl, CH_2Cl_2; (c) TBAF; (d) PTSA, CH_2Cl_2, MeOH; (e) $Pd(OH)_2$/C, H_2, MeOH; (f) allylmagnesium bromide.

We now wish to demonstrate the flexible nature of this strategy in the preparation of six additional hexoses. C-Glycosides **9**−**11** and **16**−**18** were targeted to complement the previously described compounds, representing further modifications of the central hexose. These derivatives were synthesized by the utilization of two different cyclization methods to make des C-6 and 6-deoxy sugars; the incorporation of an alternative nucleophile to include a hydroxyl at C-4 and cyclization prior to carbon homologation to prepare ring-contracted structures.

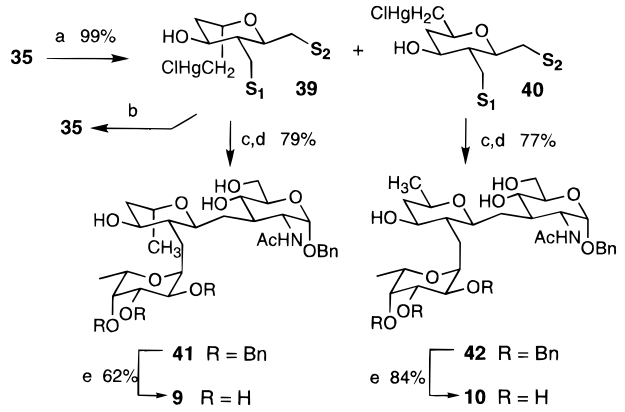
To prepare the des C-6 compounds **11** and **16**, olefin **27** was ozonized and reduced to the 1,3-diol (Scheme 3). The primary hydroxyl group was then mesylated by 1 equiv of MsCl to yield **36**. Deprotection and cyclization occurred in one pot with the addition of TBAF in THF. All that remained to be performed was the acid removal of the acetonide and benzyl hydrogenation of **37** to generate **16**. This central sugar represents the six-membered-ring pentose 2,4-dideoxy-L-ribose. Although the C-4 hydroxyl, the defining element of D or L absolute stereochemistry in five-membered sugars, has been removed, the stereochemical distiction must be made in order to establish the relative stereochemistry at C-2 and C-3. The same steps were followed to prepare compound **11**, with 2,4-dideoxy-D-xylose as the central sugar. It is important to note that compounds **37** and **38** contain a free hydroxyl which may be further functionalized via alkylation or glycosylation in order to prepare higher-order compounds.

We then focused on the C-6 deoxy sugars **9** and **10** via an alternative cyclization technique. These compounds

(51) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483.

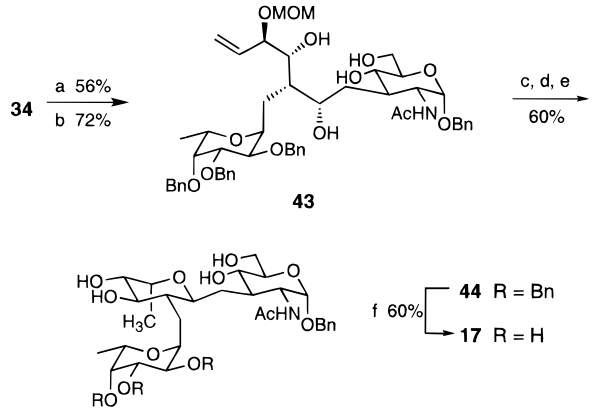
(52) Wang, Y.; Babirad, S. A.; Kishi, Y. *J. Org. Chem.* **1992**, *57*, 468−481.

Scheme 4[a]



[a] Reagents and conditions: (a) $Hg(O_2CCF_3)_2$, NaCl, THF; (b) 1 equiv of $NaBH_4$, DMF; (c) excess $NaBH_4$, DMF; (d) PTSA, CH_2Cl_2, MeOH; (e) $Pd(OH)_2/C$, H_2, MeOH.

Scheme 5[a]



[a] Reagents and conditions: (a) Brown allylboration with MOM allyl ether, (−)-Ipc_2BOMe, *t*-BuOK, *n*-BuLi, THF; (b) PTSA, CH_2Cl_2, MeOH; (c) $Hg(O_2CCF_3)_2$, NaCl, THF; (d) excess $NaBH_4$, DMF; (e) HCl, MeOH; (f) $Pd(OH)_2/C$, H_2, MeOH.

would represent an interesting permutation of the C-4 deoxy compounds **7** and **8** when compared with the des C-6, C-4 deoxy **11**. Oxymercuration−demercuration seemed to be the best route to these compounds and has been demonstrated in the literature for monosaccharides.[53] The diol **35** was intramolecularly oxymercurated with highly reactive mercury bis(trifluoroacetate) in excellent yield with no stereoselectivity observed (Scheme 4). Reductive demercurations using $NaBH_4$ on cyclic substrates of this type are typically performed with phase transfer catalysts and NaOH to discourage the reverse deoxymercuration, which would result in isolation of the ring-opened starting material used prior to mercury addition.[54] This was indeed the case when **39** was treated with 1 equiv of $NaBH_4$ in DMF, resulting in the isolation of olefin **35** as the major product However, when excess borohydride in DMF was used, reduction to the corresponding C-6 deoxy sugars occurred very smoothly to afford **41** and **42** after deprotection of the acetonide. We are presently unaware of reductive demercurations performed in DMF without NaOH, nor do we know if this represents a general method for the reduction of mercury−carbon bonds in similar systems. Compounds **41** and **42** were then fully deprotected to give the C-trisaccharide **10** with a 2,4,6-trideoxy-D-galactose center sugar and C-trisaccharide **9** with a 2,4,6-trideoxy-L-altrose center sugar, respectively. The stereochemistry of the newly formed stereogenic center was tentatively assigned through proton NMR decoupling experiments of **41** and **42**.[55]

There are many alternative nucleophiles that could be added to aldehydes **34** and **25**. Brown allylborations using a protected allylic alcohol as the carbon source would provide sugars with a C-4 hydroxyl. As an example of the progress in this area, aldehyde **34** was allylborated using MOM-protected allylalcohol and the (−)-Ipc_2BOMe chiral ligand to give **43** in reasonable yields and high enantioselectivity (Scheme 5). Allylations using THP-protected allyl alcohol occurred in unsatisfactory yields, prompting the use of the MOM-protected version. Both the TBS ether and acetonide could be removed under the mildly acidic conditions previously demonstrated. We chose to prepare a C-6 deoxy sugar and therefore added $Hg(TFA)_2$ to effect the oxymercuration. Surprisingly, the crude NMR of the product contained a single compound which was expected to have an equatorial C-6 in analogy to a literature example[53] and through a comparison of proton NMR spectra of other related examples. Following reductive demercuration using excess $NaBH_4$ in DMF and subsequent removal of the MOM protecting group under methanolic HCl conditions, compound **44** was produced. We were unable to remove the MOM protecting group with TFA or bromocatecholborane, after allylboration.[56] In both cases, the result was rapid cleaveage of the acetonide and TBS ether with the MOM group remaining. Debenzylation gave C-trisaccaride **17** with 2,6-dideoxy-L-idose as the center sugar. The stereochemistry of this ring was tentatively assigned through decoupling and NOE NMR experiments.[57]

Other nucleophiles have been investigated in our labs. Vinyl Grignard additions have been successful, more so with aldehyde **25** than **34** which gives more β-elimination, presumably due to the hard anion character at the vinyl position. One of these compounds has been converted to a furanose trisaccharide, although in poor yield. Other chiral enolate reactions can be envisioned that would provide diverse possibilities such as C-4 alkyl or amino substituents.

(53) (a) Bernotas, R. C.; Ganem, B. *Tetrahedron Lett.* **1985**, *26*, 1123. (b) Pougny, J.-R.; Nassr, M. A. M.; Sinay, P. *J. Chem. Soc., Chem. Commun.* **1981**, 375.

(54) Benhamou, M. C.; Etemad-Moghadam, G.; Speziale, V.; Lattes, A. *Synth. Commun.* **1979**, 891.

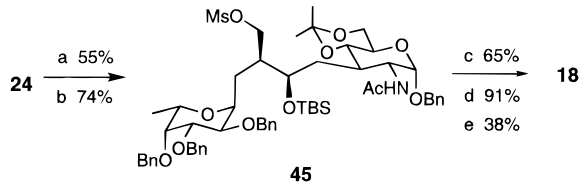
(55) For compound **41** the two methyl resonances were irradiated to identify the neighboring C-5 protons. The C-5′ proton of the central hexose was distinguished from the C-5″ proton of the of the fucose by selectively spin-saturating these resonances and looking for an effect in the upfield methylene region. Irradiation of the C-6 methyl protons of the central hexose collapsed the C-5′ resonance to a doublet of doublets having identical *J* values of 4.2 Hz. This pattern is indicative of an equatorial proton in a six-membered ring chair with two small couplings to a α methylene.

(56) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; 2nd ed.; Wiley-Interscience: New York, 1991.

(57) The C-4′, C-5′, and C-6′ protons for the central sugar were unequivocally assigned with ^1H decouplings. The C-4′ stereocenter was assumed to have an axial proton derived from the (*Z*)-boronenolate in the Brown allylboration. This was confirmed via a 9.1 Hz coupling to the C-3′ proton, also axial. Irradiation of the C-5′ proton gave an NOE with the C-6′ and C-4′ protons however, irradiation of either the C-4′ or C-6′ protons could not indicate an NOE between each other. This established a C-4′ proton to C-6′ diaxial relationship.

(58) The author has deposited atomic coordinates for structure **23** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

Scheme 6[a]



[a] Reagents and conditions: (a) 9-BBN, THF; (b) Et_3N, MsCl, CH_2Cl_2; (c) TBAF; (d) PTSA, CH_2Cl_2, MeOH; (e) $Pd(OH)_2/C$, H_2, MeOH.

Finally, we have employed the methods used to create **11** and **16** in the synthesis of a four-membered-ring hexose isostere. Despite the loss of the central sugar, alternative ring sizes can be used to examine the vectorial relationships of the C-1 and C-2 branch points by representing a distorted dihedral angle as do sugars with axial substituents at C-6 such as C-trisaccharide **7**. The alcohol resulting from the hydroboration of **24** was mesylated to yield **45**. This compound was then treated with TBAF, causing the removal of the TBS protecting group and cyclization in one step (Scheme 6). This oxetane was further deprotected to give compound **18**.

Conclusion

In conclusion, this paper presents a unique way to prepare a diverse set of C-trisaccharides in a rapid manner. In order to prepare all the possible diastereomers of a particular arrangement of functional groups using the same chemical steps, a few sacrifices were made, namely, the isolation of diastereomeric mixtures in some cases. To account for this, other reaction conditions have been developed to bias the diastereomeric mixtures so that a recursive stereochemical deconvolution procedure can be employed. This RSD strategy represents a new possibility for preparing and sorting compounds with a complex stereochemical content and may be useful for the solution phase combinatorial chemistry of these and other types of structures.

Experimental Section

General Procedures. Reactions were carried out in flame-dried glassware under an inert atmosphere of nitrogen. Solvents and reagents were distilled immediately prior to use: THF and Et_2O from sodium/benzophenone ketyl, methanol from magnesium turnings, CH_2Cl_2 from P_2O_5, and toluene from CaH_2. Anhydrous DMF, BnOH, and CH_3CN were purchased from Aldrich and used directly. The protected-sugar starting materials were azeotropically dried three times with toluene on a rotary evaporator, venting to nitrogen prior to use. All combined solvents from extractions were dried with Na_2SO_4 (except for the hydrogenation reactions), filtered, and evaporated to dryness. Thin-layer chromatography was performed on silica gel with precoated glass plates (E. Merck Brinkman, Kieselgel 60 F254, 0.25 mm) and visualized with UV light, *p*-anisaldehyde, and/or ninhydrin staining. Preparative TLC was also performed with E. Merck Brinkman plates of the appropriate thickness. Flash silica gel chromatography was performed with ICN silica, 32−63 mesh, purchased from Bodman. Columns were eluted with a linear gradient by loading the compound in CH_2Cl_2 on to silica with 100% nonpolar eluent and gradually increasing the polarity. Unless otherwise noted, columns and TLCs were eluted with hexanes and EtOAc. Crude compounds **7**−**18** were plated on a minimum amount of silica and loaded directly on the column. For these compounds IR spectra were not taken due to probable contamination with KBr, which may impede biological evaluation of them. NMR spectra were obtained on 500, 400, or 360 MHz spectrometers in $CDCl_3$, CD_3OD, or d_6-acetone. Proton and carbon spectra were referenced to residual solvent 7.26 and 77.0 ppm for chloroform, 3.3 and 49.0 ppm for methanol, and 2.3 and 29.8 ppm for acetone, respectively. For HRMS 4 ppm = $\pm 2\ \sigma$. Ozone was produced by O_2 and a Polymetrics T-816 ozone generator.

Compound 19. A solution of methyl 2,3,4-tribenzylfucoside (30.6 mg, 68.2 mmol) and 2-bromo-3-(trimethylsilyl)propene (85.2 mmol; see: Trost, B. M.; Grese, T. A.; Chan, M. T. *J. Am. Chem. Soc.* **1991**, *113*, 7350−7362 (method B) in 50 mL of CH_3CN was treated with TMSOTf (6.80 mL, 34.1 mmol). After the solution was stirred for 15 h, the reaction was quenched with 200 mL of a saturated $NaHCO_3$ solution and diluted with 200 mL of CH_2Cl_2 (TLC in 4/1 hex/EtOAc). The aqueous layer was extracted with CH_2Cl_2 (3 × 200 mL). The product was purified by chromatography to yield 30.5 g of **19** (83% yield). IR (neat): υ_{max} 2870, 1632, 1497, 1455, 1350, 1100, 1071, 735, 696 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.39 (m, 15H), 5.67 (d, 1H, J = 1.1 Hz), 5.53 (d, 1H, J = 1.5 Hz), 4.83 (d, 1H, J = 12.2 Hz), 4.79 (d, 1H, J = 12.0 Hz), 4.75 (d, 1H, J = 12.2 Hz), 4.67 (d, 1H, J = 11.9 Hz), 4.66 (d, 1H, J = 11.9 Hz), 4.57 (d, 1H, J = 11.8 Hz), 4.47 (ddd, 1H, J = 3.7, 3.7, 9.5 Hz), 4.04 (m, 1H), 3.86 (m, 3H), 2.86 (dd, 1H, J = 9.5, 15.2 Hz), 2.65 (dd, 1H, J = 3.9, 15.2 Hz), 1.42 (d, 3H, J = 6.7 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 138.6, 138.4, 137.9, 130.8, 128.3, 128.3, 128.2, 127.9, 127.8, 127.7, 127.5, 127.4, 127.4, 118.6, 76.4, 76.2, 75.4, 72.9, 72.8, 72.7, 69.0, 39.7, 14.9. HRMS (FAB): M^+ (Br 80) calcd 535.1484, found 535.1489. $[\alpha]_D$ = −37.6° (*c* 0.0127, CH_2Cl_2).

Benzyl 4,6-Isopropylidene-*N*-acetyl-α-D-glucoside. *N*-Acetyl-α-D-glucosamine (8.76 g, 39.6 mmol) was stirred overnight with 100 mL of BnOH and 2.2 mL of AcCl (30.9 mmol) at 72 °C. After cooling, the BnOH was diluted with excess Et_2O, precipitating out the benzyl glycoside as a brown solid (see: Flowers, H. M.; Shapiro, D. *J. Org. Chem.* **1965**, 2041−2043). The solid was filtered and washed with Et_2O. This crude product was combined with 200 mL of DMF and stirred for 6 h with 18 mL of 2,2-dimethoxypropane (146 mmol) and 145 mg of PTSA (0.76 mmol). Solid $NaHCO_3$ was added. After filtration and evaporation of the filtrate, chromatography was performed to isolate 8.8 g of the α-anomer (63%) and 1.8 g of the β-anomer. IR (neat): υ_{max} 3306, 2994, 2940, 1655, 1549, 1375, 1127, 1075, 737, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.28 (m, 5H), 4.83 (d, 1H, J = 11.9 Hz), 4.39 (d, 1H, J = 11.9 Hz), 4.08 (m, 1H), 3.77−3.58 (m, 5H), 1.89 (s, 3H), 1.45 (s, 3H), 1.37 (s, 3H). ^{13}C NMR (90 MHz, $CDCl_3$): δ 171.2, 136.8, 128.3, 127.9, 127.8, 99.5, 97.1, 74.3, 69.5, 63.6, 62.0, 54.0, 28.8, 18.9. HRMS (FAB): M + H calcd 352.1760, found 352.1764. $[\alpha]_D$ = +82° (*c* 0.024, $CHCl_3$).

Compound 22. Benzyl 4,6-Isopropilidene-*N*-acetyl-α-D-glucoside (8.8 g, 25.0 mmol) was dissolved in 200 mL of THF and stirred at room temperature. Deoiled KH (1.21 g, 30.1 mmol) and CS_2 (1.96 mL, 32.6 mmol) were added 45 min apart. After an 45 additional min, MeI (2 mL, 32.6 mmol) was added and the reaction was allowed to stir for another 30 min. A majority of the THF was evaporated, and the reaction was diluted with 200 mL of CH_2Cl_2, quenched with saturated NH_4Cl, and extracted with CH_2Cl_2 (3 × 200 mL); TLC in 2/1 Hex/EtOAc. Chromatography on silica gel gave 9.6 g of **22** (87%). IR (neat): υ_{max} 3304, 2996, 2946, 1669, 1516, 1374, 1198, 1117, 1051, 855 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.32 (m, 5H), 6.13 (dd, 1H, J = 9.4, 10.3 Hz), 5.92 (d, 1H, J = 9.6 Hz), 4.86 (d, 1H, J = 3.7 Hz), 4.69 (d, 1H, J = 12.0 Hz), 4.47 (d, 1H, J = 12.1 Hz), 4.43 (ddd, 1H, J = 3.8, 10.4, 10.4 Hz), 3.92 (m, 1H), 3.77 (m, 3H), 2.48 (s, 3H), 1.82 (s, 3H), 1.44 (s, 3H), 1.34 (s, 3H). ^{13}C NMR (90 MHz, $CDCl_3$): δ 217.2, 169.7, 136.4, 128.3, 128.0, 127.8, 99.6, 97.1, 78.6, 72.0, 69.6, 63.9, 62.0, 52.5, 28.7, 22.9, 18.7, 18.8. HRMS (FAB): M + H calcd 442.1358, found 442.1358.

Benzyl 3-Allyl-4,6-isopropylidene-*N*-acetyl-α-D-glucoside. The benzyl 4,6-isopropylidene-3-((methylthio)thiocarbonyl)-*N*-acetyl-α-D-glucoside (**22**) (29.0 g, 66.0 mmol), allyltributyltin hydride (50 mL), and AIBN (0.80 g, 6.6 mmol) were dissolved in 80 mL of toluene under N_2 and refluxed. After 8 h TLC showed starting material, and more AIBN was admitted to the reaction which was allowed to stir 4 h more at which

time all of the starting material had disappeared and the excess toluene was evaporated (the product has an R_f just slightly higher than the starting material in 33% EtOAc/hexanes). The crude mixture was taken up in EtOAc and brine and extracted. The product was purified by flash silica gel chromatography twice to give a yellow oil of which 11.3 g was olefinic product (46%). IR (neat): 3304, 2942, 2913, 1647, 1541, 1375, 1198, 1125, 1069, 1047 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$): δ 7.27 (m, 5H), 6.06 (d, 1H, J = 9.8 Hz), 5.81 (m, 1H), 5.16 (m, 2H), 4.70 (d, 1H, J = 3.6 Hz), 4.67 (d, 1H, J = 11.9 Hz), 4.39 (d, 1H, J = 11.9 Hz), 4.12 (m, 1H), 3.77 (m, 1H), 3.66 (m, 2H), 3.42 (dd, 1H, J = 10.1, 10.1 Hz), 2.26 (ddd, 1H, J = 4.7, 9.0, 14.0 Hz), 2.13 (dt, 1H, J = 5.2, 13.9 Hz), 1.97 (m, 1H), 1.87 (s, 3H), 1.42 (s, 3H), 1.38 (s, 3H). ^{13}C NMR (90 MHz, $CDCl_3$): δ 169.4, 137.0, 134.1, 128.2, 127.7, 127.7, 117.4, 99.1, 96.3, 70.5, 69.1, 64.6, 62.6, 49.5, 39.0, 29.6, 28.9, 22.6, 20.7, 18.7. HRMS (FAB): M + H calcd 376.2124, found 376.2115. $[\alpha]_D$ = +72.6° (*c* 0.0117, CH_2Cl_2).

Compound 20. A solution of benzyl 3-allyl-4,6-isopropylidene-*N*-acetyl-α-D-glucoside (8.6 g, 22.9 mmol) in 200 mL of CH_2Cl_2 was brought to −78 °C. Ozone was bubbled through the solution until a sky blue color persisted. After ozonide formation was complete by TLC, tributylphosphine (8.63 mL, 34.6 mmol) was added to the stirring solution, which was allowed to slowly warm to room temperature. TLC (2/1 Hex/EtOAc) confirmed conversion of ozonide to product and the solvent was evaporated. The product was purified by flash silica gel chromatography to give **20**, 6.0 g (69% yield, a higher yield of 89% was obtained on a smaller scale) of a yellow oil. IR (neat): 2940, 1723, 1661, 1539, 1373, 1267, 1202, 1136, 1076, 1042, 854, 737 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$): δ 9.58 (t, 1H, J = 1.7 Hz), 7.33 (m, 5H), 6.16 (d, 1H, J = 9.7 Hz), 4.82 (d, 1H, J = 3.6 Hz), 4.67 (d, 1H, J = 11.9 Hz), 4.42 (d, 1H, J = 11.9 Hz), 3.71 (ddd, 1H, J = 3.0, 8.1, 11.4 Hz), 4.04 (ddd, 1H, J = 2.7, 9.6, 14.5 Hz), 3.66 (m, 1H), 3.39 (dd, 1H, J = 9.1, 9.1 Hz), 2.49 (m, 1H), 2.36 (dd, 1H, J = 6.9, 11.9 Hz), 1.83 (s, 3H), 1.39 (s, 3H), 1.31 (s, 3H). ^{13}C NMR (90.5 MHz, $CDCl_3$): contaminant from triphenylphosphine oxide δ 201.2, 169.9, 136.8, 132.7, 131.9, 131.7, 131.6, 128.3, 128.3, 128.2, 127.9, 127.8, 99.4, 96.1, 72.3, 69.3, 64.9, 62.4, 51.6, 42.8, 35.9, 28.8, 22.8, 18.8. HRMS (FAB): M + H calcd 378.1917, found 378.1915. $[\alpha]_D$ = +70.8° (*c* 0.0154, CH_2Cl_2).

Compounds 23 and 24. A 0.5% $NiCl_2/CrCl_2$ mixture (300 mg, 2.4 mmol) was heated to 180 °C in a sand bath under vacuum for 3+ days. Once the mixture had turned a grayish green it was cooled and vented to N_2. A separate flask containing aldehyde **20** (150 mg, 0.4 mmol) and vinyl bromide **19** (650 mg, 1.2 mmol) was azeotroped on a high-vacuum line with distilled toluene, venting to N_2. In a glovebox, a solution of aldehyde and vinyl bromide in 3 mL of 4:1 THF:DMF was transferred to the flask containing the chromium. After 2 days all of the aldehyde had been consumed and the reaction was quenched with 10 mL of saturated NH_4Cl; TLC in 2/1 Hex/EtOAc. Extractions with EtOAc (3 × 20 mL) gave an oil that was purified by flash silica gel chromatography to give a 2:1 mixture of allylic alcohol diastereomers, 240 mg (72%). IR (neat): 3351, 2926, 1725, 1655, 1453, 1269, 1167, 1071, 713 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.29 (m, 20H), 5.09 (s, 1H), 4.95 (s, 1H), 4.91−4.42 (m, 9H), 4.23−4.05 (m, 2H), 3.89 (m, 2H), 3.79 (m, 1H), 3.71 (m, 3H), 2.34 (d, 1H, J = 5.3 Hz), 1.76 (s, 3H), 1.58 (m, 4H), 2.10−1.89 (m, 1H), 1.49 (s, 3H), 1.41 (s, 3H); major diastereomer 6.30 (d, 1H, J = 8.8 Hz), 3.40 (t, 1H, J = 3.7 Hz), 1.15 (d, 3H, J = 6.5 Hz); minor diastereomer 6.00 (d, 1H, J = 9.2 Hz), 4.80 (d, 1H, J = 3.2 Hz), 1.20 (d, 3H, J = 6.5 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 170.0, 170.5, 148.4, 148.2, 138.4, 138.4, 138.1, 137.1, 128.3, 128.2, 128.2, 128.2, 128.0, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.4, 127.4, 127.2, 127.2, 113.0, 112.5, 99.6, 99.4, 95.9, 95.9, 74.5, 73.2, 72.9, 72.8, 72.7, 72.0, 69.3, 69.2, 64.8, 64.8, 62.5, 51.6, 38.0, 35.6, 35.5, 28.9, 28.9, 22.6, 22.6, 18.9, 15.3. HRMS (FAB): M + H calcd 836.4374, found 836.4384.

To a solution of the allylic alcohol (158 mg, 0.189 mmol) in 4.5 mL of CH_2Cl_2, at 0 °C, was added 2,6-lutidine (44.0 μL, 0.379 mmol) followed by TBSOTf (53.0 μL, 0.227 mmol). After 0.5 h the reaction was warmed to room temperature and quenched with 5 mL of saturated $NaHCO_3$. Following extractions with CH_2Cl_2 (3 × 15 mL) the two diastereomers were separated on silica gel (TLC in 3/1 Hex/EtOAc) to yield a major and minor compound: total weight 162.8 mg (91%), 37.3 mg of the minor diastereomer **23** (eluted first), 18.5 mg of a mixture, and 107.0 mg of the major diastereomer **24** (eluted second). **Compound 23.** IR (neat): 2926, 2857, 1661, 1512, 1497, 1455, 1377, 1258, 1204, 1115, 1074, 698 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.30 (m, 20H), 5.69 (d, 1H, J = 8.9 Hz), 5.02 (s, 1H), 4.89 (s, 1H), 4.82 (d, 1H, J = 3.5 Hz), 4.73 (d, 1H, J = 11.9 Hz), 4.71 (d, 1H, J = 11.9 Hz), 4.67 (d, 1H, J = 12.1 Hz), 4.60 (d, 1H, J = 11.8 Hz), 4.58 (d, 1H, J = 11.8 Hz), 4.53 (d, 1H, J = 11.6 Hz), 4.42 (d, 1H, J = 11.8 Hz), 4.23 (m, 1H), 4.18 (m, 1H), 3.92 (m, 1H), 3.88−3.80 (m, 2H), 3.36 (dd, 1H, J = 9.1, 9.1 Hz), 2.31 (dd, 1H, J = 4.0, 14.5 Hz), 2.18 (dd, 1H, J = 9.3, 14.5 Hz), 2.01 (m, 1H), 1.89 (s, 3H), 1.59 (m, 1H), 1.38 (s, 3H), 1.32 (s, 3H), 0.93 (d, 3H, J = 6.4 Hz), 0.86 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 169.8, 149.5, 138.7, 138.6, 138.4, 137.4, 128.4, 128.3, 128.2, 127.9, 127.8, 127.6, 127.5, 127.5, 127.4, 110.5, 99.3, 96.5, 75.9, 75.6, 75.0, 73.0, 69.5, 68.4, 65.4, 62.8, 52.3, 36.8, 36.0, 29.1, 26.0, 23.2, 19.0, 18.1, 15.3, −4.3, −4.9. HRMS (FAB): M + H calcd 950.5239, found 950.5235. **Compound 24.** IR (neat): 2928, 1672, 1537, 1454, 1372, 1117, 1071, 698 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.35−7.15 (m, 21H), 5.02 (d, 1H, J = 1.8 Hz), 4.97 (d, 1H, J = 10.9 Hz), 4.91 (s, 1H), 4.84 (d, 1H, J = 11.9 Hz), 4.70 (m, 3H), 4.70 (m, 2H), 4.58 (d, 1H, J = 11.9 Hz), 4.46 (d, 1H, J = 10.9 Hz), 4.39 (d, 1H, J = 11.9 Hz), 4.33 (m, 1H), 4.07 (m, 1H), 3.80−3.67 (m, 6H), 3.60 (d, 1H, J = 2.4 Hz), 4.43 (dd, 1H, J = 9.5, 9.5 Hz), 2.87 (dd, 1H, J = 2.8,14.3 Hz), 2.31 (t, 1H, J = 13.2 Hz), 1.55 (s, 3H), 1.43 (s, 3H), 1.41 (s, 3H), 1.40 (m, 1H), 0.93 (d, 3H, J = 6.4 Hz), 0.87 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 170.8, 145.8, 138.8, 138.7, 138.3, 137.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.7, 127.7, 127.6, 127.5, 127.5, 127.3, 117.1, 99.0, 95.8, 79.3, 78.1, 75.5, 75.4, 75.0, 72.9, 72.8, 71.8, 69.3, 67.4, 64.8, 62.8, 51.6, 39.2, 34.5, 29.3, 28.6, 25.9, 22.0, 19.0, 18.4, 16.6, −4.9, −5.0. HRMS (FAB): M + H calcd 950.5239, found 950.5240. $[\alpha]_D$ = +25.3° (*c* 0.0119, CH_2Cl_2).

Compound 25. The TBS ether **24** (333 mg, 0.351 mmol) was dissolved in 10 mL of THF and cooled to 0 °C. A 0.5 M solution of 9-BBN in hexanes (1.75 mmol) was added dropwise, and the solution was allowed to stir for 0.5 h and then for 1 h at room temperature. The reaction was recooled to 0 °C and quenched with successive addition of 1 mL of EtOH, 4 mL of a pH 7 phosphate buffer, and 1.5 mL of 30% H_2O_2. The reaction was warmed to room temperature and stirred for 2 h at which time the flask was diluted with brine and extracted with EtOAc (3 × 30 mL). The product was purified by flash silica gel chromatography (TLC in 2/1 Hex/EtOAc) to give a yellow oil, 188 mg (55%). IR (neat): 3438, 2928, 2857, 1663, 1455, 1454, 1379, 1262, 1202, 1119, 1069, 1028, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.31 (m, 20H), 5.51 (d, 1H, J = 9.7 Hz), 4.83−4.41 (m, 10H), 4.12−3.60 (m, 14H), 3.48 (m, 2H), 3.40 (dd, 1H, J = 9.6, 9.6 Hz), 1.94 (m, 1H), 1.88 (s, 3H), 1.87−1.57 (m, 4H), 1.48(s, 3H), 1.39 (s, 3H), 1.20 (d, 3H, J = 8.5 Hz), 0.83 (s, 9H), 0.08 (s, 3H), 0.05 (s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 169.9, 138.5, 138.4, 138.1, 137.0, 128.4, 128.4, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 127.4, 127.3, 99.4, 96.2, 77.8, 76.0, 75.2, 74.8, 73.4, 73.4, 72.9, 72.8, 69.4, 64.4, 62.6, 60.3, 52.5, 36.1, 33.4, 29.0, 25.8, 25.8, 23.0, 18.9, 17.8, 17.7, 15.5, 14.1, −4.3, −4.6. HRMS (FAB): M + H calcd 968.5344, found 968.5364. $[\alpha]_D$ = +31.7° (*c* 0.0820, $CDCl_3$).

To a solution of the alcohol (17.6 mg, 0.018 mmol) in 1 mL of CH_2Cl_2 was added a freshly prepared solution of Dess−Martin periodinane (DMP, 39 mg, 0.091 mmol) in 0.5 mL of CH_2Cl_2. This solution was prepared by stirring the DMP with 0.5 mL of CH_2Cl_2 and one drop of pyridine for 20 min. The reaction was finished after 2 h and was quenched with 2 mL of 1.5 M sodium thiosulfate and 2 mL of saturated $NaHCO_3$. After the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), the product was purified on silica gel (TLC in 2/1 Hex/EtOAc) to give **25**, 16.6 mg (97%). IR (neat): 2930, 2859, 1719, 1682, 1497, 1454, 1373, 1260, 1207, 1117, 1071, 1047, 1028, 735, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 9.76 (d, 1H, J = 1.52 Hz), 7.31 (m, 20H), 5.62 (d, 1H, J = 9.6 Hz), 4.85 (d,

1H, J = 11.7 Hz), 4.72 (m, 6H), 4.60 (d, 1H, J = 11.6 Hz), 4.43 (d, 1H, J = 11.8 Hz), 4.17 (m, 4H), 3.98 (m, 1H), 2.58 (b, 1H), 2.16 (m, 1H), 1.92 (m, 1H), 1.86 (s, 3H), 1.73 (m, 1H), 1.61 (m, 2H), 1.43 (s, 3H), 1.34 (s, 3H), 1.11 (d, 3H, J = 6.3 Hz), 0.82 (s, 9H), 0.06 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 203.4, 169.9, 138.6, 138.5, 128.5, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.0, 128.0, 127.7, 127.7, 127.5, 127.5, 127.4, 99.4, 96.3, 74.9, 73.4, 72.9, 70.5, 69.5, 65.2, 62.6, 54.0, 52.0, 36.1, 29.0, 25.8, 25.7, 23.1, 18.9, 17.8, −4.2, −4.6. HRMS (FAB): M + H calcd 966.5188, found 966.5190.

Compounds 26 and 27. To a stirred solution of aldehyde **25** (41 mg, 0.043 mmol) in 1.7 mL of THF cooled to −78 °C was added a 1.0 M solution of allylmagnesium bromide (0.127 mmol, Aldrich). After 0.5 h of continued stirring, the reaction was quenched with saturated ammonium chloride and extracted with excess CH_2Cl_2. The two resultant diastereomers were separated on silica gel (TLC in 2/1 Hex/EtOAc) to yield major (**26**) and minor (**27**) compounds in a 1:2 ratio, total weight 37.3 mg (88%). **Compound 26.** IR (neat): 3449, 2924, 2857, 1742, 1684, 1530, 1456, 1377, 1350, 1254, 1115 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (m, 1H), 6.06 (d, 1H, J = 9.2 Hz), 5.82 (m, 1H), 5.06 (m, 2H), 4.85 (d, 1H, J = 11.7 Hz), 4.73−4.61 (m, 6H), 4.55 (d, 1H, J = 11.7 Hz), 4.39 (d, 1H, J = 11.8 Hz), 4.21 (m, 1H), 4.14 (m, 1H), 4.08−3.98 (m, 3H), 3.88 (b, 1H), 3.80 (dt, 2H, J = 3.0, 8.5 Hz), 3.67 (m, 4H), 3.32 (dd, 1H, J = 9.3, 9.3 Hz), 2.34 (dt, 1H, J = 7.4, 14.5 Hz), 2.15 (m, 1H), 2.04 (m, 1H), 1.84 (s, 3H), 1.77 (m, 2H), 1.68 (b, 1H), 1.61 (bd, 1H, J = 9.3 Hz), 1.48 (s, 3H), 1.42 (s, 3H), 1.04 (d, 3H, J = 6.2 Hz), 0.80 (s, 9H), 0.05 (s, 3H), −0.02 (s, 3H). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 169.9, 138.8, 138.5, 138.3, 137.0, 135.7, 128.4, 128.4, 128.2, 128.2, 128.0, 127.7, 127.6, 127.5, 127.5, 116.7, 99.7, 95.9, 78.7, 76.6, 76.3, 73.8, 73.8, 73.2, 72.9, 71.6, 69.9, 69.4, 69.3, 68.2, 65.1, 62.7, 53.5, 38.8, 36.1, 33.9, 29.2, 25.8, 22.7, 19.1, 17.7, 16.0, −3.9, −4.8. HRMS (FAB): M + H calcd 1008.5657, found 1008.5662. $[\alpha]_D$ = +24.0° (*c* 0.0095, $CDCl_3$). **Compound 27.** IR (neat): 3440, 2928, 2665, 1530, 1350, 1070, 1044, 733, 698 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 (m, 20H), 5.87 (m, 1H), 5.68 (d, 1H, J = 9.2 Hz), 5.10 (m, 2H), 4.79 (d, 1H, J = 1.6 Hz), 4.75−4.55 (m, 10H), 4.41 (d, 1H, J = 11.7 Hz), 4.10 (m, 1H), 4.02 (m, 1H), 3.92 (m, 4H), 3.84−3.68 (m, 6H), 3.43 (dd, 1H, J = 9.0, 9.0 Hz), 2.33 (m, 1H), 2.26 (m, 1H), 1.96 (m, 1H), 1.85 (m, 1H), 1.79 (s, 3H), 1.74 (m, 2H), 1.64 (br, 2H), 1.48 (s, 3H), 1.40 (s, 3H), 1.24 (d, 3H, J = 6.7 Hz), 0.82 (s, 9H), 0.05 (s, 3H), −0.01 (s, 3H). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 169.7, 138.6, 138.1, 137.3, 136.4, 128.4, 128.3, 128.3, 128.3, 128.1, 128.0, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 116.6, 99.5, 96.3, 75.0, 73.4, 73.1, 73.0, 71.4, 69.5, 68.8, 65.3, 62.7, 52.6, 38.7, 35.7, 29.2, 26.1, 26.0, 26.0, 22.9, 19.1, 17.9, 15.3, −4.1, −4.2. HRMS (FAB): M + H calcd 1008.5657, found 1008.5648.

Asymetric Route to Compound 26. (+)-Ipc$_2$BOMe (50 mg, 0.155 mmol) was dissolved in 0.5 mL of THF, and the solution was cooled to −78 °C. A 1.0 M solution of allylmagnesium bromide (0.110 mmol, Aldrich) was added slowly to the reaction. After the solution was stirred for 1 h, the cold bath was removed and the reaction was warmed to room temperature, allowed to stir for an additional 15 min, and then recooled to −78 °C. Aldehyde **25** (50 mg, 0.052 mmol) was added to 300 μL of THF. The reaction was stirred at −78 °C for 6 h and was then allowed to slowly warm to room temperature over 12 h. At this time 200 μL of 3 N NaOH and 200 μL of 30% H_2O_2 were added, and the reaction was stirred for an additional 3 h. The reaction was diluted with 5 mL of brine and extracted with CH_2Cl_2 (4 × 25 mL). The solvent was evaporated and chromatographed on silica (TLC in 2/1 Hex/EtOAc) to give 22.1 mg of a major compound (eluted first) and 3.7 mg of a minor compound (eluted second) that spectroscopically match the diastereomers created in the nonasymmetric allylation, 48% total yield.

Asymmetric Route to Compound 27. **26** (22.1 mg, 0.024 mmol) was dissolved in 0.5 mL of CH_2Cl_2, treated with a 0.5 mL solution of CH_2Cl_2 containing Dess−Martin periodinane (20 mg, 0.047 mmol), and allowed to stir for 1 h. The reaction was quenched with 3 mL of 1.5 M sodium thiosulfate and 3 mL of saturated $NaHCO_3$. After the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), the solvent was evaporated and a crude ^{1}H NMR confirmed oxidation of the homoallylic alcohol. The resultant ketone was dissolved in 900 μL of THF and treated with an excess of a 2.0 M $LiBH_4$ solution (200 μL, 0.400 mmol) at 0 °C. After TLC showed disappearance of all of the starting ketone, the reaction was quenched with 5 mL of a saturated solution of NH_4Cl and extracted with CH_2Cl_2 (4 × 20 mL). Preparatory TLC in 2/1 Hex/EtOAc was performed (20 cm × 20 cm plate, 0.25 mm thick) to yield 6.0 mg of a minor compound (eluted first) and 15.0 mg of a major compound (eluted second) that spectroscopically match the diastereomers created in the nonasymmetric allylation, 95% total yield.

Compound 28. The TBS-protected homoallylic alcohol **26** (51 mg, 0.051 mmol) in 400 μL of Et_2O was cooled to 0 °C. A 1.0 M solution of TBAF (0.100 mmol) was added and the reaction stirred for 1 h. The solvent was evaporated and the oil was purified with silica gel chromatography (TLC in 1/1 Hex/EtOAc) to yield 44 mg of **28** (97%). IR (neat): υ_{max} 3341, 2924, 1655, 1541, 1497, 1455, 1375, 1204, 1119, 1069, 1039, 698 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 (m, 20H), 6.01 (d, 1H, J = 9.2 Hz), 5.78 (m, 1H), 5.07 (m, 2H), 4.80 (d, 1H, J = 3.5 Hz), 4.78 (d, 1H, J = 12.0 Hz), 4.72 (d, 1H, J = 12.0 Hz), 4.71 (d, 1H, J = 11.6 Hz), 4.68 (d, 1H, J = 11.8 Hz), 4.65 (d, 1H, J = 11.7 Hz), 4.59 (d, 1H, J = 11.8 Hz), 4.57 (d, 1H, J = 11.6 Hz), 4.45 (d, 1H, J = 11.9 Hz), 4.15 (m, 1H), 4.05 (t, 1H, J = 6.2 Hz), 3.97 (m, 2H), 3.86 (b, 2H), 3.80 (m, 1H), 3.75 (m, 2H), 3.69 (m, 2H), 3.44 (dd, 1H, J = 9.7, 9.7 Hz), 3.38 (b, 1H), 3.29 (b, 1H), 2.29 (m, 1H), 2.13 (m, 1H), 2.03 (m, 1H), 1.87 (s, 3H), 1.75 (m, 4H), 1.53 (b, 1H), 1.42 (s, 3H), 1.32 (s, 3H), 1.21 (d, 3H, J = 6.8 Hz). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 170.1, 138.7, 138.5, 138.2, 137.2, 135.3, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 128.6, 127.5, 127.5, 117.3, 99.6, 96.3, 76.1, 74.3, 73.3, 73.0, 71.4, 70.6, 69.6, 68.4, 65.1, 62.7, 52.3, 42.1, 38.9, 36.9, 34.8, 29.7, 29.1, 23.0, 19.1, 15.6 ppm. HRMS (FAB): M + H calcd 894.4792, found 894.4810. $[\alpha]_D$ = +23.0° (*c* 0.0078, $CHCl_3$).

Compounds 12 and 13. **28** (15 mg, 0.0168 mmol) was combined with MCPBA (11.6 mg, 0.0673 mmol) and NaH_2PO_4 (16.0 mg, 0.135 mmol) in 2 mL of CH_2Cl_2, and the solution was stirred for 24 h sealed with a glass stopper. The reaction was quenched with 10 mL of brine and extracted with CH_2Cl_2 (4 × 15 mL) to yield an inseparable mixture of epoxide diastereomers that was isolated with silica gel chromatography (5% MeOH in CH_2Cl_2), 9.4 mg (63%). IR (neat): υ_{max} 3339, 2923, 2853, 1727, 1655, 1539, 1454, 1377, 1267, 1206, 1119, 1071, 1041, 735, 695 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 (m, 40H), 6.08 (d, 1H, J = 9 Hz), 6.04 (d, 1H, J = 9 Hz), 4.80−4.45 (m, 20H), 4.27 (bd, 1H), 4.22 (bd, 1H), 4.14 (m, 1H), 4.08 (m, 1H), 4.03−3.82 (m, 2H), 3.80−3.63 (m, 16H), 3.45 (dt, 3H, J = 1.8, 8.9 Hz), 3.07 (m, 2H), 2.78 (t, 1H, J = 4.7 Hz), 2.73 (t, 1H, J = 4.7 Hz), 2.51 (m, 2H), 2.05 (m, 4H), 1.89 (s, 6H), 1.42 (s, 3H), 1.32 (s, 3H), 1.25 (s, 6H), 1.25 (d, 3H, J = 5.9 Hz), 1.21 (d, 3H, J = 6.4 Hz). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 170.2, 138.6, 138.5, 138.4, 138.4, 138.2, 138.1, 137.1, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.0, 128.0, 127.9, 127.8, 127.7, 127.7, 127.5, 127.5, 127.4, 127.4, 99.6, 99.5, 96.3, 96.2, 74.3, 74.2, 73.3, 73.0, 71.2, 69.6, 69.4, 68.9, 68.7, 65.0, 65.0, 62.6, 52.0, 50.5, 50.3, 47.0, 46.6, 43.4, 42.9, 36.7, 36.6, 34.8, 29.6, 29.0, 22.9, 19.0. HRMS (FAB): M + H calcd 910.4742, found 910.4754.

The epoxide from **28** (9.3 mg, 10.2 μmol) was dissolved in 1 mL of CH_2Cl_2 and stirred overnight with CSA (1.2 mg, 5 μmol). The reaction was then quenched with 10 mL of saturated $NaHCO_3$ and extracted with CH_2Cl_2 (3 × 25 mL). The crude (9−10 mg) was taken directly on to the hydrogenation reaction listed below; TLC in 5% MeOH/CH_2Cl_2. IR (neat): υ_{max} 3403, 2925, 1656, 1528, 1350, 1047, 733, 698 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 (m, 40H), 5.61 (d, 1H, J = 9.0 Hz), 5.49 (d, 1H, J = 9.0 Hz), 4.82−4.41 (m, 18H), 4.08 (m, 1H), 4.06 (m, 1H), 3.98 (m, 5H), 3.90−3.59 (m, 19H), 3.53 (m, 2H), 3.44 (m, 1H), 3.31 (m, 1H), 2.04 (m, 4H), 1.87−1.43 (m, 12H), 1.75 (s, 3H), 1.66 (s, 3H), 1.25 (m, 6H). HRMS (FAB): $(M - C_7H_7O)^+$ calcd 762.3853, found 762.3862.

The crude from the CSA cyclization (9−10 mg) was dissolved in 2 mL of dry MeOH. This was stirred with 9 mg of $Pd(OH)_2$ on carbon under a H_2 atmosphere until all starting material

was consumed. The solvent was filtered through a bed of Celite, isolating the carbon bound $Pd(OH)_2$. The MeOH was evaporated, and the oil was chromatographed on silica gel (linear gradient 0−20% MeOH/CH_2Cl_2) to yield inseparable polyols **12** and **13**, 5.2 mg (87% from the epoxide). ^{1}H NMR (500 MHz, CD_3OD): δ 7.32 (m, 10H), 4.76 (d, 2H, J = 21.1 Hz), 4.72 (d, 1H, J = 3.0 Hz), 4.51 (d, 2H, J = 12.1 Hz), 4.09 (m, 1H), 4.03 (m, 2H), 3.97 (m, 1H), 3.92−3.73 (m, 8H), 3.68−3.59 (m, 10H), 3.55−3.44 (m, 6H), 2.24 (bt, 1H, J = 12.2 Hz), 2.15 (b, 2H), 1.95 (s, 3H), 1.95 (s, 3H), 1.87 (m, 2H), 1.81 (m, 1H), 1.74−1.57 (m, 8H), 1.53 (m, 1H), 1.48 (m, 1H), 1.22 (d, 3H, J = 6.8 Hz), 1.20 (d, 3H, J = 7.5 Hz). HMQC with a BIRD pulse (500 × 125 MHz, CD_3OD) indicates the following ^{13}C resonances: δ 129.0, 128.4, 96.2, 96.1, 80.2, 80.0, 75.2, 74.6, 74.6, 73.4, 73.0, 72.1, 71.7, 70.9, 70.8, 69.6, 69.6, 69.8, 69.5, 69.1, 68.6, 65.8, 65.8, 64.2, 64.2, 62.7, 62.7, 52.4, 52.0, 49.7, 47.8, 44.0, 39.2, 37.2, 33.2, 33.0, 32.9, 30.5, 26.1, 24.9, 24.7, 22.3, 16.1. HRMS (FAB): M + H calcd 600.3020, found 600.3020.

Compound 29. The TBS-protected homoallylic alcohol **27** (14.0 mg, 0.0139 mmol) in 0.70 mL of THF was cooled to 0 °C. A 1.0 M solution of TBAF (0.021 mmol) was added and the reaction stirred for 1 h. The solvent was evaporated, and the oil was purified with silica gel chromatography (TLC 1/1 Hex/EtOAc) to yield 9 mg of **29** (72%). IR (neat): 3425, 2924, 2855, 1659, 1653, 1539, 1497, 1454, 1377, 1265, 1206, 1118, 1072, 1042, 735, 698 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 (m, 20H), 6.06 (d, 1H, J = 9.1 Hz), 5.84 (m, 1H), 5.08 (m, 2H), 4.82 (d, 1H, J = 3.6 Hz), 4.76 (d, 1H, J = 13.0 Hz), 4.71 (d, 1H, J = 11.6 Hz), 4.67 (m, 2H), 4.63 (d, 1H, J = 11.7, Hz), 4.57 (d, 1H, J = 11.7 Hz), 4.54 (d, 1H, J = 11.8 Hz), 4.45 (d, 1H, J = 11.8 Hz), 4.06 (m, 1H), 3.92 (m, 2H), 3.80 (m, 4H), 3.71 (m, 4H), 3.45 (dd, 1H, J = 9.0, 9.0 Hz), 2.35 (m, 1H), 2.18 (m, 1H), 2.06 (m, 2H), 1.82 (s, 3H), 1.73−1.52 (m, 8H), 1.43 (s, 3H), 1.37 (s, 3H), 1.23 (d, 3H, J = 6.6 Hz). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 170.1, 138.6, 138.5, 138.2, 137.2, 135.8, 128.5, 128.4, 128.4, 128.3, 128.1, 128.1, 128.0, 127.9, 127.9, 127.6, 127.6, 127.4, 117.3, 99.7, 96.3, 75.9, 74.6, 73.4, 72.9, 72.5, 71.8, 69.6, 68.6, 65.1, 62.7, 53.4, 51.9, 45.1, 39.4, 36.9, 35.2, 29.7, 29.1, 23.0, 22.7, 19.1, 15.5, 14.1. HRMS (FAB): M + H calcd 894.4792, found 894.4789. $[\alpha]_D$ = +18.0° (c 0.005, $CHCl_3$).

Compounds 14 and 15. **29** (5.2 mg, 6.2 μmol) was dissolved in 750 μL of CH_2Cl_2 and treated with MCPBA (3 mg, 18.5 μmol) for 12 h at which time another 3 mg of MCPBA was added due to incomplete formation of product. After 12 h CSA (1.5 mg, 6.2 mmol) was added directly to the reaction mixture and allowed to stir for an additional 24 h. The reaction was quenched with 10 mL of saturated $NaHCO_3$ and extracted with EtOAc (4 × 25 mL). The C-glycosides were chromatographed by preparatory TLC (10% MeOH/CH_2Cl_2) to yield the benzylated precursors to compounds **14** and **15**, 4.3 mg (80%). IR (neat): υ_{max} 3357, 2924, 1719, 1655, 1455, 1377, 1262, 1094, 735, 698 cm^{-1}. ^{1}H NMR (500 MHz, d_6-acetone): δ 7.34 (m, 40H), 4.90−4.45 (m, 18H), 4.20−3.43 (m, 30H), 2.12 (m, 4H), 1.89 (s, 3H), 1.87 (s, 3H), 1.77−1.36 (m, 12H), 1.27 (d, 3H, J = 6.4 Hz), 1.18 (d, 3H, J = 6.4 Hz). HMQC with a BIRD pulse (500 × 125 MHz, d_6-acetone) indicates the following ^{13}C resonances: δ 137.3, 105.1, 104.9, 88.0, 86.5, 85.8, 85.7, 85.6, 85.2, 83.9, 82.7, 82.8, 81.5, 81.5, 81.5, 79.8, 79.7, 79.6, 79.3, 77.0, 76.9, 76.1, 74.6, 74.3, 74.1, 71.8, 71.8, 60.5, 59.6, 53.3, 50.3, 48.1, 44.6, 41.9, 41.8, 41.7, 38.3, 38.2, 33.3, 33.2, 31.8, 31.5, 30.4, 30.3, 25.0, 24.1. HRMS (FAB): M + H calcd 870.4428, found 870.4415.

Compounds 14 and 15. The tetrabenzylated precursors (2 mg) were dissolved in 1 mL of dry MeOH. This was stirred with 3.0 mg of $Pd(OH)_2$ on carbon under a H_2 atmosphere for 2 h. The solvent was filtered through a bed of Celite, isolating the carbon bound $Pd(OH)_2$. The MeOH was evaporated, and the oil was chromatographed on silica gel (linear gradient 0−20% MeOH/CH_2Cl_2) to yield three main fractions. Fraction 1 contains a 9:1 mixture of trisaccharide diastereomers (0.9 mg), fraction 2 an approximate equal molar mixture (0.5 mg), and fraction 3 a 1:7 mixture of diastereomers (0.5 mg). **Fraction 1, compound 14.** ^{1}H NMR (500 MHz, CD_3OD): δ 7.34 (m, 5H), 4.78 (d, 1H, J = 1.7 Hz), 4.76 (d, 1H, J = 12.3 Hz), 4.51 (d, 1H, J = 12.2 Hz), 4.11 (m, 2H), 3.98−3.86 (m, 3H), 3.83 (m, 2H), 3.74 (m, 1H), 3.71−3.60 (m, 3H), 3.56 (dd, 1H, J = 3.5, 11.4 Hz), 3.44 (dd, 1H, J = 6.8, 11.4 Hz), 1.95 (s, 3H), 1.79 (dd, 1H, J = 4.9, 15.3 Hz), 1.75 (m, 1H), 1.68 (m, 1H), 1.59 (m, 2H), 1.53 (m, 1H), 1.45 (m, 1H), 1.22 (d, 3H, J = 6.5 Hz). **Fraction 3, compound 15.** ^{1}H NMR (500 MHz, CD_3OD): δ 7.34 (m, 5H), 4.76 (d, 1H, J = 12.0 Hz), 4.71 (d, 1H, J = 3.3 Hz), 4.51 (d, 1H, J = 12.2 Hz), 4.10 (m, 2H), 3.97 (dd, 1H, J = 3.3, 12.2 Hz), 3.92 (m, 2H), 3.80 (m, 3H), 3.62 (m, 5H), 3.55 (m, 1H), 2.21 (m, 1H), 1.95 (s, 3H), 1.89 (m, 1H), 1.73 (m, 2H), 1.59 (m, 3H), 1.44 (m, 1H), 1.16 (d, 3H, J = 6.4 Hz). HMQC with a BIRD pulse (500 × 125 MHz, CD_3OD) indicates the following ^{13}C resonances: δ 129.1, 69.2, 74.4, 73.8, 71.6, 70.7, 70.5, 70.3, 69.5, 69.3, 67.8, 66.4, 66.1, 62.8, 62.7, 51.6, 41.0, 32.9, 30.3, 30.1, 22.1, 20.0, 16.6. HRMS (FAB): M + H calcd 600.3020, found 600.3021.

Compound 30. **27** (21 mg, 0.021 mmol) was dissolved in 0.5 mL of CH_2Cl_2 and cooled to 0 °C. The reaction was treated with 2,6-lutidene (10 μL, 0.084 mmol) and then with TBSOTf (12 μL, 0.050 mmol). After the solution was stirred for 0.5 h, the reaction was warmed to room temperature, quenched with 2 mL of saturated NH_4Cl, and extracted with CH_2Cl_2 (4 × 25 mL). Silica gel chromatography (TLC in 2/1 Hex/EtOAc) gave 20 mg of the bis-TBS ether (85%). IR (neat): 3353, 2928, 1682, 1456, 771, 1256, 1047 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 (m, 20H), 5.79 (m, 1H), 5.02 (d, 1H, J = 6.5 Hz), 4.97 (d, 1H, J = 10.2 Hz), 4.93 (d, 1H, J = 11.0 Hz), 4.69 (m, 5H), 4.62 (d, 1H, J = 11.6 Hz), 4.53 (d, 1H, J = 11.7 Hz), 4.39 (d, 1H, J = 11.6 Hz), 4.21 (t, 1H, J = 7.8 Hz), 4.12 (m, 2H), 3.99 (m, 2H), 3.81 (m, 3H), 3.71 (m, 4H), 3.53 (b, 1H), 3.33 (dd, 1H, J = 8.3, 8.3 Hz), 2.12 (b, 2H), 1.98 (m, 2H), 1.86 (s, 3H), 1.71 (m, 4H), 1.49 (s, 3H), 1.43 (s, 3H), 1.29 (m, 4H), 0.82 (s, 9H), 0.80 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), −0.01 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.0, 139.1, 138.6, 138.5, 137.0, 128.6, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 127.5, 127.4, 127.3, 99.7, 96.1, 74.0, 72.8, 69.5, 65.0, 62.8, 39.2, 35.6, 29.7, 29.4, 26.2, 26.0, 25.9, 22.6, 19.1, 18.0, 17.9, −3.9, −4.0, -4.0, −4.4. HRMS (FAB): M + H calcd 1122.6522, found 1122.6525. $[\alpha]_D$ = +0.5° (c 0.020, CH_2Cl_2).

The bis-TBS ether (19 mg, 0.0169) was dissolved in 300 μL of t-BuOH and 300 μL of H_2O prior to adding $K_3Fe(CN)_6$ (50 mg), K_2CO_3 (25 mg), and the chiral ligand $(DHQD)_2$·pyr (2 mg). This was stirred until a homogeneous mixture was obtained and then cooled to 0 °C. At this point, potassium osmate (0.5 mg) was added and the reaction stirred for 4 h. This was quenched with 3 mL of a saturated solution of sodium sulfite and extracted with CH_2Cl_2 (4 × 25 mL). Chromatography (TLC in 2/1 Hex/EtOAc) gave a minor (2.5 mg, eluted first) and a major compound **30** (12.5 mg, eluted second) in a 1:5 ratio; total yield 77%. IR (neat): 3387, 2928, 1680, 1522, 1456, 1381, 1258, 1209, 1048 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (m, 20H), 4.96 (d, 1H, J = 11.6 Hz), 4.77 (d, 1H, J = 11.6 Hz), 4.71 (m, 5H), 4.59 (d, 1H, J = 11.6 Hz), 4.52 (d, 1H, J = 11.7 Hz), 4.39 (d, 1H, J = 11.6 Hz), 4.29 (d, 1H, J = 8.7 Hz), 4.24 (dd, 1H, J = 5.5, 11.3 Hz), 4.18 (b, 1H), 4.11 (m, 2H), 3.80 (m, 3H), 3.68 (m, 2H), 3.60 (d, 1H, J = 6.0 Hz), 3.57 (dd, 1H, J = 3.2, 11.0 Hz), 3.49 (b, 1H), 3.35 (dd, 1H, J = 7.9, 10.9 Hz), 3.33 (m, 1H), 1.98 (m, 4H), 1.91 (s, 3H), 1.49 (s, 3H), 1.45 (s, 3H), 1.42 (m, 1H), 1.30 (m, 1H), 0.96 (d, 1H, J = 6.21 Hz), 0.82 (s, 9H), 0.81 (s, 9H), 0.15 (s, 3H), 0.06 (s, 3H), 0.02 (s, 3H), −0.02 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.1, 139.1, 138.5, 138.3, 136.9, 128.7, 128.4, 128.3, 128.2, 128.1, 128.0, 127.6, 127.6, 127.4, 99.9, 96.0, 79.8, 77.9, 75.9, 74.6, 74.3, 72.8, 70.6, 69.5, 69.4, 67.7, 67.1, 64.9, 62.8, 54.0, 53.4, 37.8, 35.8, 34.9, 29.7, 29.4, 25.9, 25.8, 22.6, 19.0, 17.9, 17.8, 16.9. HRMS (FAB): M + H calcd 1156.6577, found 1156.6577. $[\alpha]_D$ = −8.0° (c 0.012, CH_2Cl_2).

Compound 31. The bis-TBS ether diol (12.5 mg, 0.0108 mmol) was dissolved in 400 μL of CH_2Cl_2 and cooled to 0 °C. After addition of Et_3N (4 μL, 0.040 mmol) a molar solution of MsCl in CH_2Cl_2 was added in two portions until no starting material remained by TLC (0.0108 mmol). The reaction was transferred directly onto a preparatory TLC plate (eluent 2/1 Hex/EtOAc, 0.25 mm thick, 20 cm × 10 cm) to isolate 11.5 mg of the primary mesylate after elution (86%). IR (neat): 3364, 2928, 1684, 1522, 1456, 1360, 1258, 1177, 1048 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (m, 20H), 6.22 (b, 1H), 4.97 (d, 1H,

J = 11.7 Hz), 4.79 (d, 1H, J = 11.3 Hz), 4.68 (m, 5H), 4.59 (d, 1H, J = 11.6 Hz), 4.53 (d, 1H, J = 11.7 Hz), 4.39 (d, 1H, J = 11.6 Hz), 4.30 (d, 1H, J = 8.9 Hz), 4.26−4.08 (m, 5H), 4.00 (m, 2H), 3.80 (m, 2H), 3.68 (m, 2H), 3.59 (d, 1H, J = 6.0 Hz), 3.48 (b, 1H), 3.32 (dd, 1H, J = 9.0, 9.0 Hz), 3.03 (s, 3H), 2.27−1.94 (m, 5H), 1.91 (s, 3H), 1.68 (m, 2H), 1.49 (s, 3H), 1.43 (s, 3H), 0.95 (d, 3H, J = 5.8 Hz), 0.83 (s, 9H), 0.82 (s, 9H), 0.14 (s, 3H), 0.07 (s, 3H), 0.03 (s, 3H), −0.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 139.1, 138.4, 138.3, 136.9, 128.7, 128.4, 128.3, 128.2, 128.1, 128.0, 127.6, 127.4, 127.3, 99.9, 96.0, 79.9, 77.9, 77.2, 75.8, 74.6, 74.4, 72.8, 70.5, 69.5, 67.2, 66.9, 64.9, 62.8, 37.4, 37.3, 35.8, 34.9, 29.7, 29.4, 25.9, 5.8, 22.6, 19.1, 17.9, 17.8, 16.9, 14.1, −3.8, −4.0, −4.5, −4.8. HRMS (FAB): M + H calcd 1234.6352, found 1234.6375. $[\alpha]_D$ = −5.2° (*c* 0.012, CH_2Cl_2).

The primary mesylate (11.4 mg, 0.0092 mmol) was dissolved in 0.5 mL of THF, treated with deoiled NaH (2.5 mg, 0.104 mmol), and stirred for 0.5 h. TLC showed incomplete formation of product, and an additional amount of NaH was admitted to the reaction (1 mg, 0.042 mmol). After 0.5 h the reaction was quenched with 1.5 mL of saturated NH_4Cl and then with 1.5 mL of brine. The reaction was extracted with CH_2Cl_2 (3 × 25 mL) and submitted to silica gel chromatography (TLC in 2/1 Hex/EtOAc) to yield 9.0 mg of the epoxide **31** (86%). IR (neat): 3355, 2928, 1682, 1512, 1456, 1372, 1258, 1047 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 (m, 20H), 6.29 (b, 1H), 4.96 (d, 1H, J = 11.6 Hz), 4.77 (d, 1H, J = 11.5 Hz), 4.74 (d, 1H, J = 11.9 Hz), 4.69 (m, 3H), 4.59 (d, 1H, J = 11.6 Hz), 4.52 (d, 1H, J = 11.7 Hz), 4.38 (d, 1H, J = 11.7 Hz), 4.26 (m, 1H), 4.21 (dd, 1H, J = 5.6, 11.4 Hz), 4.13 (m, 3H), 3.80 (m, 2H), 3.69 (m, 2H), 3.61 (m, 1H), 3.48 (b, 1H), 3.32 (dd, 1H, J = 9.1, 9.1 Hz), 2.92 (m, 1H), 2.74 (dd, 1H, J = 4.0, 5.1 Hz), 2.41 (d, 1H, J = 2.7, 5.2 Hz), 2.20 (b, 1H), 2.00 (m, 3H), 1.90 (s, 3H), 1.70 (m, 4H), 1.50 (s, 3H), 1.47 (s, 3H), 0.95 (d, 3H, J = 4 Hz), 0.83 (s, 9H), 0.79 (s, 9H), 0.11 (s, 3H), 0.08 (s, 3H), 0.01 (s, 3H), −0.04 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.1, 139.1, 138.5, 138.4, 137.0, 128.7, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.6, 127.6, 127.5, 127.3, 99.9, 96.0, 79.8, 77.9, 75.9, 74.6, 74.2, 72.7, 70.6, 69.4, 67.2, 64.9, 62.8, 50.6, 48.1, 37.7, 35.8, 35.0, 29.7, 29.4, 25.9, 25.8, 22.7, 22.6, 19.0, 17.9, 17.9, 16.9, 14.1, −3.8, −3.9, −4.7, −4.7. HRMS (FAB): M + H calcd 1138.6471, found 1138.6469. $[\alpha]_D$ = −8.9° (*c* 0.090, CH_2Cl_2).

Compound 32. The TBS-protected epoxide **31** (8.9 mg, 0.0078 mmol) was dissolved in 400 μL of THF and treated with a 1.0 M solution of TBAF in THF (0.027 mmol). After 1 h the reaction was quenched with 4 mL of brine and extracted with CH_2Cl_2 (4 × 25 mL). Chromatography using preparatory TLC (eluent 1/2 hex/EtOAc, 0.25 mm thick, 20 cm × 10 cm) yielded 5 mg of the epoxide diol **32** (70%). IR (neat): 3416, 2924, 1655, 1541, 1454, 1375, 1070 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 (m, 20H), 6.07 (d, 1H, J = 9.2 Hz), 4.81 (d, 1H, J = 3.5 Hz), 7.74 (d, 1H, J = 11.8 Hz), 4.73 (d, 1H, J = 11.9 Hz), 4.70−4.60 (m, 5H), 4.56 (d, 1H, J = 11.7 Hz), 4.06 (m, 1H), 3.97 (m, 4H), 3.80−3.65 (m, 10H), 3.45 (dd, 1H, J = 9.1, 9.1 Hz), 3.14 (m, 1H), 2.79 (dd, 1H, J = 4.7, 4.7 Hz), 2.53 (dd, 1H, J = 2.8, 4.8 Hz), 2.05 (m, 2H), 1.83 (s, 3H), 1.68 (m, 2H), 1.61 (m, 1H), 1.52 (m, 2H), 1.43 (s, 3H), 1.35 (s, 3H), 1.26 (b, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.2, 138.6, 138.4, 138.1, 137.2, 128.5, 28.4, 128.4, 128.3, 128.1, 128.0, 127.9, 127.6, 127.6, 127.5, 99.7, 96.3, 75.7, 74.5, 73.3, 73.2, 73.0, 71.6, 70.3, 69.6, 68.8, 65.0, 62.7, 51.8, 50.7, 47.3, 46.4, 37.2, 36.9, 34.8, 29.7, 29.1, 23.0, 19.1. HRMS (FAB): M + H calcd 910.4742, found 910.4753. $[\alpha]_D$ = +18° (*c* 0.005, CH_2Cl_2).

Compound 33. The epoxide diol (4.9 mg, 0.0054 mmol) was dissolved in 400 μL of CH_2Cl_2 and treated with a catalytic amount of CSA (<1 mg). After the solution was stirred for 5 h the reaction was transferred directly onto a preparatory TLC plate (0.25 mm thick, 20 cm × 10 cm) to isolate 4.2 mg of **33** after elution (5% MeOH in CH_2Cl_2, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (m, 20H), 5.81 (d, 1H, J = 9.6 Hz), 4.78 (d, 1H, J = 3.5 Hz), 4.76 (d, 1H, J = 11.8 Hz), 4.70 (d, 1H, J = 11.8 Hz), 4.68 (d, 1H, J = 11.8 Hz), 4.59 (d, 1H, J = 11.9 Hz), 4.57 (d, 1H, J = 11.8 Hz), 4.55 (d, 1H, J = 11.8 Hz), 4.48 (d, 1H, J = 12.1 Hz), 4.45 (d, 1H, J = 11.9 Hz), 4.11 (m, 1H), 4.03 (dd, 1H, J = 3.2, 6.2 Hz), 3.96 (m, 3H), 3.82 (dd, 1H, J = 3.9, 13.0 Hz), 3.76 (m, 1H), 3.72 (m, 5H), 3.61 (dd, 1H, J = 2.6, 11.6 Hz), 3.55 (dd, 1H, J = 9.8, 9.8 Hz), 3.46 (dd, 1H, J = 7.8, 11.8 Hz), 2.03 (m, 1H), 1.77 (s, 3H), 1.68 (m, 4H), 1.44 (m, 4H), 1.28 (d, 3H, J = 6.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.0, 138.5, 138.3, 138.0, 137.3, 128.5, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9, 127.7, 127.4, 96.0, 73.9, 73.3, 73.1, 72.8, 72.7, 72.3, 69.7, 69.4, 68.9, 66.0, 64.5, 62.7, 50.5, 43.7, 39.1, 34.3, 31.3, 29.7, 23.0, 14.1.

Compound 14. Compound **33** (4.2 mg, 0.0048 mmol) was dissolved in 2 mL of dry MeOH. This was stirred with 8 mg of $Pd(OH)_2$ on carbon under a H_2 atmosphere until all starting material was consumed. The solvent was filtered through a bed of Celite, isolating the carbon bound $Pd(OH)_2$. The MeOH was evaporated, and the oil was chromatographed on silica gel (linear gradient 0−20% MeOH/CH_2Cl_2) to yield compound **14** as a pure diastereomer, 2.2 mg (76% yield). ^{1}H NMR (500 MHz, CD_3OD): δ 7.38 (d, 2H, J = 7.0 Hz), 7.33 (dd, 2H, J = 7.2, 7.7 Hz), 7.26 (d, 1H, J = 12.0 Hz), 4.78 (d, 1H, J = 3.2 Hz), 4.76 (d, 1H, J = 12.0 Hz), 4.51 (d, 1H, J = 12.0 Hz), 4.11 (m, 1H), 4.00−3.63 (m, 10H), 3.56 (m, 1H), 3.43 (m, 2H), 2.15 (m, 1H), 1.95 (s, 3H), 1.79 (dd, 1H, J = 5.5, 13.7 Hz), 1.73 (m, 1H), 1.67 (m, 1H), 1.61−1.47 (m, 4H), 1.22 (d, 3H, J = 6.5 Hz). HMQC with a BIRD pulse (500 × 125 MHz, CD_3OD) indicates the following ^{13}C resonances: δ 129.0, 128.7, 128.4, 96.2, 75.9, 75.7, 74.4, 73.1, 71.8, 70.9, 69.4, 69.3, 66.8, 66.0, 66.0, 62.6, 62.6, 52.8, 44.9, 39.0, 36.3, 33.4, 30.4, 22.6, 22.5, 22.3, 15.9. HRMS (FAB): M + H calcd 600.3020, found 600.3018. $[\alpha]_D$ = +43° (*c* 0.0019, MeOH).

Compound 34. The TBS ether **23** (2.0 g, 2.1 mmol) was dissolved in 40 mL of THF and cooled to 0 °C. A 0.5 M solution of 9-BBN in hexanes (8.0 mmol) was added dropwise, and the solution was allowed to stir for 0.5 h at 0 °C and then for 0.5 h at room temperature. The reaction was recooled to 0 °C and quenched with successive addition of 8 mL of EtOH, 16 mL of a pH 7 phosphate buffer, 3 mL of 3 N NaOH, and 3 mL of 30% H_2O_2. The reaction stirred for 15 min at 0 °C, warmed to room temperature, and stirred for 0.5 h at which time the flask was diluted with 50 mL of brine, 50 mL of saturated NH_4Cl, and 100 mL of EtOAc and stirred for 40 min. The reaction was extracted with EtOAc (3 × 100 mL). The product was purified by flash silica gel chromatography (TLC in 2/1 Hex/EtOAc) to give a yellow oil, 1.2 g (60%). IR (neat): 3308, 2930, 1662, 1653, 1539, 1455, 1373, 1253, 1205, 1070, 837, 735, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (m, 20H), 5.87 (d, 1H, J = 9.8 Hz), 4.78 (d, 1H, J = 11.8 Hz), 4.72 (m, 4H), 4.68 (d, 1H, J = 11.8 Hz), 4.62 (d, 1H, J = 11.9 Hz), 4.61 (d, 1H, J = 11.8 Hz), 4.57 (d, 1H, J = 11.7 Hz), 4.45 (d, 1H, J = 11.8 Hz), 4.27 (dt, 1H, J = 3.6, 11.7 Hz), 4.00 (m, 2H), 3.90 (m, 1H), 3.85−3.58 (m, 9H), 3.43 (t, 1H, J = 9.6 Hz), 1.93 (m, 1H), 1.94 (s, 3H), 1.83 (m, 1H), 1.74−1.44 (m, 4H), 1.50 (s, 3H), 1.33 (s, 3H), 1.20 (d, 3H, J = 6.6 Hz), 0.86 (s, 9H), 0.07 (s, 3H), 0.03 (s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 170.3, 138.6, 138.5, 138.4, 137.0, 128.5, 128.3, 128.2, 128.2, 128.2, 128.1, 128.1, 127.8, 127.6, 127.6, 127.5, 127.5, 99.2, 96.2, 77.4, 76.7, 75.6, 73.4, 72.9, 69.6, 68.1, 65.1, 62.5, 59.7, 51.4, 37.2, 36.2, 36.1, 35.7, 31.0, 29.2, 25.8, 23.1, 19.0, 17.8, 15.6, −4.1, −4.9. HRMS (FAB): M + H calcd 968.5344, found 968.5359. $[\alpha]_D$ = +13.8° (*c* 0.0474, $CHCl_3$).

To a solution of alcohol (1.08 g, 1.24 mmol) in 20 mL of CH_2Cl_2 was added a freshly prepared solution of Dess−Martin periodinane (DMP, 710 mg, 1.67 mmol) in 20 mL of CH_2Cl_2. This solution was prepared by stirring the DMP with 20 mL of CH_2Cl_2 for 20 min. The reaction was opened to the atmosphere for 30 min, and then 10 mL of undistilled CH_2Cl_2 was added. After an additional 1 h of stirring the reaction was quenched with 25 mL of 1.5 M sodium thiosulfate and 25 mL of saturated $NaHCO_3$. After the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL), the product was purified on silica gel (TLC in 2/1 Hex/EtOAc) to give **34** 1.05 g (97%). IR (neat): 3272, 2929, 1717, 1652, 1539, 1516, 1455, 1373, 1308, 1265, 1204, 1074, 837, 734, 698 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.62 (d, 1H, J = 3.7 Hz), 7.33 (m, 20H), 5.86 (d, 1H, J = 9 Hz), 4.76−4.45 (m, 7H), 4.59 (d, 1H, J = 11.6 Hz), 4.54 (d, 1H, J = 11.6 Hz), 4.48 (d, 1H, J = 12.0 Hz), 4.13 (m, 1H), 3.95 (m, 2H), 3.85 (br, 1H), 3.75 (m, 3H), 3.66 (m, 2H), 3.41 (dd, 1H, J = 9.6, 9.6 Hz), 2.56 (m, 1H), 2.16 (ddd,

1H, J = 3.1, 11.7, 14.2 Hz), 1.94 (s, 3H), 1.80 (q, 1H, J = 10.5 Hz), 1.73 (m, 1H), 1.68 (m, 1H), 1.49 (s, 3H), 1.46 (m, 1H), 1.36 (s, 3H), 1.23 (d, 3H, J = 6.6 Hz), 0.87 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 206.6, 170.5, 138.6, 138.5, 138.1, 137.2, 128.5, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 99.2, 96.1, 75.9, 74.0, 73.0, 72.9, 69.4, 68.5, 65.0, 62.5, 53.4, 51.5, 50.6, 36.8, 36.1, 29.2, 25.8, 23.0, 19.0, 17.9, −4.1, −4.9. HRMS (FAB): M + H calcd 966.5188, found 966.5187. $[\alpha]_D$ = +28.5° (c 0.0332, $CHCl_3$).

Compound 35. To a stirred solution of aldehyde **35** (40 mg, 0.0415 mmol) in 2 mL of THF, cooled to 0 °C, was added a 1.0 M solution of allylmagnesium bromide (0.125 mmol, Aldrich). After 30 min of continued stirring the reaction was quenched with saturated NH_4Cl and extracted with CH_2Cl_2. The crude reaction mixture, showing only one spot by TLC (2/1 Hex/EtOAc), was dissolved in 2 mL of THF and treated with 1 M TBAF (0.0415 mmol) at 0 °C. After 2 h the reaction was quenched with 2 mL of a saturated solution of NH_4Cl and 2 mL of H_2O and extracted with EtOAc. Silica gel chromatography isolated the major compound **35**, 18.2 mg (50%). IR (neat): 3416, 2924, 1659, 1537, 1497, 1454, 1373, 1206, 1119, 1072, 1028, 735, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): contaminated with ethyl acetate δ 7.31 (m, 20H), 5.80 (m, 1H), 5.17 (d, 1H, J = 9.8 Hz), 5.04 (m, 2H), 4.83−4.64 (m, 7H), 4.60 (d, 1H, J = 11.8 Hz), 4.56 (d, 1H, J = 11.8 Hz), 4.45 (d, 1H, J = 11.8 Hz), 4.13−3.70 (m, 11H), 3.50 (dd, 1H, J = 9.0, 9.0 Hz), 2.31 (m, 1H), 2.13 (m, 1H), 1.85 (m, 1H), 1.84 (s, 3H), 1.82 (m, 2H), 1.49 (s, 3H), 1.34 (s, 3H), 1.30 (m, 1H), 1.20 (d, 3H, J = 6.5 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 170.5, 138.9, 138.6, 138.5, 137.0, 135.8, 128.7, 128.4, 128.3, 128.3, 128.1, 127.9, 127.7, 127.6, 127.5, 127.4, 116.8, 100.0, 96.3, 77.4, 77.3, 76.5, 73.7, 73.3, 73.3, 73.1, 71.1, 69.6, 68.1, 65.2, 62.6, 51.5, 46.0, 40.8, 38.7, 34.6, 29.0, 23.2, 21.1, 19.2, 16.0, 14.2. HRMS (FAB): M + H calcd 894.4792, found 894.4800. $[\alpha]_D$ = +20.9° (c 0.0091, $CHCl_3$).

Tetrabenzylated C-Trisaccharide Precursors of 7 and 8. **35** (82.0 mg, 0.092 mmol) was dissolved in 1 mL of CH_2Cl_2 and treated with MCPBA (45 mg, 0.261) for 4 h. Upon completion of the epoxidation, catlytic CSA (1.0 mg) was added directly to the reaction mixture and allowed to stir for an additional 15 h. The C-glycosides were separated by preparatory TLC (5% MeOH/CH_2Cl_2) to yield the benzylated precursors to compound **8**, 25.0 mg (top band), and precursor to **7**, 24.0 mg (bottom band); total yield 61%. **Tetrabenzyl Precursor to 8.** IR (neat): υ_{max} 3359, 2923, 1717, 1653, 1455, 1377, 1260, 1049, 735, 698 cm^{-1}. ^{1}H NMR (500 MHz, d_6-acetone): δ 7.30 (m, 20H), 4.85 (d, 1H, J = 11.5 Hz), 4.79 (s, 2H), 4.75 (d, 1H, J = 12.1 Hz), 4.73 (d, 1H, J = 11.5 Hz), 4.70 (d, 1H, J = 3.4 Hz), 4.60 (d, 1H, J = 11.5 Hz), 4.59 (d, 1H, J = 11.6 Hz), 4.47 (d, 1H, J = 12.1 Hz), 4.18 (m, 1H), 3.96 (m, 1H), 3.94 (m, 1H), 3.85 (m, 1H), 3.82 (m, 1H), 3.80 (m, 1H), 3.69−3.61 (m, 4H), 3.47−3.32 (m, 5H), 2.14 (dd, 1H, J = 3.3, 14.5 Hz), 2.07 (m, 1H), 1.89 (m, 3H), 2.05 (s, 3H), 1.79 (dd, 1H, J = 4.0, 11.7 Hz), 1.69 (ddd, 1H, J = 2.6, 6.4, 14.9 Hz), 1.58 (m, 2H), 1.20 (d, 3H, J = 6.4 Hz). HMQC with a BIRD pulse (500 × 125 MHz, d_6-acetone) indicates the following ^{13}C resonances: δ 147.5, 115.7, 98.2, 97.6, 97.3, 96.7, 96.6, 93.8, 93.5, 92.1, 92.0, 91.4, 89.2, 88.3, 87.5, 85.1, 82.4, 71.5, 66.1, 59.9, 57.6, 51.1, 49.2, 45.0, 44.9, 42.0, 35.7. HRMS (FAB): M + H calcd 870.4428, found 870.4430. **Tetrabenzyl Precursor to 7**. IR (neat): υ_{max} 3359, 2925, 1721, 1655, 1455, 1377, 1262, 1049, 735, 698 cm^{-1}. ^{1}H NMR (500 MHz, d_6-acetone): δ 7.33 (m, 20H), 4.85 (d, 1H, J = 11.6 Hz), 4.79 (s, 2H), 4.75 (d, 1H, J = 12.2 Hz), 4.68 (d, 1H, J = 3.3 Hz), 4.67 (d, 1H, J = 11.6 Hz), 4.64 (d, 1H, J = 11.8 Hz), 4.61 (d, 1H, J = 11.6 Hz), 4.47 (d, 1H, J = 12.1 Hz), 4.29 (m, 1H), 4.06 (m, 1H), 3.92 (m, 2H), 3.88 (dd, 1H, J = 2.4, 8.5 Hz), 3.84 (d, 1H, J = 2.0 Hz), 3.78 (m, 2H), 3.70−3.58 (m, 4H), 3.48 (dd, 1H, J = 4.2, 11.5 Hz), 3.25 (dd, 1H, J = 9.4, 9.4 Hz), 2.00 (m, 1H), 1.90 (m, 2H), 1.86 (s, 3H), 1.81 (m, 2H), 1.66 (ddd, 1H, J = 2.0, 7.3, 13.7 Hz), 1.58 (ddd, 1H, J = 5.2, 8.4, 13.4 Hz), 1.46 (m, 1H), 1.21 (d, 3H, J = 6.3 Hz). HMQC with a BIRD pulse (500 × 125 MHz, CD_3OD) indicates the following ^{13}C resonances: δ 136.8, 134.2, 132.0, 132.0, 99.4, 81.2, 80.9, 80.3, 79.7, 78.4, 77.1, 76.9, 76.5, 76.2, 74.0, 73.8, 73.8, 73.2, 73.0, 72.4, 71.3, 76.9, 76.8, 76.0, 65.7, 47.0, 44.0, 37.9, 35.7, 33.2, 32.4, 26.1, 19.3. HRMS (FAB): M + H calcd 870.4428, found 870.4429. $[\alpha]_D$ = +0.030° (c 0.0024, $CHCl_3$).

Compound 8. The tetrabenzylated precursor (2.5 mg, 2.87 μmol) was dissolved in 1 mL of dry MeOH. This was stirred with 3.6 mg of $Pd(OH)_2$ on carbon under a H_2 atmosphere for 3 h. The solvent was filtered through a bed of Celite, isolating the carbon bound $Pd(OH)_2$. The MeOH was evaporated, and the oil was chromatographed on silica gel (linear gradient 0−20% MeOH/CH_2Cl_2) to yield polyol **8**. ^{1}H NMR (500 MHz, CD_3OD): δ 7.32 (m, 5H), 4.75 (d, 1H, J = 12.0 Hz), 4.68 (d, 1H, J = 3.2 Hz), 4.52 (d, 1H, J = 12.1 Hz), 4.16 (m, 1H), 4.03 (dd, 1H, J = 3.4, 12.1 Hz), 3.89−3.82 (m, 3H), 3.70−3.58 (m, 6H), 3.50−3.42 (m, 3H), 3.33 (m, 1H), 2.11 (m, 1H), 1.97 (m, 2H), 1.94 (s, 3H), 1.81−1.69 (m, 3H), 1.59 (m, 2H), 1.20 (d, 3H, J = 6.5 Hz). HMQC with a BIRD pulse (500 × 125 MHz) indicates the following ^{13}C resonances: δ 127, 96.4, 78.8, 77.4, 74.7, 74.4, 73.3, 72.0, 69.5, 69.4, 69.4, 66.2, 63.0, 62.9, 53.6, 47.2, 39.9, 33.0, 30.4, 25.0, 22.3, 16.3. HRMS (FAB): M + H calcd 600.3020, found 600.3021. $[\alpha]_D$ = +60° (c 0.011, MeOH).

Compound 7. The tetrabenzylated precursor (2−3 mg) was dissolved in 1 mL of dry MeOH. This was stirred with 3.6 mg of $Pd(OH)_2$ on carbon under a H_2 atmosphere for 3 h. The solvent was filtered through a bed of Celite, isolating the carbon bound $Pd(OH)_2$. The MeOH was evaporated, and the oil was chromatographed on silica gel (linear gradient 0−20% MeOH/CH_2Cl_2) to yield polyol **7**, 2.0 mg (>95%). ^{1}H NMR (500 MHz, CD_3OD): δ 7.31 (m, 5H), 4.75 (d, 1H, J = 12.1 Hz), 4.69 (d, 1H, J = 3.4 Hz), 4.51 (d, 1H, J = 12.1 Hz), 4.05 (m, 2H), 3.89−3.81 (m, 5H), 3.75−3.61 (m, 7H), 3.51 (dd, 1H, J = 4.3, 11.6 Hz), 2.07 (m, 1H), 1.96 (m, 1H), 1.94 (s, 3H), 1.82−1.73 (m, 3H), 1.66 (m, 1H), 1.56 (m, 1H), 1.47 (m, 1H), 1.20 (d, 3H, J = 6.4 Hz). HMQC with a BIRD pulse (500 × 125 MHz, CD_3OD) indicates the following ^{13}C resonances: δ 124, 96.1, 74.3, 74.3, 74.1, 72.2, 71.4, 70.9, 70.3, 69.6, 68.7, 63.4, 63.0, 62.8, 53.5, 44.9, 40.1, 34.9, 33.5, 30.4, 25.8, 22.5, 16.5. HRMS (FAB): M + H calcd 600.3020, found 600.3026. $[\alpha]_D$ = +40° (c 0.011, MeOH).

Compound 36. The homoallylic alcohol **27** (23 mg, 0.0257 mmol) was dissolved in 2 mL of MeOH and cooled to −78 °C. After 20 s of bubbling ozone through the reaction, 9 mg of $NaBH_4$ (0.238 mmol) was added and the solution was stirred for 15 min as the reaction mixture warmed to RT. The solvent was then evaporated without quench and was redissolved in 300 μL of CH_2Cl_2 and 2 drops of MeOH and placed directly onto a preparatory TLC plate (25 mm thick, 20 cm × 20 cm) and eluted with hexanes/EtOAc, 1/2; 16.4 mg of the diol was isolated (71% yield). This diol (0.0160 mmol) was dried and dissolved in 400 μL of CH_2Cl_2. After 7 μL of Et_3N (0.05 mmol) was added, 1.3 μL of MsCl (0.016 mmol) was syringed in and the reaction was allowed to stir for 0.5 h. This reaction mixure was then transferred directly onto a preparatory TLC plate and eluted with 1/1 Hex/EtOAc to result in the isolation of 13.5 mg of compound **36** (77% yield). IR (neat): υ_{max} 3444, 2928, 1663, 1497, 1455, 1356, 1175, 1069, 837, 735, 698 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 (m, 20H), 5.66 (d, 1H, J = 9.4 Hz), 4.76 (d, 1H, J = 3.4 Hz), 4.72 (d, 1H, J = 11.9 Hz), 4.70 (d, 1H, J = 11.9 Hz), 4.68 (d, 1H, J = 12.0 Hz), 4.60 (d, 1H, J = 12.0 Hz), 4.59 (d, 1H, J = 10.6 Hz), 4.56 (d, 1H, J = 11.4 Hz), 4.53 (d, 1H, J = 11.7 Hz), 4.41 (d, 1H, J = 11.7 Hz), 4.38 (m, 1H), 4.05 (m, 1H), 4.00 (m, 3H), 3.86 (m, 1H), 3.78 (m, 2H), 3.68 (m, 3H), 3.44 (dd, 1H, J = 9.5, 9.5 Hz), 3.13 (b, 1H), 2.97 (s, 3H), 1.90 (m, 2H), 1.81 (s, 3H), 1.70 (m, 1H), 1.47 (s, 3H), 1.38 (s, 3H), 1.25 (m, 5H), 0.82 (s, 9H), 0.04 (s, 3H), −0.02 (s, 3H). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 169.8, 138.5, 138.5, 138.0, 137.2, 128.5, 128.4, 128.4, 128.3, 128.2, 128.0, 127.8, 127.7, 127.6, 127.6, 127.5, 99.5, 96.3, 75.3, 74.9, 73.4, 73.0, 72.9, 71.6, 69.6, 69.5, 69.1, 68.2, 67.2, 65.3, 62.7, 52.4, 37.0, 36.0, 33.9, 33.7, 29.7, 29.2, 25.9, 24.0, 23.0, 19.1, 17.9, 15.1, 14.2, −4.1, −4.3. HRMS (FAB): M + H calcd 1090.5382, found 1090.5376. $[\alpha]_D$ = +18.6° (c 0.013.4, CH_2Cl_2).

Compound 37. Mesylate **36** (13 mg, 0.012 mmol) was dissolved in 0.6 mL of Et_2O and treated with 24 μL of a 1.0 M solution of TBAF in THF (0.024 mmol) and an additional 100 μL of THF. This reaction was allowed to stir for 2 h until, by TLC, the product spot appeared just below the starting material and above the TBS-deprotected uncyclized material.

Then 0.5 mL of CH_2Cl_2 was added and the reaction mixture was placed directly on a preparatory TLC plate and eluted with 1/1 Hex/EtOAc to give 8.0 mg of compound **37** (76% yield). IR (neat): υ_{max} 3420, 2924, 1661, 1539, 1455, 1375, 1204, 1071, 737, 698 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.33 (m, 20H), 6.16 (d, 1H, J = 8.6 Hz), 4.87 (d, 1H, J = 3.5 Hz), 4.75 (d, 1H, J = 12.2 Hz), 4.72 (d, 1H, J = 13.3 Hz), 4.58 (d, 1H, J = 12.1 Hz), 4.54 (s, 2H), 4.53 (d, 1H, J = 13.6 Hz), 4.46 (d, 1H, J = 12.0 Hz), 4.41 (d, 1H, J = 11.9 Hz), 4.21 (dt, 1H, J = 6.4, 6.4 Hz), 4.00 (b, 2H), 3.87 (dd, 1H, J = 3.1, 5.5 Hz), 3.84−3.59 (m, 10H), 3.4 (m, 2H), 3.27 (b, 1H), 2.11 (m, 1H), 1.9 (s, 3H), 1.74 (m, 6H), 1.41 (d, 3H, J = 7.3 Hz), 1.36 (s, 3H), 1.31 (s, 3H). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 170.2, 138.5, 138.3, 137.7, 137.5, 128.5, 128.4, 128.4, 128.2, 128.1, 127.9, 127.9, 127.7, 127.7, 127.6, 127.6, 99.2, 96.5, 78.8, 75.3, 75.2, 74.2, 73.9, 73.3, 73.0, 71.7, 70.5, 69.6, 65.1, 63.7, 62.9, 62.5, 53.4, 52.4, 45.3, 35.8, 33.1, 33.0, 29.7, 23.3, 19.2, 13.3. HRMS (FAB): M + H calcd 880.4636, found 880.4635. $[\alpha]_D$ = +45° (c 0.0082, CH_2Cl_2).

Compound 16. Compound **37** (8.1 mg, 0.0092 mmol) was dissolved in 0.5 mL of CH_2Cl_2 and 3 drops of MeOH. A catalytic amount of CSA (<0.2 mg) was added to the flask which was allowed to stir for 16 h. The reaction mixture was then transferred directly onto a preparatory TLC plate (25 mm thick, 20 cm × 10 cm) and eluted with 5% MeOH in CH_2Cl_2 to isolate 5.6 mg of the triol (73% yield). IR (neat): υ_{max} 3413, 2925, 1725, 1659, 1539, 1455, 1377, 1053, 735, 698 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.30 (m, 20H), 5.85 (d, 1H, J = 9.6 Hz), 4.79 (d, 1H, J = 3.6 Hz), 4.76 (d, 1H, J = 11.7 Hz), 4.69 (d, 1H, J = 11.7 Hz), 4.67 (d, 1H, J = 11.8 Hz), 4.56 (d, 1H, J = 11.7 Hz), 4.54 (d, 1H, J = 11.7 Hz), 4.51 (s, 2H), 4.46 (d, 1H, J = 11.8 Hz), 4.00 (b, 1H), 3.95 (m, 1H), 3.93 (m, 2H), 3.90−3.82 (m, 3H), 3.80−3.72 (m, 5H), 3.67 (m, 2H), 3.40 (dd, 1H, J = 9.5, 9.5 Hz), 1.96 (m, 2H), 1.82 (s, 3H), 1.78 (ddd, 1H, J = 3.1, 5.4, 12.7 Hz), 1.71 (m, 3H), 1.60 (ddd, 1H, J = 1.9, 7.6, 15.4 Hz), 1.46 (m, 3H), 1.28 (d, 3H, J = 6.7 Hz). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 170.0, 138.3, 138.2, 137.9, 137.1, 128.5, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.7, 127.4, 95.8, 75.1, 74.1, 73.4, 72.7, 71.9, 71.3, 69.5, 69.0, 63.6, 63.5, 62.5, 50.7, 43.2, 38.7, 32.9, 32.9, 29.7, 23.1. HRMS (FAB): M + H calcd 840.4323, found 840.4326. $[\alpha]_D$ = +55° (c 0.0056, CH_2Cl_2).

The triol (5.6 mg, 0.0067 mmol) was dissolved in 2 mL of dry MeOH. This was stirred with 29 mg of $Pd(OH)_2$ on carbon under a H_2 atmosphere for 12 h before 10 μL of AcOH was added and the concentration of the MeOH was reduced to 700 μL. After the solution was stirred for another 6 h, the solvent was filtered through a bed of Celite, isolating the carbon bound $Pd(OH)_2$. The MeOH was evaporated, and the oil was chromatographed on silica gel (linear gradient 0−20% MeOH/CH_2Cl_2) to yield compound **16**, 3.0 mg (79% yield). ^1H NMR (400 MHz, CD_3OD/D_2O, 1/1): δ 7.38 (m, 5H), 4.78 (d, 1H, J = 3.5 Hz), 4.75 (d, 1H, J = 12.2 Hz), 4.52 (d, 1H, J = 12.2 Hz), 4.06 (b, 1H), 3.97 (m, 1H), 3.91 (m, 1H), 3.89 (dd, 1H, J = 5.5, 9.4 Hz), 3.81−3.64 (m, 9H), 3.43 (dd, 1H, J = 9.8, 9.8 Hz), 2.10 (m, 1H), 1.94 (s, 3H), 1.74 (m, 4H), 1.52 (m, 3H), 1.20 (d, 3H, J = 6.5 Hz). ^{13}C NMR (100.6 MHz, CD_3OD/D_2O, 1/1): δ 173.9, 138.7, 129.5, 129.2, 129.0, 96.1, 76.1, 74.4, 72.3, 71.6, 71.1, 70.0, 69.7, 69.0, 66.9, 62.7, 62.3, 52.7, 44.4, 38.7, 34.1, 33.6, 22.8, 16.5. $[\alpha]_D$ = +70° (c 0.003, CD_3OD).

Compound 38. The olefin (17 mg, 0.019 mmol) from allylmagnesium bromide addition to aldehyde **35** was ozonized following the conditions in the synthesis of **16** to give 11.2 mg of the diol (0.011 mmol, 66% yield). This diol was then mesylated as before with 4.6 μL of Et_3N (0.033 mmol) and 0.88 μL of MsCl (0.011 mmol) to isolate 8.5 mg of the primary mesylate (0.0078 mmol, 71% yield). This mesylate was then dissolved in 0.5 mL of THF and treated with 50 μL of a TBAF solution, 1 M in THF (0.050 mmol), and stirred for 12 h. The THF was evaporated, and the oil was redissolved in CH_2Cl_2, transferred to a preparatory TLC plate (25 mm thick, 20 cm × 10 cm), and eluted to give 7.1 mg of the cyclized monoalcohol **38** analogous to compound **37** (96% yield). IR (neat): υ_{max} 3418, 2925, 1655, 1455, 1377, 1200, 1067, 735, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.32 (m, 20H), 6.19 (d, 1H, J = 8.2 Hz), 4.86 (d, 1H, J = 3.5 Hz), 4.76 (d, 1H, J = 11.9 Hz), 4.75 (d, 1H, J = 12.0 Hz), 4.70 (d, 1H, J = 11.6 Hz), 4.67 (d, 1H, J = 10.9 Hz), 4.63 (d, 1H, J = 11.6 Hz), 4.59 (d, 1H, J = 11.4 Hz), 4.56 (d, 1H, J = 10.8 Hz), 4.45 (d, 1H, J = 12.0 Hz), 4.12 (m, 1H), 4.00 (b, 2H), 3.95 (dd, 1H, J = 3.3, 8.2 Hz), 3.93 (m, 1H), 3.84−3.67 (m, 9H), 3.65 (dd, 1H, J = 1.4, 8.8 Hz), 3.24 (dd, 1H, J = 9.7, 9.7 Hz), 2.14 (m, 1H), 1.92 (s, 3H), 1.84 (m, 1H), 1.75 (m, 2H), 1.57 (m, 1H), 1.39 (m, 1H), 1.36 (s, 3H), 1.34 (s, 3H), 1.27 (d, 3H, J = 6.6 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 169.8, 138.7, 138.4, 138.1, 137.6, 128.4, 128.4, 128.3, 128.2, 128.0, 127.9, 127.9, 127.7, 127.6, 127.5, 99.5, 96.4, 77.2, 73.7, 73.1, 72.7, 72.1, 69.5, 68.6, 65.1, 65.0, 62.8, 61.7, 53.6, 42.0, 34.6, 33.8, 31.4, 29.7, 29.2, 23.4, 19.0, 15.3. HRMS (FAB): $(M - C_7H_7O)^+$ calcd 772.4061, found 772.4083. $[\alpha]_D$ = +1.6° (c 0.0061, CH_2Cl_2).

Compound 11. Compound **38** (6.1 mg, 0.0069 mmol) was dissolved in 0.5 mL of CH_2Cl_2 and 3 drops of MeOH. A catalytic amount of PTSA (<0.1 mg) was added to the flask which was allowed to stir for 16 h. The reaction mixture was then transferred directly onto a preparatory TLC plate (25 mm thick, 20 cm × 10 cm) and eluted with 5% MeOH in CH_2Cl_2 to isolate 4.1 mg of the triol (70% yield).

The triol (4.0 mg, 0.0048 mmol) was dissolved in 700 μL of dry MeOH. This was stirred with 11 mg of $Pd(OH)_2$ on carbon under a H_2 atmosphere for 45 min and filtered through a bed of Celite, isolating the carbon bound $Pd(OH)_2$. The MeOH was evaporated, and the oil was chromatographed on silica gel (linear gradient 0−20% MeOH/CH_2Cl_2) to yield compound **11**, 2.0 mg (74% yield). ^1H NMR (500 MHz, CD_3OD): δ 7.38 (d, 2H, J = 7.2 Hz), 7.32 (dd, 2H, J = 7.1, 7.1 Hz), 7.27 (t, 1H, J = 7.2 Hz), 4.75 (d, 1H, J = 11.9 Hz), 4.68 (d, 1H, J = 3.4 Hz), 4.50 (d, 1H, J = 11.9 Hz), 4.07 (m, 2H), 3.80 (m, 4H), 3.70 (m, 2H), 3.65 (m, 4H), 3.49 (dd, 1H, J = 9.7, 9.7 Hz), 3.18 (dd, 1H, J = 9.7, 9.7 Hz), 1.94 (s, 3H), 1.82 (m, 2H), 1.65 (m, 2H), 1.56 (m, 2H), 1.38 (m, 2H), 1.17 (d, 3H, J = 6.5 Hz). ^{13}C NMR (125.7 MHz, CD_3OD): δ 173.5, 139.1, 129.5, 129.4, 128.9, 96.6, 77.3, 74.9, 72.7, 72.2, 71.1, 69.9, 69.8, 68.8, 64.0, 63.0, 53.7, 42.5, 41.4, 35.0, 34.9, 30.8, 22.7, 16.7. HRMS (FAB): M + H calcd 570.2914, found 570.2908. $[\alpha]_D$ = +18° (c 0.002, MeOH).

Compounds 39 and 40. Diol **35** (31.6 mg, 0.0343 mmol) was dissolved in 2.5 mL of THF and stirred with 30 mg of $Hg(O_2CCF_3)_2$ (0.0686 mmol) for 20 min, 15 mL of brine was added, and the reaction was allowed to stir for an additional 30 min. The reaction mixture was then transferred to a separatory funnel and extrated with CH_2Cl_2 (4 × 25 mL), dried, and evaporated. The two diastereomers were separated on preparatory TLC plates (1/2 Hex/EtOAc) to give two compounds, a top band containing 18.3 mg of **40** (46% yield) and a bottom band containing 21.0 mg of **39** (53% yield); total yield, 99%. **Compound 39.** IR (neat): υ_{max} 4313, 2930, 1659, 1539, 1455, 1375, 1202, 1069, 735, 698 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$): δ 7.33 (m, 20H), 5.78 (d, 1H, J = 9.6 Hz), 4.78−4.69 (m, 5H), 4.65 (d, 1H, J = 11.6 Hz), 4.58 (d, 1H, J = 11.8 Hz), 4.50 (d, 1H, J = 11.8 Hz), 4.43 (d, 1H, J = 11.8 Hz), 4.25 (m, 1H), 4.10 (m, 1H), 3.97 (m, 1H), 3.90−3.60 (m, 9H), 3.43 (dd, 1H, J = 10.0, 10.0 Hz), 2.21 (m, 1H), 2.12 (dd, 1H, J = 4.5, 11.8 Hz), 2.04 (s, 3H), 1.95 (m, 2H), 1.74 (m, 1H), 1.57 (m, 4H), 1.46 (s, 3H), 1.38 (s, 3H), 1.24 (d, 3H, J = 7.0 Hz). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 170.0, 138.6, 138.5, 138.3, 137.1, 128.5, 128.4, 128.4, 128.3, 128.3, 128.0, 127.9, 127.7, 127.6, 127.6, 99.5, 96.3, 77.2, 76.4, 76.0, 73.3, 73.1, 69.6, 68.4, 67.9, 67.5, 65.0, 63.4, 62.8, 52.9, 40.1, 38.6, 37.0, 31.3, 29.4, 25.5, 23.2, 19.3, 15.5, 14.1. HRMS (FAB): M + H calcd 1130.4108, found 1130.4111. $[\alpha]_D$ = +2.3° (c 0.021, CH_2Cl_2). **Compound 40.** IR (neat): υ_{max} 3413, 2928, 1655, 1522, 1455, 1375, 1200, 1075, 735, 698 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.30 (m, 20H), 5.51 (d, 1H, J = 10.0 Hz), 4.79 (d, 1H, J = 11.8 Hz), 4.76 (d, 1H, J = 12.0 Hz), 4.76 (d, 1H, J = 3.7 Hz), 4.72 (d, 1H, J = 11.8 Hz), 4.71 (d, 1H, J = 11.7 Hz), 4.65 (d, 1H, J = 11.4 Hz), 4.59 (d, 1H, J = 11.8 Hz), 4.55 (d, 1H, J = 11.3 Hz), 4.50 (m, 1H), 4.43 (d, 1H, J = 11.6 Hz), 4.24 (m, 1H), 3.90−3.70 (m, 10H), 3.51 (m, 2H), 3.27 (dd, 1H, J = 9.4, 9.4 Hz), 2.36 (dd, 1H, J = 4.7, 11.7 Hz), 2.05 (m, 2H), 1.97 (d, 1H, J = 4.2, 11.9 Hz), 1.95 (s, 3H), 1.85 (m, 2H), 1.76 (m, 1H), 1.54 (m, 1H), 1.45 (m, 1H), 1.40 (s, 3H), 1.31 (s, 3H), 1.24 (d, 3H, J = 6.6 Hz). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 169.9, 138.5, 138.4, 137.9, 137.3, 128.5, 128.4, 128.4, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.6, 127.5, 99.3, 96.5, 77.5, 76.2, 76.0, 73.9, 73.6, 73.0, 71.6, 70.7,

69.5, 68.5, 65.0, 62.8, 60.4, 51.3, 45.7, 45.3, 38.3, 37.0, 29.1, 27.8, 23.6, 18.7, 15.8, 14.1. HRMS (FAB): $(M - Cl)^+$ calcd 1094.4350, found 1094.4347. $[\alpha]_D = +16°$ (*c* 0.018, CH_2Cl_2).

Compound 41. Organomercury compound **39** (15.0 mg, 0.0133 mmol) was dissolved in 0.5 mL of DMF and treated with 16 mg of $NaBH_4$ (0.423 mmol). After 45 min of stirring, 10 mL of brine was added and the reaction stirred for an additional hour. The reaction mixture was transferred to a separatory funnel and extracted with CH_2Cl_2 (3 × 25 mL). The crude oil was redissolved in CH_2Cl_2 and 2 drops of MeOH, combined with catalytic PTSA (2 grains), and stirred for 12 h. This reaction mixture was then transferred directly onto a preparatory TLC plate and eluted with 5% MeOH in CH_2Cl_2 to yield 9.0 mg of **41** (79% yield). IR (neat): υ_{max} 3339, 2926, 1655, 1541, 1497, 1455, 1375, 1049, 735, 698 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$): δ 7.32 (m, 20H), 5.63 (d, 1H, J = 9.5 Hz), 4.79 (d, 1H, J = 11.9 Hz), 4.78 (d, 1H, J = 11.1 Hz), 4.71 (m, 3H), 4.65 (d, 1H, J = 11.5 Hz), 4.59 (d, 1H, J = 12.0 Hz), 4.56 (d, 1H, J = 11.8 Hz), 4.45 (d, 1H, J = 11.7 Hz), 4.24 (m, 2H), 3.94−3.76 (m, 10H), 3.68 (dq, 1H, J = 4.7, 4.7 Hz), 3.35 (m, 2H), 2.00 (bd, 1H, J = 15.3 Hz), 1.80 (dd, 1H, J = 4.4, 14.6 Hz), 1.75 (s, 3H), 1.67 (m, 2H), 1.50 (dd, 1H, J = 7.5, 15.2 Hz), 1.33 (m, 1H), 1.24 (d, 3H, J = 6.9 Hz), 1.22 (d, 3H, J = 6.6 Hz). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 170.2, 138.6, 138.2, 138.0, 137.0, 128.5, 128.3, 128.2, 128.1, 128.1, 128.0, 128.0, 127.8, 127.6, 127.5, 127.4, 95.6, 77.7, 77.1, 75.9, 74.2, 73.5, 73.0, 72.2, 71.7, 69.2, 68.5, 67.7, 67.5, 63.4, 51.1, 45.1, 43.6, 37.8, 34.8, 29.6, 27.7, 23.1, 18.3, 15.6. HRMS (FAB): M + H calcd 854.4479, found 854.4476. $[\alpha]_D = +5.6°$ (*c* 0.0090, CH_2Cl_2).

Compound 9. 41 (9.0 mg, 0.0105 mmol) was dissolved in 1 mL of dry MeOH. This was stirred with 20 mg of $Pd(OH)_2$ on carbon under a H_2 atmosphere for 1.5 h and filtered through a bed of Celite, isolating the carbon bound $Pd(OH)_2$. The MeOH was evaporated, and the oil was chromatographed on silica gel (linear gradient 0−20% MeOH/CH_2Cl_2) to yield compound **9**, 3.8 mg (62% yield). ^1H NMR (400 MHz, CD_3OD): δ 7.32 (m, 5H), 4.75 (d, 1H, J = 12.0 Hz), 4.72 (d, 1H, J = 3.5 Hz), 4.50 (d, 1H, J = 12.0 Hz), 4.22 (m, 1H), 4.05 (m, 1H), 3.83 (m, 5H), 3.66 (m, 6H), 3.27 (dd, 1H, J = 9.5, 9.5 Hz), 1.95 (m, 1H), 1.93 (s, 3H), 1.70 (m, 5H), 1.41 (m, 1H), 1.21 (m, 7H). ^{13}C NMR (100.6 MHz, CD_3OD): δ 173.1, 138.9, 129.3, 129.2, 128.7, 96.3, 74.8, 74.4, 72.4, 72.0, 71.1, 69.8, 69.0, 68.6, 67.2, 62.9, 53.3, 45.1, 41.6, 38.7, 35.1, 30.2, 26.1, 22.7, 19.4, 16.6. HRMS (FAB): M + H calcd 504.3071, found 504.3070. $[\alpha]_D = +32°$ (*c* 0.0038, MeOH).

Compound 42. Organomercury compound **40** (18.2 mg, 0.0161 mmol) was treated under the same conditions reported for compound **41**, using 20 mg of $NaBH_4$ (0.530 mmol) followed by catalytic PTSA to give 10.6 mg of **42** (79% yield). IR (neat): υ_{max} 3341, 2925, 1655, 1542, 1497, 1455, 1375, 1059, 735, 698 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.31 (m, 20H), 5.23 (d, 1H, J = 10.0 Hz), 4.81 (d, 1H, J = 11.8 Hz), 4.79 (d, 1H, J = 11.9 Hz), 4.75 (d, 1H, J = 11.6 Hz), 4.72 (m, 1H), 4.72 (d, 1H, J = 3.7 Hz), 4.65 (d, 1H, J = 11.3 Hz), 4.59 (d, 1H, J = 11.7 Hz), 4.58 (d, 1H, J = 11.3 Hz), 4.45 (d, 1H, J = 11.6 Hz), 4.30 (m, 1H), 4.00−3.75 (m, 7H), 3.68 (dq, 1H, J = 4.6, 4.6 Hz), 3.67 (b, 1H), 3.50 (m, 2H), 3.28 (dd, 1H, J = 9.7, 9.7 Hz), 2.97 (dd, 1H, J = 9.9, 9.9 Hz), 2.11 (bd, 1H, J = 15.5 Hz), 1.94 (ddd, 1H, J = 1.2, 4.6, 11.2 Hz), 1.81 (ddd, 1H, J = 3.6, 10.0, 14.6 Hz), 1.72 (s, 3H), 1.70 (m, 1H), 1.49 (m, 1H), 1.37 (dd, 1H, J = 6.5, 9.9 Hz), 1.21 (m, 6H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 170.2, 138.6, 138.2, 138.0, 137.0, 128.5, 128.3, 128.2, 128.2, 128.1, 128.0, 128.0, 127.8, 127.6, 127.5, 127.4, 95.7, 80.6, 78.0, 77.5, 76.0, 73.6, 73.1, 72.4, 71.9, 69.3, 68.5, 63.4, 51.2, 44.5, 43.3, 42.2, 34.3, 29.6, 27.6, 23.1, 21.1, 15.7. HRMS (FAB): $(M - C_7H_7O)^+$ calcd 746.3904, found 746.3901. $[\alpha]_D = 0.0°$ (*c* 0.010, CH_2Cl_2).

Compound 10. 42 (10.6 mg, 0.0124 mmol) was dissolved in 1 mL of dry MeOH. This was stirred with 20 mg of $Pd(OH)_2$ on carbon under a H_2 atmosphere for 1.5 h and filtered through a bed of Celite, isolating the carbon bound $Pd(OH)_2$. The MeOH was evaporated, and the oil was chromatographed on silica gel (linear gradient 0−20% MeOH/CH_2Cl_2) to yield compound **10**, 6.1 mg (84% yield). ^1H NMR (400 MHz, CD_3OD): δ 7.35 (m, 5H), 4.76 (d, 1H, J = 12.0 Hz), 4.71 (d, 1H, J = 3.5 Hz), 4.51 (d, 1H, J = 12.0 Hz), 4.13 (m, 1H), 3.85 (m, 4H), 3.70−3.55 (m, 6H), 3.24 (dd, 1H, J = 9.7, 9.7 Hz), 3.24 (dd, 1H, J = 9.3, 9.3 Hz), 2.00 (bd, 1H, J = 17.1 Hz), 1.93 (s, 3H), 1.90 (ddd, 1H, J = 1.8, 5.4, 15.3 Hz), 1.26 (m, 1H), 1.19 (d, 3H, J = 6.5 Hz), 1.18 (d, 3H, J = 6.2 Hz). ^{13}C NMR (100.6 MHz, CD_3OD): δ 173.3, 139.1, 129.4, 129.4, 128.9, 96.4, 80.3, 74.8, 74.6, 73.7, 73.0, 72.5, 72.1, 71.3, 70.1, 69.9, 69.3, 63.0, 53.4, 46.6, 44.1, 41.6, 35.2, 30.7, 25.3, 22.7, 21.6, 16.6. HRMS (FAB): $(M - C_7H_7O)^+$ calcd 476.2496, found 476.2492. $[\alpha]_D = +36°$ (*c* 0.0061, MeOH).

Compound 43. *t*-BuOK (36 mg, 0.032 mmol) was dissolved in 1 mL of THF, and 82 μL of the MOM-protected allyl alcohol (0.064 mmol) was syringed in and allowed to stir for 15 min prior to cooling the flask to −78 °C. At this time, 120 μL of a 2.0 M solution of *n*-BuLi in pentane (0.024 mmol) was added dropwise followed by continued stirring for 1.5 h. Then 152 mg of (−)-Ipc_2BOMe was added in 280 μL of THF. After 3 h of stirring, 69.0 μL of BF_3OEt_2 (0.056 mmol) was added followed immediately by 154 mg of aldehyde **34** (0.016 mmol). The reaction mixture stirred at −78 °C for 4 h and was then allowed to warm to 10 °C slowly overnight, 12 h. The reaction was quenched with 1 mL of 3 N NaOH and 1 mL of 30% H_2O_2 and stirred for 4 h to insure complete oxidation of the boron. The contents of the flask were diluted with 15 mL of brine and transferred to a separatory funnel and extracted with CH_2Cl_2 (4 × 30 mL). Column chromatography (2/1 Hex/EtOAc) isolated 95 mg of the alcohol (57% yield). IR (neat): υ_{max} 3428, 2928, 1682, 1499, 1455, 1774, 1262, 1071, 837, 735, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.32 (m, 20H), 5.77 (ddd, 1H, J = 6.1, 10.6, 16.9 Hz), 5.64 (d, 1H, J = 10.0 Hz), 5.34 (dd, 1H, J = 0.8, 17.2 Hz), 5.01 (d, 1H, J = 11.8 Hz), 4.89 (d, 1H, J = 11.7 Hz), 4.78−4.61 (m, 9H), 4.42 (d, 1H, J = 11.7 Hz), 4.24 (m, 1H), 4.15 (dd, 1H, J = 2.6, 10.7 Hz), 4.08 (m, 2H), 3.98 (ddd, 1H, J = 3.5, 10.2, 11.4 Hz), 3.82 (d, 1H, J = 9.1 Hz), 3.79 (dd, 1H, J = 4.0, 9.3 Hz), 3.71 (dd, 1H, J = 3.0, 9.0 Hz), 3.67 (m, 3H), 3.59 (m, 1H), 3.43 (dd, 1H, J = 9.4, 9.4 Hz), 3.35 (s, 3H), 2.08 (m, 1H), 1.72 (m, 1H), 1.66 (m, 1H), 1.63 (ddd, 1H, J = 4.8, 9.8, 14.4 Hz), 1.50 (s, 3H), 1.37 (m, 2H), 1.31 (s, 3H), 1.26 (s, 3H), 1.11 (d, 3H, J = 6.4 Hz), 0.83 (s, 9H), 0.04 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 170.2, 138.7, 138.7, 138.6, 137.2, 136.0, 128.5, 128.3, 128.3, 128.2, 128.2, 128.1, 127.8, 127.6, 127.5, 127.5, 127.5, 99.3, 96.5, 94.6, 78.2, 77.2, 76.1, 74.2, 72.9, 72.8, 71.1, 69.5, 67.4, 65.3, 62.6, 55.5, 51.4, 36.1, 35.1, 29.7, 29.3, 25.8, 23.1, 19.0, 17.8, 16.7, −4.2, −4.7. HRMS (FAB): M + H calcd 1068.5868, found 1068.5875. $[\alpha]_D = -12°$ (*c* 0.017, CH_2Cl_2).

The alcohol (13 mg, 0.012 mmol) was dissolved in 1 mL of CH_2Cl_2 and 100 μL of MeOH, and the solution was stirred for 4 h with catalytic PTSA (<0.2 mg). The solution was evaporated and redissolved in CH_2Cl_2 for transfer onto a preparatory TLC plate and eluted with 5% MeOH in CH_2Cl_2 to yield 8.1 mg of the tetrol **43** (72% yeild). IR (neat): υ_{max} 3326, 2925, 1655, 1541, 1455, 1375, 1210, 1028, 735, 698 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.33 (m, 20H), 5.62 (d, 1H, J = 9.8 Hz), 5.52 (ddd, 1H, J = 2.0, 8.3, 17.5 Hz), 5.23 (dd, 1H, J = 1.1, 10.4 Hz), 5.16 (d, 1H, J = 17.1 Hz), 4.80 (d, 1H, J = 11.7 Hz), 4.76 (d, 1H, J = 11.9 Hz), 4.75 (d, 1H, J = 11.3 Hz), 4.73 (m, 2H), 4.70 (d, 1H, J = 12.0 Hz), 4.69 (d, 1H, J = 11.9 Hz), 4.68 (m, 1H), 4.59 (d, 1H, J = 11.7 Hz), 4.56 (m, 2H), 4.45 (d, 1H, J = 11.8 Hz), 3.94 (m, 5H), 3.85 (dd, 1H, J = 4.5, 11.2 Hz), 3.77 (m, 7H), 3.71 (dd, 1H, J = 4.7, 9.3 Hz), 3.40 (dd, 1H, J = 9.4, 9.4 Hz), 3.36 (s, 3H), 1.97 (bd, 1H, J = 15.0 Hz), 1.64 (b, 1H), 1.50 (ddd, 1H, J = 9.2, 9.2, 15.3 Hz), 1.20 (d, 3H, J = 6.5 Hz). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 170.1, 138.6, 138.5, 138.3, 137.3, 133.8, 128.6, 128.4, 128.3, 128.1, 128.1, 128.0, 128.0, 127.9, 127.7, 127.6, 127.6, 127.4, 127.1, 95.7, 94.1, 79.9, 78.1, 76.2, 74.9, 74.0, 73.7, 73.4, 73.0, 72.1, 71.9, 69.3, 68.5, 63.7, 55.8, 51.1, 43.9, 43.7, 37.1, 29.7, 23.2, 20.8, 15.8. HRMS (FAB): M + H calcd 914.4691, found 914.4694. $[\alpha]_D = -2.5°$ (*c* 0.0081, CH_2Cl_2).

Compound 44. Compound **43** (8.0 mg, 0.0088 mmol) was dissolved in 800 μL of THF and stirred with 15 mg of $Hg(O_2CCF_3)_2$ for 30 min before addition of 8 mL of brine and 45 min of further stirring. The reaction was then transferred to a separatory funnel and extracted with CH_2Cl_2 (3 × 25 mL). The crude oil was checked for reaction completion by ^1H NMR and then redissolved in 800 μL of DMF. This solution was treated

with 8.0 mg of $NaBH_4$ (0.22 mmol) and stirred for 30 min. At this point, 4 mL of brine was added, the reaction was stirred for 1.5 h, and the solution was extracted again with CH_2Cl_2 (3 × 25 mL). This crude oil was also checked for reaction completion by ^{1}H NMR prior to dissolving the oil in 2 mL of MeOH and 200 μL of CH_2Cl_2. One drop of concentrated HCl was added and the reaction stirred overnight for 11 h and then for 2 h after the addition of 2 more drops of acid. The MeOH was evaporated and redissolved in CH_2Cl_2. This solution was dried without extraction and placed on a preparatory TLC plate (5% MeOH/CH_2Cl_2) to give 4.5 mg of **44** (60% overall yield). IR (neat): υ_{max} 3359, 2925, 1655, 1541, 1455, 1375, 1055, 735, 698 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 (m, 20H), 5.60 (d, 1H, *J* = 9.7 Hz), 4.79 (d, 1H, *J* = 12.0 Hz), 4.76 (d, 1H, *J* = 4.6 Hz), 4.73 (d, 1H, *J* = 10.3 Hz), 4.69 (m, 2H), 4.65 (d, 1H, *J* = 11.5 Hz), 4.59 (d, 1H, *J* = 12.2 Hz), 4.56 (d, 1H, *J* = 12.0 Hz), 4.45 (d, 1H, *J* = 11.7 Hz), 4.25 (m, 1H), 3.92 (m, 1H), 3.85 (m, 3H), 3.78 (m, 2H), 3.69 (m, 1H), 3.54 (m, 1H), 3.29 (dq, 1H, *J* = 9.4, 9.4 Hz), 2.05 (bd, 1H, *J* = 15.4 Hz), 1.82 (m, 1H), 1.71 (s, 3H), 1.65 (m, 2H), 1.51 (m, 1H), 1.43 (m, 1H), 1.29 (d, 3H, *J* = 6.7 Hz), 1.29 (d, 3H, *J* = 6.8 Hz). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 170.3, 138.6, 138.3, 138.0, 137.1, 128.6, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 127.7, 127.6, 127.5, 95.7, 77.7, 75.9, 73.8, 73.6, 73.3, 73.1, 72.4, 72.3, 71.8, 71.7, 69.4, 68.8, 63.4, 51.3, 44.1, 43.3, 34.5, 29.7, 27.5, 23.1, 22.7, 14.1, 12.0. HRMS (FAB): M + H calcd 870.4428, found 870.4407. $[\alpha]_D$ = −20° (*c* 0.0046, CH_2Cl_2).

Compound 17. Compound **44** (4.5 mg, 0.0052 mmol) and 8 mg of $Pd(OH)_2$ on carbon were dissolved in 1 mL of MeOH. The reaction was stirred under a hydrogen atmosphere for 2.5 h at which time the reaction was filtered through a bed of Celite to filter out the carbon bound Pd. The solvent was evaporated, and the oil was chromatographed on silica gel (linear gradient 0−20% MeOH/CH_2Cl_2) to yield 1.9 mg of **17** (62% yield). ^{1}H NMR (400 MHz, CD_3OD): δ 7.33 (m, 5H), 4.75 (d, 1H, *J* = 11.9 Hz), 4.71 (d, 1H, *J* = 3.5 Hz), 4.52 (d, 1H, *J* = 12.1 Hz), 4.15 (m, 1H), 4.09 (dd, 1H, *J* = 6.1, 6.8 Hz), 3.85 (m, 4H), 3.64 (m, 5H), 3.47 (dd, 1H, *J* = 5.7, 9.1 Hz), 1.96 (m, 1H), 1.94 (s, 3H), 1.82 (m, 1H), 1.70 (m, 1H), 1.42 (m, 3H), 1.22 (d, 3H, *J* = 6.9 Hz), 1.20 (d, 3H, *J* = 6.4 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 173.4, 139.1, 129.4, 129.4, 128.9, 96.4, 74.7, 74.7, 74.3, 73.7, 73.4, 72.6, 72.1, 71.0, 70.1, 69.9, 69.3, 63.0, 53.4, 46.0, 41.4, 34.8, 22.7, 16.6, 12.6. $[\alpha]_D$ = +40° (*c* 0.0015, CH_3OH).

Compound 45. The primary alcohol (32 mg, 0.033 mmol) was dissolved in 0.5 mL of CH_2Cl_2 followed by the addition of 7.0 μL of Et_3N (0.10 mmol). After the solution was stirred for 15 min, 6 μL of MsCl (0.078 mmol) was added and the reaction stirred for an additional 0.5 h before being quenched with 4 mL of saturated sodium bicarbonate. The mixture was extracted with CH_2Cl_2 (4 × 25 mL), and 25.6 mg of mesylate **45** was isolated from preparatory TLC (2/1 Hex/EtOAc, 74% yield). IR (neat): υ_{max} 3384, 2930, 1678, 1455, 1358, 1048, 699 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (m, 20H), 5.83 (d, 1H, *J* = 9.7 Hz), 4.82 (d, 1H, *J* = 11.7 Hz), 4.74 (d, 1H, *J* = 11.8 Hz), 4.71 (d, 1H, *J* = 3.5 Hz), 4.70−4.66 (m, 3H), 4.59 (d, 1H, *J* = 11.6 Hz), 4.57 (d, 1H, *J* = 11.7 Hz), 4.41 (d, 1H, *J* = 11.8 Hz), 4.25 (dd, 1H, *J* = 6.2, 9.8 Hz), 4.19 (dd, 1H, *J* = 7.5, 9.9 Hz), 4.70 (m, 2H), 4.00 (m, 1H), 3.92 (ddd, 1H, *J* = 3.6, 9.9, 11.7 Hz), 3.37 (dd, 1H, *J* = 9.7, 9.7 Hz), 2.95 (s, 3H), 2.07 (m, 1H), 1.91 (m, 1H), 1.82 (s, 3H), 1.71 (m, 3H), 1.66 (dd, 1H, *J* = 6.5, 12.1 Hz), 1.48 (s, 3H), 1.41 (s, 3H), 1.39 (m, 1H), 1.16 (d, 3H, *J* = 6.3 Hz), 0.81 (s, 9H), 0.04 (s, 3H), −0.02 (s, 3H). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 170.0, 138.6, 138.5, 138.1, 137.0, 128.4, 128.3, 128.3, 128.2, 128.0, 127.9, 127.8, 127.6, 127.5, 127.4, 99.6, 96.1, 78.4, 76.2, 76.1, 74.2, 73.6, 72.8, 70.6, 69.6, 69.4, 68.0, 65.2, 62.7, 53.4, 52.7, 39.2, 36.8, 35.9, 33.6, 31.5, 29.0, 25.9, 23.0, 18.9, 17.9, 16.0, −4.0, −4.6. HRMS (FAB): M + H calcd 1046.5120, found 1046.5109. $[\alpha]_D$ = +16.8° (*c* 0.0256, $CHCl_3$).

Compound 18. Compound **45** (25 mg, 0.024 mmol) was dissolved in 1 mL of THF and stirred with 120 μL of a 1 M TBAF solution in THF (0.120 mmol) for 24 h. The solution was diluted with 5 mL of brine and extracted with CH_2Cl_2 (3 × 30 mL). The crude oil was chromatographed on preparatory TLC (2/1 Hex/EtOAc) to yield 13 mg of the fully protected oxetane (65% yield). IR (neat): υ_{max} 3306, 2932, 1662, 1541, 1454, 1374, 1266, 1204, 1118, 856 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 (m, 20H), 6.22 (d, 1H, *J* = 8.4 Hz), 4.87 (d, 1H, *J* = 3.2 Hz), 4.72 (d, 1H, *J* = 12.0 Hz), 4.71 (d, 1H, *J* = 14.2 Hz), 4.68 (d, 1H, *J* = 12.1 Hz), 4.65 (d, 1H, *J* = 12.1 Hz), 4.60 (d, 1H, *J* = 11.5 Hz), 4.58 (d, 1H, *J* = 11.8 Hz), 4.50 (m, 2H), 4.43 (d, 1H, *J* = 11.8 Hz), 4.23 (dd, 1H, *J* = 6.6, 6.6 Hz), 3.93−3.85 (m, 3H), 3.80−3.74 (m, 3H, 3.69−3.62 (m, 3H), 3.41 (m, 1H), 2.59 (m, 1H), 1.96 (m, 1H), 1.93 (s, 3H), 1.85 (m, 2H), 1.68 (m, 4H), 1.41 (s, 3H), 1.32 (s, 3H), 1.24 (d, 1H, *J* = 6.6 Hz). HRMS (FAB): M + H calcd 836.4374, found 836.4369. $[\alpha]_D$ = +50° (*c* 0.013, $CHCl_3$).

The fully protected oxetane (13.0 mg, 0.0155) was dissolved in MeOH and treated with catalytic PTSA (<0.2 mg). After disappearance of starting material the MeOH was evaporated and the reaction was redissolved in CH_2Cl_2. The reaction was quenched with 10 mL of saturated sodium bicarbonate and extracted with CH_2Cl_2 (3 × 25 mL) and chromatographed (TLC in 5% MeOH/CH_2Cl_2) to give 11.2 mg of the tetrabenzylated diol precursor to compound **18** (91% yield). IR (neat): υ_{max} 3306, 2929, 1653, 1547, 1455, 1374, 1107, 1026, 735, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (m, 20H), 5.73 (d, 1H, *J* = 9.3 Hz), 4.87 (d, 1H, *J* = 3.5 Hz), 4.75−4.48 (m, 8H), 4.13−3.90 (m, 5H), 3.82−3.67 (m, 9H), 3.46 (m, 1H), 3.22 (dd, 1H, *J* = 9.8, 9.8 Hz), 3.05 (b, 1H), 2.09 (m, 2H), 1.94 (s, 3H), 1.73 (m, 4H), 1.34 (d, 3H, *J* = 6.7 Hz). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 169.6, 138.6, 138.4, 138.1, 137.2, 128.6, 128.4, 128.4, 128.3, 128.2, 128.1, 128.1, 128.0, 127.8, 127.6, 127.6, 127.4. HRMS (FAB): M + H calcd 796.4061, found 796.4078. $[\alpha]_D$ = +58° (*c* 0.0096, $CHCl_3$).

The benzylated diol and 10 mg of $Pd(OH)_2$ on carbon were dissolved in 1.5 mL of MeOH. The reaction was stirred under a hydrogen atmosphere for 4 h at which time the reaction was filtered through a bed of Celite to filter out the carbon bound Pd. The solvent was evaporated, and the oil was chromatographed on silica gel (linear gradient 0−20% MeOH/CH_2Cl_2) to yield 3.1 mg of **18** (38% yield). IR (neat): υ_{max} 3368, 2926, 1653, 1559, 1455, 1375, 1024 cm^{-1}. ^{1}H NMR (500 MHz, CD_3OD): δ 7.32 (m, 5H), 4.85 (d, 1H, *J* = 3.4 Hz), 4.78 (d, 1H, *J* = 12.0 Hz), 4.53 (d, 1H, *J* = 12.0 Hz), 4.16 (m, 1H), 4.09 (m, 1H), 3.90 (dd, 1H, *J* = 3.4, 11.8 Hz), 3.87 (dd, 1H, *J* = 5.4, 9.0 Hz), 3.77 (m, 2H), 3.68 (m, 1H), 3.65 (dd, 1H, *J* = 3.5, 9.1 Hz), 3.63 (m, 2H), 3.61 (dd, 1H, *J* = 5.7, 11.8 Hz), 3.53 (dd, 1H, *J* = 5.6, 10.7 Hz), 3.21 (dd, 1H, *J* = 9.9, 9.9 Hz), 2.22 (m, 1H), 2.15 (m, 1H), 1.91 (s, 3H), 1.83 (m, 2H), 1.76 (m, 1H), 1.21 (d, 3H, *J* = 6.5 Hz). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 173.0, 139.2, 129.4, 129.3, 128.8, 96.7, 82.6, 78.5, 75.8, 75.4, 72.6, 72.1, 70.2, 70.1, 69.9, 68.9, 63.6, 63.3, 54.1, 44.7, 43.6, 34.1, 30.8, 24.8, 22.4, 16.6. HRMS (FAB): M + H calcd 526.2652, found 526.2653. $[\alpha]_D$ = +80° (*c* 0.003, CH_2Cl_2).

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Supporting Information Available: ^{1}H NMR spectra for all compounds reported (55 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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