Preferred Conformation of *C*-Glycosides. 10. Synthesis and Conformational Analysis of Carbon Trisaccharides†

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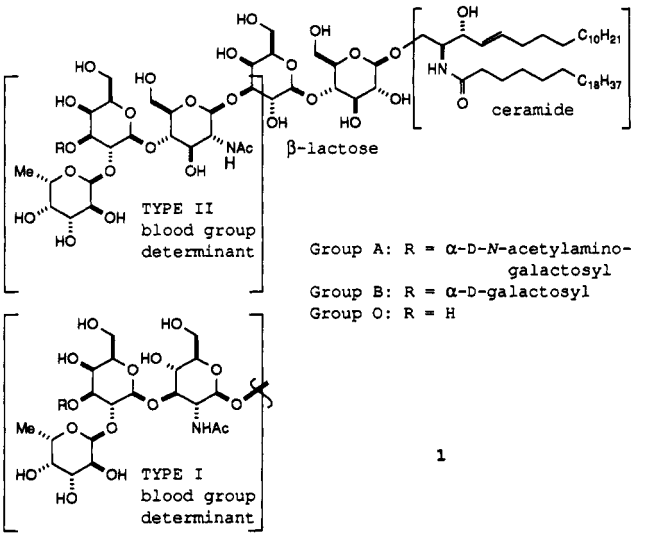
A flexible and efficient synthesis of the carbon trisaccharide **2** related to the Type II O(H) blood group determinant has been developed. This route was applied to the synthesis of the trisaccharides **3**, **4**, and **5**. The preferred solution conformations of compounds **2–5** were determined on the basis of vicinal coupling constants in the ^{1}H NMR spectrum. Each of the four trisaccharides adopts a distinct and well-defined solution conformation in accord with the predictions made on the basis of the preference of the C-glycosidic bond for the "exo-anomeric" conformation and the analysis of 1,3-diaxial-like interactions around the C-aglyconic bond.

The relationship between the conformation of carbohydrates and their binding affinity to biomacromolecules has been used to study the steric requirements of receptor sites.[1] A variety of structural modifications have been employed to generate conformationally modified analogues. Often, these modifications alter only the size of a given moiety or affect the conformation in an unpredictable way. Alternatively, recourse has been made to ring systems or tethers in order to lock the structure into a well-defined conformation.[2] To our knowledge, few attempts have been made to control the conformational behavior of carbohydrates by rationally manipulating the intrinsic steric interactions of these substrates.

In preceding publications,[3] it was shown that the conformation of carbohydrates can be predicted solely on the basis of (a) the preference of the C-glycosidic bond for the "exo-anomeric" conformation and (b) the consideration of 1,3-diaxial-like interactions as revealed by diamond lattice analysis.

We decided to prepare the carbon analogue of a biologically significant substrate and demonstrate two issues on the basis of this analysis. First, we wish to show that the conformation of this compound can be predicted and that this prediction can be proven experimentally. Second, we wish to demonstrate that the compound can be induced to adopt different, yet predictable and well-defined conformations as a result of specific, rationally designed structural modifications. This approach relies exclusively on the analysis of acyclic steric constraints. The Type II O(H) blood group determinant trisaccharide[1,4] and its carbon analogue are ideally suited for this purpose.

The Type II ABO(H) blood group antigen is a membrane-bound glycosphingolipid of structure **1** consisting of a variable oligosaccharide linked via a β-lactosyl spacer to the terminal hydroxyl group of ceramide. The blood group determinant also appears in the plasma of certain individuals (secretors) as a water-soluble glycoprotein, bound by a 3-*O*-(β-D-galactosyl)-α-D-*N*-acetylglucosamine disaccharide to a serine or threonine residue of the conjugate peptide.



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Conformational Analysis

The conformational analysis of the blood group determinant trisaccharide and its carbon analogues can be broken down into the conformation across the C.1′–C.α–C.4 linkage of the galactosyl–glucosamine moiety and the conformation across the C.1″–C.α'–C.2′ linkage of the fucosyl-galactose moiety. No significant interaction between the two conformational systems is expected. The conformational studies on the monoglycosides and the 1,4-linked disaccharides[3] have shown that the glycosidic conformation is essentially independent of the substituent at the 2-position. The 2′-fucosylmethyl functionality should therefore have little bearing on the conformation of the C.1′–C.α–C.4 bridge. Conversely, the galactosyl–glucosamine system should not affect the conformational behavior across the fucosyl–galactose bridge. While the presence of the C.1′–C.α bond of the galactosylmethyl group is relevant in determining the 1,3-interactions influencing the conformation around the C.2′–C.α' bond, the conformation around C.1′–C.α–C.4 is only relevant in determining longer range (1,4- and 1,5-) interactions, whose effect we expect to be nominal. The trisaccharide can therefore be analyzed as a first approximation in terms of

† Taken in part from Goekjian, P. G. Ph.D. Dissertation, Harvard University, 1990. For Part 9 of this series, see: Wang, Y.; Goekjian, P. G.; Ryckman, D. H.; Miller, W. H.; Babirad, S. A.; Kishi, Y. *J. Org. Chem.*, previous paper in this issue.

(1) See, for example: Lemieux, R. U. *Frontiers of Chemistry*; Laidler, K. J., Ed.; Pergamon: New York, 1982; and references cited therein.
(2) For a recent example, see: Lindh, I.; Hindsgaul, O. *J. Am. Chem. Soc.* **1991**, *113*, 216.
(3) (a) Goekjian, P. G.; Wu, T.-C.; Kishi, Y. *J. Org. Chem.* **1991**, *56*, 6412. Wu, T.-C.; Goekjian, P. G.; Kishi, Y. *J. Org. Chem.* **1987**, *52*, 4819. (b) Goekjian, P. G.; Wu, T.-C.; Kang, H.-Y.; Kishi, Y. *J. Org. Chem.* **1991**, *56*, 6422. Goekjian, P. G.; Wu, T.-C.; Kang, H.-Y.; Kishi, Y. *J. Org. Chem.* **1987**, *52*, 4823. (c) Wang, Y.; Babirad, S. A.; Kishi, Y. *J. Org. Chem.*, in press. Babirad, S. A.; Wang, Y.; Kishi, Y. *J. Org. Chem.* **1987**, *52*, 1370. (d) Wang, Y.; Goekjian, P. G.; Ryckman, D. M.; Miller, W. H.; Babirad, S. A.; Kishi, Y. *J. Org. Chem.*, in press. Babirad, S. A.; Wang, Y.; Goekjian, P. G.; Kishi, Y. *J. Org. Chem.* **1987**, *52*, 4825. Wang, Y.; Goekjian, P. G.; Ryckman, D. M.; Kishi, Y. *J. Org. Chem.* **1988**, *53*, 4151. Miller, W. H.; Ryckman, D. M.; Goekjian, P. G.; Wang, Y.; Kishi, Y. *J. Org. Chem.* **1988**, *53*, 5580.
(4) (a) Hounsell, E. F. *Chem. Soc. Rev.* **1987**, *16*, 161. Watkins, W. M. *Biochem. Soc. Symp.* **1974**, *40*, 125. (b) Yan, Z.-Y.; Rao, B. N. N.; Bush, C. A. *J. Am. Chem. Soc.* **1987**, *109*, 7663.

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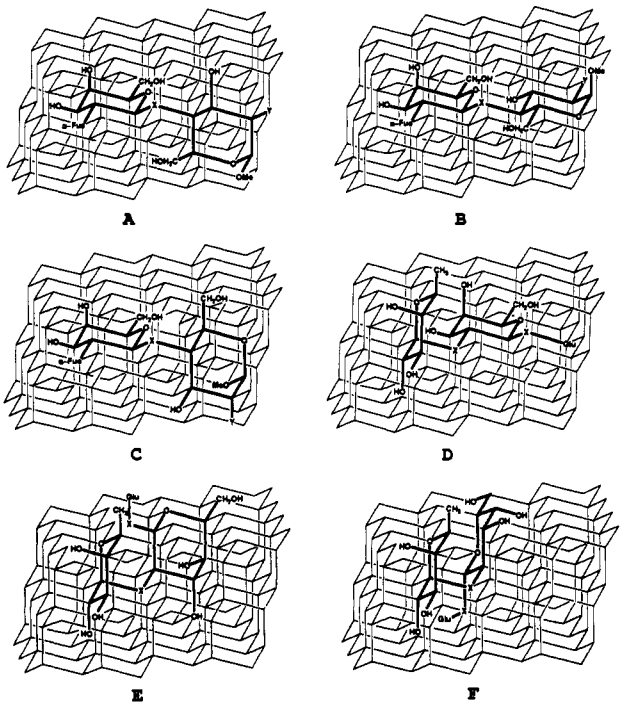
two independent disaccharide systems.

The conformational behavior of the β(1,4)-linkage is expected to be similar to that of methyl *C*-cellobioside.[3d] The conformation around the C-glycosidic bond is predicted to be such that the C.α–C.4 bond is antiperiplanar to the pyranose C.1′–C.2′ bond, i.e., the "exo-anomeric" conformation. Analysis of the three staggered conformers around the C-aglyconic bond indicates that all three suffer from unfavorable steric interactions. Conformer C has two gauche interactions (C.α–C.1′/C.3–C.4 and C.α–C.1′/C.4–C.5) and one 1,3-diaxial-like interaction (C.1′–0.5′/C.4–C.5); conformer B has two 1,3-diaxial-like interactions (C.1′–0.5′/C.3–C.4 and C.1′–C.α/C.3–O.3); conformer A has one 1,3-diaxial-like interaction (C.α–C.1′/C.5–C.6).



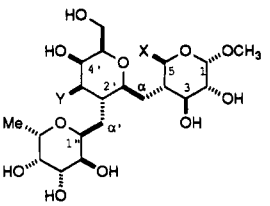
The conformation across the fucosyl–galactose linkage is analyzed in the same manner. The C.1″–C.α′ bond is expected to exist in the depicted "exo-anomeric" conformation. Consideration of the three staggered rotamers around the C.α′–C.2′ bond shows that none of them is free of unfavorable steric interactions. Conformer F has two gauche interactions (C.α′–C.1″/C.1′–C.2′ and C.α′–C.1″/C.2′–C.3′) and one 1,3-diaxial-like interaction (C.1″–0.5″/C.2′–C.3′); E has two 1,3-diaxial-like interactions (C.1″–0.5″/C.1′–C.2′ and C.α′–C.1″/C.α–C.1′); D has one 1,3-diaxial-like interaction (C.α′–C.1″/C.3′–O.3′).

On the basis of the results observed for the monoglycosides and the 1,4-linked disaccharides,[3] distortion is expected to occur primarily around the C-aglyconic bond. The trisaccharide is therefore predicted to exist in a conformation with both C-glycosidic bonds, C.1′–C.α and C.1″–C.α′, in the "exo-anomeric" conformation. Both C-aglyconic bonds, C.α–C.4 and C.α′–C.2′, are predicted to exist in a flexible conformation, i.e., either as a mixture of conformers or as a single twisted conformer.

The conformation of the blood group determinant trisaccharide can be controlled by modifying the 1,3-diaxial-like interactions which are responsible for the distortion around the C-aglyconic bonds. If the C.3′-hydroxyl group is removed, the fucosyl–galactose system is expected to adopt the ideal staggered conformer D, while leaving the conformation across the galactosyl–glucosamine linkage unaffected. Similarly, removal of the C.5-hydroxymethyl group will allow the galactosyl–glucosamine system to adopt conformer A predominantly, without affecting the conformation of the fucosyl–galactose system. Finally, removal of both the C.3′-hydroxyl group and the C.5-hydroxymethyl group should produce an analogue which exists predominantly in an ideal staggered conformation across both linkages (AD). We predict that four different conformers of the blood group determinant trisaccharide can thus be accessed through the use of small but strategically chosen structural modifications. The Type II O(H) determinant trisaccharide is ideal for this study because both the C.5-hydroxymethyl and the C.3-hydroxyl group are readily available for structural modification.

Results and Discussion

Synthesis. The terminal residue of the Type II O(H) blood group determinant trisaccharide is β-D-acetylglucosamine. Neither the 2-acetamido group nor the configuration of the methyl glycoside is expected to have a substantial effect on the conformational behavior of the compound. In view of the possible technical difficulties associated with the presence of the acetamide functionality (e.g., poor solubility, reactivity, the presence of an acidic proton), the 2-acetamido group was replaced with a hydroxyl. In addition, the axial methyl glycoside was found to be far more amenable to the early stages of the synthesis. Thus, for purely practical reasons, the synthesis and conformational analysis were developed first on the α-D-gluco compound **2**. We were confident, however, that the analogue of the natural product could be readily obtained by adapting the synthesis to the β-D-acetylglucosamine case.[5]



2: X=CH_2OH, Y=OH
3: X=H, Y=OH
4: X=CH_2OH, Y=H
5: X=H, Y=H

It was necessary to develop a synthetic route to the carbon trisaccharide that was both efficient enough to provide reasonable quantities of the trisaccharides and flexible enough to allow for the preparation of the 5-deshydroxymethyl and the 3′-deoxy compounds. Formation of the C.2′–C.α′ bond by aldol condensation[6] may provide an efficient access to the carbon trisaccharide, via readily available carbon mono- and disaccharides.

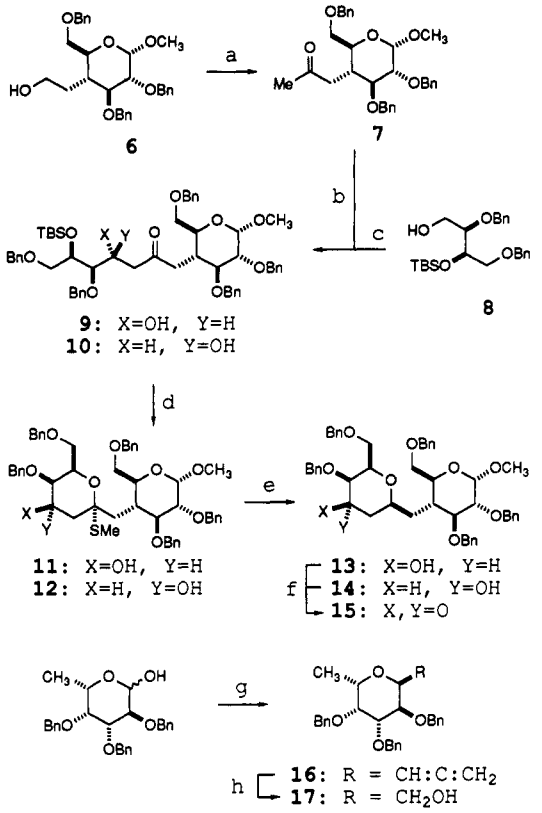
The synthesis of the substrates for the aldol condensation is shown in Scheme I. The primary alcohol **6**, readily available in large scale from methyl 2,3,6-*O*-tribenzyl-α-D-glucopyranoside,[3c] was converted to the methyl ketone **7**. Oxidation of the primary alcohol **8** and aldol condensation with the methyl ketone in toluene yielded a 4:1 ratio of hydroxy ketones **9** and **10**.[7] Since the hydroxyl stereochemistry was to be removed in the oxidation to the

(5) Subsequent investigations in these laboratories have shown that the β-D-acetylglucosamine analogue can be carried through the synthesis, following exactly the synthetic route developed for the glucose series. Feng, B.; Kishi, Y. Unpublished results.

(6) See for example: (a) Yu, K.-L.; Handa, S.; Tsang, R.; Fraser-Reid, B. *Tetrahedron* **1991**, *42*, 189. Yu, K. L.; Fraser-Reid, B. *Chem. Commun.* **1989**, 1442. (b) Chapleur, Y.; Euvrard, M.-N. *Chem. Commun.* **1987**, 884.

(7) The stereochemistry was assigned on the basis of the observed coupling constants between the C.2′ and C.3′ protons in the ^1H NMR of the derived thioketals: J = 12.0 and 5.1 Hz for **11** (derived from **9**) and J = <1 and 4.2 Hz for **12** (derived from **10**).

Scheme I[a]



[a] Reagents and conditions: (a) (i) Swern oxidation; (ii) MeMgBr, THF, 0 °C; (iii) Swern oxidation; (b) (i) LiHMDS, THF; (ii) aldehyde; (c) Swern oxidation; (d) (i) TBAF, THF; (ii) MeSH, $Bf_3 \cdot Et_2O$, CH_2Cl_2; (e) Bu_3SnH, AIBN, toluene; (f) Swern oxidattion; (g) $TMSCH_2C{\equiv}CH$, TMSOTf, CH_3CN; (h) (i) O_3, CH_3OH; (ii) Me_2S; (iii) $NaBH_4$.

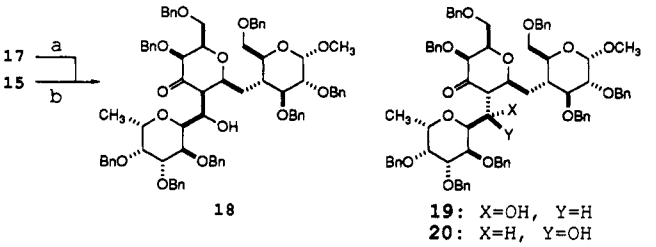
disaccharide ketone, both compounds were carried on. Treatment of each isomer with TBAF in THF yielded the hemiketals which were treated with methanethiol and boron trifluoride etherate in methylene chloride to yield the thioketals **11** and **12**. Tributyltin hydride reduction[3c] in toluene gave stereospecifically the 2′-deoxy carbon disaccharides **13** and **14**, which were oxidized to give the disaccharide ketone **15**.

Treatment of the *p*-nitrobenzyl ester of 2,3,4-*O*-tribenzyl-L-fucose with propargyltrimethylsilane and TMSOTf in acetonitrile yielded the allene **16**.[3c] Ozonolysis of the allene followed by sodium borohydride reduction led to the primary alcohol **17**.

A large variety of reaction conditions[8] are available for the aldol condensation, and many were developed specifically with delicate cases in mind. In view of the sensitive nature of the aldehyde, and on the basis of model studies, we felt that the magnesium enolate offered the best combination of mild reaction conditions and high yields of aldol products in hindered systems.[9]

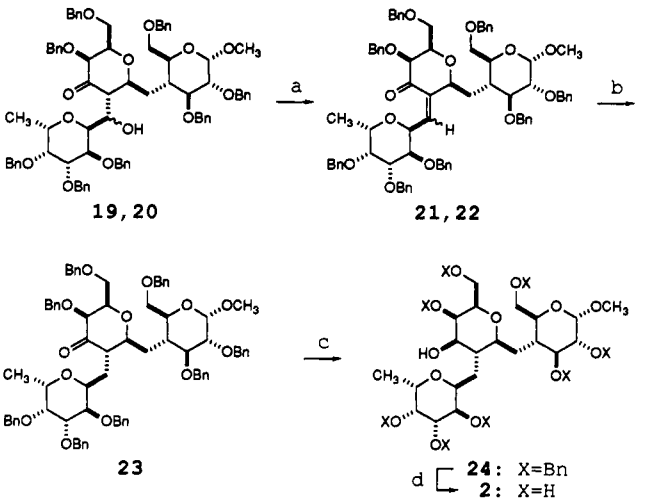
Direct formation of the magnesium enolate using dicyclohexylamidomagnesium bromide[10] was unsuccessful. Treatment of the ketone **15** with the base in THF followed

Scheme II[a]



[a] Reagents and conditions: (a) Swern oxidation, (b) (i) LiHMDS, TMEDA or HMPA, THF; (ii) $MgBr_2$; (iii) aldehyde.

Scheme III[a]



[a] Reagents and conditions: (a) (i) MsCl, NEt_3, Et_2O; (ii) NH_3, THF; (b) Bu_3SnH, AIBN, toluene; (c) $NaBH_4$, MeOH; (d) $Pd(OH)_2/C$, H_2, MEOH.

by addition of an excess of the aldehyde derived from **17** gave only the reduced ketone **13**. The magnesium enolate was therefore prepared by transmetalation of the lithium enolate with magnesium bromide. Three bases—lithium dicyclohexylamide, lithium diisopropylamide (LDA), and lithium hexamethyldisilazane (LiHMDS)—were investigated in the enolization step. LiHMDS was found to be markedly superior.[11] Thus, the ketone in THF at −78 °C was treated with LiHMDS (3 equiv)[12] and HMPA, followed by the addition of $MgBr_2$. Addition of the aldehyde led to three aldol products **18**–**20** in a 3.2:1.7:1 ratio by ^1H NMR. The stereochemistry at C.2′ was assigned unambiguously on the basis of the coupling constants around the pyranose rings.[13]

The equatorial aldol products **19** and **20** were cleanly dehydrated by formation of the mesylate and treatment of the crude mesylate with liquid ammonia in THF.[14] Similar treatment of the axial aldol product **18**, however,

(8) For recent reviews on crossed aldol reactions, see: (a) Heathcock, C. H. The Aldol Addition Reaction. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: Orlando, 1984; Vol. 3, Chapter 3, p 111. (b) Mukaiyama, T. *Org. React.* **1982**, *28*, 203.

(9) Kishi, Y.; Hatakeyama, S.; Lewis, M. D. *Frontiers of Chemistry*; Laidler, K. J., Ed.; Pergamon: New York, 1982. Lewis, M. D. Ph.D. Dissertation, Harvard University, 1983.

(10) Fukuyama, T.; Akasaka, K.; Karanewsky, D. S.; Wang, C.-L. J.; Schmid, G.; Kishi, Y. *J. Am. Chem. Soc.* **1979**, *101*, 262.

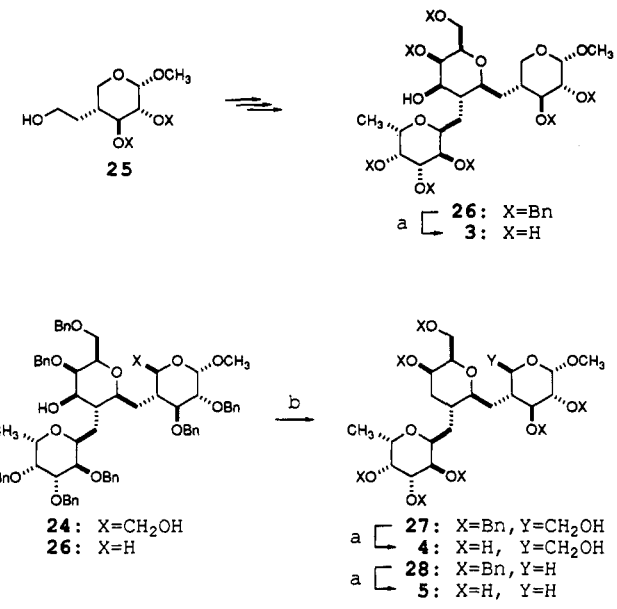
(11) LDA and LiHMDS are known to give very different results in certain systems. See, for example: Koreeda, M.; Chen, Y. P. L. *Tetrahedron Lett.* **1981**, *22*, 15.

(12) Beutelman, H. P.; Xie, L.; Saunders, W. H. *J. Org. Chem.* **1989**, *54*, 1703 and references cited therein.

(13) The stereochemistry of the C.α′ hydroxyl group was assigned tentatively on the basis of the vicinal coupling constants between the C.1″ and the C.α′ protons: J = 9.4 Hz for **19** and J = 3.5 Hz for **20**. If the carbon backbone is assumed to adopt an extended conformation (i.e., the "exo-anomeric" conformation), the C.α′ hydroxy is erythro to the pyranose oxygen in **19** and threo in **20**. Since this stereocenter does not exist in the final product, however, this assignment is not critical for this synthesis.

(14) Treatment of β-hydroxy ketones with MsCl and triethylamine normally leads to dehydration in situ. In this case, however, the mesylate was isolated cleanly. Subsequent treatment of the mesylate with amine bases other than ammonia resulted in the recovery of unreacted mesylate.

Scheme IV[a]



[a] Reagents and conditions: (a) $Pd(OH)_2/C$, H_2, MeOH; (b) (i) NaH, CS_2, MeI; (ii) Bu_3SnH, AIBN, toluene.

led only to recovery of the mesylate. Despite investigating a large number of reagents and conditions, including a variety of activating groups, various Mitsonobu-type reagents,[15] and tin hydride radical deoxygenation conditions,[16] we were unable to convert the axial aldol product **18** either to the enone or to the trisaccharide ketone.

It was therefore necessary to modify the original aldol condensation conditions in order to obtain selectively the equatorial aldol products **19** and **20**. A variety of conditions were investigated. Using TMEDA instead of HMPA resulted in a striking reversal of the selectivity at C.2′. Treatment of the ketone **15** with LiHMDS (3 equiv), TMEDA, and $MgBr_2$, followed by addition of the aldehyde, led to almost exclusive formation of the equatorial products **19** and **20** in 1:2 ratio. A plausible explanation to account for the change in selectivity, based on the work of House,[17] is that TMEDA enhances the reversibility of the initial formation of the β-alkoxy ketone, thus favoring the thermodynamically favored C.2′-equatorial aldol product.[18]

Mesylation of **19** and **20** followed by treatment with liquid ammonia gave the enones **21** and **22**, which were reduced with tributyltin hydride[19] in the presence of a catalytic amount of AIBN in refluxing benzene to yield exclusively the C.2′-equatorial ketone **23** (Scheme III). Sodium borohydride reduction of the C.3′ carbonyl proceeded with the desired stereoselectivity to yield the protected carbon trisaccharide **24**. Hydrogenolysis of the protecting groups provided the polyol **2**.

This synthetic scheme allows for efficient preparation of the 5-deshydroxymethyl *C*-trisaccharide **3**, the 3′-deoxy *C*-trisaccharide **4**, and the 3′-deoxy-5-deshydroxymethyl *C*-trisaccharide **5** (Scheme IV). The 5-deshydroxymethyl primary alcohol **25** is available from the synthesis of the 5-deshydroxymethyl analogue of the *C*-cellobiose.[3c] This compound could be carried through the same sequence as the parent compound to provide the 5-deshydroxymethyl heptabenzyl trisaccharide **26**.[20]

Since the synthetic route propitiously leaves the trisaccharide unprotected at the 3′-position, deoxygenation can be performed directly on compounds **24** and **26**. Conversion to the xanthates followed by tributyltin hydride reduction yields the protected 3′-deoxy trisaccharide **27** and the 3′-deoxy-5-deshydroxymethyl compound **28**. Deprotection of **26**, **27**, and **28** gave the polyols **3**, **4**, and **5**.

Table I. ^{1}H NMR Data (500 MHz, 2.5% Methanol-d_4/Pyridine-d_5) for Compound 2 at Room Temperature

proton	chemical shift (δ, pattern, coupling constants)
H.1	5.11 (d, J = 3.6 Hz)
H.2	3.99 (dd, J = 3.6, 9.3 Hz)
H.3	4.37–4.42 (buried)
H.4	2.25 (dddd, J = 3.7, 4.0, 10.9, 10.9 Hz)
H.5	4.37–4.42 (buried)
H.6	4.37–4.42 (buried)
H.6	4.05 (dd, J = 5.7, 11.6 Hz)
H.α	1.97 (ddd, J = 4.0, 9.5, 15.1 Hz)
H.α	2.78 (br dd, J = 3.7, 15.1 Hz)
H.1′	3.89 (br dd, J = 9.5, 10.1 Hz)
H.2′	2.46 (dddd, J = 2.3, 5.5, 9.9, 10.1 Hz)
H.3′	3.99 (dd, J = 2.9, 9.9 Hz)
H.4′	4.18 (br d, J = 2.9 Hz)
H.5′	3.75 (br dd, J = 4.1, 7.6 Hz)
H.6′	4.11 (dd, J = 4.1, 11.5 Hz)
H.6′	4.42 (dd, J = 7.6, 11.5 Hz)
H.α′	2.37 (ddd, J = 4.7, 5.5, 14.7 Hz)
H.α′	2.53 (ddd, J = 2.3, 9.8, 14.7 Hz)
H.1″	4.96 (ddd, J = 4.7, 5.2, 9.8 Hz)
H.2″	4.66 (dd, J = 5.2, 8.7 Hz)
H.3″	4.36 (dd, J = 2.4, 8.7 Hz)
H.4″	4.19 (dd, J = 2.2, 2.4 Hz)
H.5″	4.44 (dq, J = 2.2, 6.5 Hz)
H.6″	1.57 (d, J = 6.5 Hz)

NMR Analysis. The ^{1}H NMR spectrum of the carbon trisaccharide **2** was measured in 2.5% methanol-d_4/pyridine-d_5.[21] The signals were assigned on the basis of the 2D-COSY. All coupling constants were determined by first-order analysis (Table I). The coupling constants around the pyranose rings show that they adopt the expected chair forms.

The coupling constants observed around the two C-glycosidic bonds ($J_{H.1'-H\alpha}$ = 9.5, 0.5 Hz; $J_{H.1''-H\alpha'}$ = 9.8, 4.7 Hz) indicate that both adopt the expected "exo-anomeric" conformation. The coupling constants around the C-aglyconic bond ($J_{H.4-H.\alpha}$ = 3.7, 4.0 Hz; $J_{H.2'-H.\alpha'}$ = 5.5, 2.3 Hz) point either to a mixture of conformers or to a single distorted conformer. In the latter case, applying a modified Karplus curve[22] yields the approximate dihedral angles (ϕ, Ψ) = (−75°, −120°), (ϕ',Ψ') = (−75°, −110°).[23,24]

The carbon trisaccharide adopts the "exo-anomeric" conformation around both C-glycosidic bonds and a distorted conformation around both C-aglyconic bonds.

(15) Mitsonobu, O. *Synthesis* **1981**, 1.
(16) Barton, D. H. R.; Motherwell, W. B. *Pure Appl. Chem.* **1981**, *53*, 15.
(17) House, H. O.; Crumrine, D. S.; Teranishi, A. Y.; Olmstead, H. D. *J. Am. Chem. Soc.* **1973**, *95*, 3310.
(18) Alternatively, TMEDA may inhibit the chelation of the magnesium cation to the C.4′ oxygen. See: Van Draanen, N. A.; Arseniyadis, S.; Crimmins, M. T.; Heathcock, C. H. *J. Org. Chem.* **1991**, *56*, 2499.
(19) Neumann, W. P. *Synthesis* **1987**, 665 and references cited therein.
(20) The 5-deshydroxymethyl compound is also available by differentially protecting the C.6 hydroxyl group as a *p*-methoxybenzyl ether, followed by decarbonylation at a late stage. The present route, however, was found to be more efficient.
(21) The use of methanol-d_4/pyridine-d_5 as solvent was necessary to resolve the important signals in the ^{1}H NMR.
(22) Haasnoot, C. A. G.; de Leeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783.
(23) The dihedral angle ϕ is defined as (O.5–C.1–C.α–C.*n*) and Ψ as (C.1–C.α–C.*n*–C.*n* + 1).
(24) This is in remarkable agreement with the results found for the parent blood group determinant trisaccharide. (a) Lemieux, R. U.; Rock, K.; Delbaere, L. T. J.; Koto, S.; Roa, V. S. *Can. J. Chem.* **1980**, *58*, 631. (b) Yan, Z.-Y.; Rao, B. N. N.; Bush, C. A. *J. Am. Chem. Soc.* **1987**, *109* 7663.

Table II. Selected ^{1}H NMR (500 MHz) Coupling Constants for Compounds 2–5, 24, and 26–28 at Room Temperature[a]

compd	H1′–Xα	H1′–Yα	Xα–H4	Yα–H4	H1″–Xα′	H1″–Yα′	Xα′–H2′	Yα′–H2′
2	9.5	0.5	4.0	3.7	9.8	4.7	2.3	5.5
24	10.7	1.2	2.1	5.5	10.2	3.4	2.8	6.2
3	10.6	1	2.9	10.7	10.6	2.8	1	6[b]
26	8.3	2.3	2.7	10.7	10.4	3.1	3.1	6.3
4	9.4	1	3.6	4.0	12.1	3.0	2.6	11.0
27	10.2	1	2.7	5.1	11.4	2	3.0	12
5	9.6	3.2	2.0	10.1	12.1	3.0	2.8	10.9
28	7.5	2.7	2.3	10.8	11.5	2.7	2.8	10.9

[a] Benzylated compounds 24 and 26–28 were recorded in both $CDCl_3$ and C_6D_6. Polyols were recorded in the following solvents: 2, 2.5% CD_3OD/pyridine-d_5; 3, D_2O; 4, CD_3OD; 5 33% CD_3OD/D_2O. [b] The coupling constant was estimated on the basis of a PANIC simulation.

Again, distortion occurs preferentially around the aglyconic bond rather than the glycosidic bond. The preference of the C-glycosidic bond for the "exo-anomeric" conformation has held true for all cases studied to date. This includes the monoglycosides, the disaccharides, and now the trisaccharide. The conformation of the carbon trisaccharide, as determined from the ^{1}H NMR coupling constants, provides experimental evidence of the predictive value of our analysis.

The significant ^{1}H NMR data for compounds 2, 3, 4, and 5 and their protected forms 24, 26, 27, and 28 are summarized in Table II. Comparison of the 5-deshydroxymethyl analogue 3 with the parent trisaccharide 2 shows no change in the behavior across the C.1″–C.α′–C.2′ fucosyl–galactose bridge. The coupling constants between C.α′ and C.2′ are relatively unchanged: 5.5 and 2.3 Hz for 2, 6 and 1 Hz for 3. However, a clear conformational preference for the extended conformation A is observed around the glucose C.α–C.4 bond. The vicinal coupling constants across this bond change dramatically from 3.7 and 4.0 Hz for 2 to the more "ideal" 10.7 and 2.9 Hz for 3.

Conversely, the 3′-deoxy compound 4 shows no change across the C.1′–C.α–C.4 galactosyl–glucose linkage, but a clear preference for the conformer D across the C.2′–C.α′–C.1″ bonds. Again, this is clear from comparison of the observed coupling constants: $J_{4,\alpha}$ = 2 (4.0, 3.7 Hz), vs 4 (3.6, 4.0 Hz); $J_{2',\alpha'}$ = 2 (2.3, 5.5 Hz) vs 4 (2.6, 11.0 Hz).

Finally, the 3′-deoxy-5-deshydroxymethyl *C*-trisaccharide 5 shows a strong preference for a single conformation across both linkages. The coupling constants between C.4 and C.α are 2.0 and 10.1 Hz; the coupling constants between C.2′ and C.α′ are 2.8 and 10.9 Hz. Based on the observed vicinal coupling constants, it has been shown that each of the four trisaccharides exhibits a unique conformational behavior which coincides with the predictions based on our analysis.

Finally, as was the case with the monoglycosides and the carbon disaccharides, there is little difference between the preferred conformation of the polyols and their protected forms. This implies that electrostatic interactions and hydrogen bonds do not play a central role in the overall conformation of the trisaccharides.

It should be noted that this analysis is equally applicable to the parent oxygen compounds. The conformational similarity of carbon and oxygen linked disaccharides has been demonstrated experimentally.[3d] The structural modifications described above are therefore expected to have the same conformational ramifications in the natural Type II O(H) blood group determinant trisaccharide.

Conclusions

An efficient synthesis of the carbon analogue 2 of a trisaccharide related to the Type II O(H) blood group determinant has been developed. The 5-deshydroxymethyl analogue 3, the 3′-deoxy analogue 4, and the 3′-deoxy-5-deshydroxymethyl analogue 5 were also prepared. It was demonstrated that these structural modifications, strategically chosen on the basis of the analysis of 1,3-diaxial-like interactions, can be used to induce the carbon trisaccharide to adopt either the preferred solution conformation observed for the naturally occurring substances or an ideal extended conformation around each of the interannular linkages. The carbon trisaccharides 2–5 were predicted to adopt four different conformations on the basis of the preference of the C-glycosidic bond for the "exo-anomeric" conformation and the diamond lattice analysis of 1,3-diaxial-like interactions. The conformation of the four trisaccharides, determined experimentally on the basis of the ^{1}H NMR vicinal coupling constants, validate these predictions.

Experimental Section

General Experimental Procedures. Only selected spectral data are presented in the Experimental Section. For general procedures, see ref 3C.

Methyl Ketone 7. The primary alcohol 6 (2.80 g, 5.68 mmol) was oxidized to the aldehyde by the usual Swern procedure.[3c] A stirred solution of the crude aldehyde in THF (50 mL) at 0 °C under argon was treated with methylmagnesium bromide (1.9 M in *n*-Bu_2O, 13.6 mmol). The reaction mixture was stirred at room temperature for 20 min. Aqueous workup (ether) and filtration through silica gel yielded a crude mixture of secondary alcohols which was azeotroped with toluene and used without further purification. The crude secondary alcohols were oxidized by the usual Swern procedure to yield the ketone 7 as a clear colorless oil (2.10 g, 4.16 mmol, 73% yield). IR (neat): 1708 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.90 (3 H, s), 3.38 (3 H, s), 3.48 (2 H, d, *J* = 3.8 Hz), 3.59 (1 H, dd, *J* = 3.5, 9.2 Hz), 3.66–3.74 (2 H), 4.67 (1 H, d, *J* = 3.5 Hz). ^{13}C NMR ($CDCl_3$): δ 29.36, 206.96. HRMS (FAB, NaI): calcd for $C_{31}H_{36}O_6$ (M + Na) 527.2410, found 527.2410. $[\alpha]_D$: +14.6° (*c* 1.97, $CHCl_3$).

1,3-*O*-Dibenzyl-2,4-*O*-anisylidenethreitol (29), 1,3-*O*-Dibenzyl-4-*O*-(*p*-methoxybenzyl)threitol (30), and 1,3-*O*-Dibenzyl-2-*O*-(*tert*-butyldimethylsilyl)-4-*O*-(*p*-methoxybenzyl)threitol (31). See supplementary material for procedures and analytical data.

1,3-*O*-Dibenzyl-2-*O*-(*tert*-butyldimethylsilyl)threitol (8). A stirred solution of the (methoxybenzyl)threitol 31 (1.68 g, 3.13 mmol) in methylene chloride (25 mL) and pH 7.0 buffer (75 mL) at 0 °C was treated with DDQ (portionwise, 1.7 g, 7.5 mmol). The reaction mixture was stirred at 0 °C for 4 h. Aqueous workup (ether; Na_2SO_3), $NaBH_4$/methanol treatment of the crude product (anisaldehyde elutes with the primary alcohol), and silica gel chromatography (flash silica, 10% ethyl acetate:hexanes) yielded the primary alcohol 8 as a clear colorless oil (1.040 g, 2.50 mmol, 80% yield). IR (neat): 3462 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.05 (3 H, s), 0.06 (3 H, s), 0.89 (9 H, s), 2.42 (1 H, br dd, *J* = 5.8, 6.0 Hz), 3.53 (1 H, dd, *J* = 5.8, 10.0 Hz), 3.57 (1, H, ddd, *J* = 4.9, 5.0, 5.1 Hz), 3.66 (1 H, dd, *J* = 3.8, 10.0 Hz), 3.68 (1 H, m), 3.78 (1 H, br ddd, *J* = 5.0, 5.7, 11.4 Hz), 4.04 (1 H, ddd, *J* = 3.8, 5.5, 5.5 Hz). ^{13}C NMR ($CDCl_3$): δ −4.97. HRMS (FAB, NaI): calcd for

$C_{24}H_{36}O_4Si$ (M + Na) 439.2281, found 439.2299. $[\alpha]_D$: +15.2° (*c* 2.14, $CHCl_3$).

Monocyclic Aldol Products 9 and 10. The primary alcohol 8 (2.00 g, 4.92 mmol) was oxidized to the aldehyde by the usual Swern procedure. A stirred solution of HMDS (0.57 mL, 2.7 mmol) in THF (5 mL) at −78 °C under argon was treated with *n*-BuLi (2.05 M in hexanes, 1.06 mL, 2.45 mmol). The reaction mixture was stirred at −78 °C for 5 min and 0 °C for 15 min. The mixture was cooled to −78 °C, and a solution of the ketone 7 (1.05 g, 2.08 mmol) was added dropwise. The reaction mixture was stirred at −78 °C for 20 min. A solution of the aldehyde (half of above, ca. 2.46 mmol) was added dropwise. The reaction was stirred for 10 min and quenched with saturated NH_4Cl. Aqueous workup and size exclusion chromatography (JAI LC-908, chloroform) followed by silica gel chromatography (flash silica, 35% ethyl acetate/hexanes) yielded the aldol products as clear colorless oils (9 (erythro): 935 mg, 1.02 mmol, 49% yield; (threo): 200 mg, 0.220 mmol, 11% yield). **Erythro Diasteriomer 9.** IR (neat): 3469, 1709 cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.02 (3 H, s), 0.04 (3 H, s), 0.86 (9 H, s), 2.30 (1 H, m), 2.36 (1 H, dd, *J* = 9.2, 16.0 Hz), 2.43 (2 H, m), 2.59 (1 H, dd, *J* = 2.7, 16.0 Hz), 3.29 (1 H, dd, *J* = 3.8, 7.7 Hz), 3.37 (3 H, s), 3.44 (2 H, d, *J* = 4.0 Hz), 3.66 (1 H, dd, *J* = 4.1, 9.8 Hz), 3.71 (1, H, dd, *J* = 9.6, 10.5 Hz), 3.76 (1 H, ddd, *J* = 3.8, 4.0, 10.6 Hz), 4.07 (1 H, ddd, *J* = 3.8, 4.0, 6.6 Hz), 4.16 (1 H, m), 4.66 (1 H, d, *J* = 3.5 Hz). ^{13}C NMR ($CDCl_3$): δ 209.08. HRMS (FAB, NaI): calcd for $C_{55}H_{70}O_{10}Si$ (M + Na) 941.4636, found 941.4657. $[\alpha]_D$: +21.7° (*c* 1.67, $CHCl_3$). **Threo Diasteriomer 10.** IR (Neat): 3511, 1712 cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.01 (3 H, s), 0.03 (3 H, s), 0.87 (9 H, s), 2.17 (1 H, dd, *J* = 3.3, 15.8 Hz), 2.25 (1 H, dddd, *J* = 5.1, 5.4, 10.6, 10.6 Hz), 2.34 (1 H, dd, *J* = 5.1, 17.0 Hz), 2.40 (1 H, dd, *J* = 5.4, 17.0 Hz), 2.51 (1 H, dd, *J* = 9.7, 15.7 Hz), 2.72 (1 H, d, *J* = 5.5 Hz), 3.18 (1 H, dd, *J* = 3.2, 5.6 Hz), 3.37 (3 H, s), 3.43 (2 H, m), 3.50 (1 H, dd, *J* = 5.4, 10.2 Hz), 3.53–3.58 (2 H), 3.72 (1 H, dd, *J* = 9.4, 10.5 Hz), 3.78 (1 H, ddd, *J* = 3.7, 3.9, 10.5 Hz), 3.99 (1 H, ddd, *J* = 3.8, 5.5, 5.5 Hz), 4.11 (1 H, m), 4.66 (1 H, d, *J* = 3.5 Hz). ^{13}C NMR ($CDCl_3$): δ 208.18. HRMS (FAB, NaI): calcd for $C_{55}H_{70}O_{10}Si$ (M + Na) 941.4636, found 941.4675. $[\alpha]_D$: +9.9° (*c* 1.18, $CHCl_3$).

Disaccharide Thioketals 11 and 12. A stirred solution of the erythro aldol product 9 (3.04 g, 3.34 mmol) in THF (20 mL) was treated with TBAF·$3H_2O$ (2.1 g, 6.7 mmol). The reaction mixture was stirred at room temperature for 30 min. The reaction mixture was filtered through silica gel and concentrated in vacuo. Silica gel chromatography (flash silica, 50% ethyl acetate/hexanes) yielded the hemiketal as a clear colorless oil (2.23 g). A stirred solution of the hemiketal (half of above, 1.12 g) in methylene chloride (20 mL) was cooled to −78 °C under argon. Methyl mercaptan (5 mL) was condensed into the reaction mixture, and BF_3·Et_2O (0.08 M in methylene chloride, 5 mL, 0.4 mmol) was added at −15 °C via a syringe pump over a period of 2 h. Aqueous workup (CH_2Cl_2) and silica gel chromatography (flash silica, 25% ethyl acetate/hexanes) yielded the thioketal 11 as a clear colorless oil (1.11 g, 1.35 mmol, 81% yield). The threo aldol product 10 (23.4 mg, 0.0255 mmol) was converted to the gulo thioketal 12 (16.1 mg, 0.0193 mmol, 76% yield; clear colorless oil) by the same procedure. **C.3′ Equatorial (Galacto) Isomer 11.** IR (neat): 3482 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.32 (1 H, dd, *J* = 5.1, 14.0 Hz), 1.47 (1 H, d, *J* = 10.3 Hz), 1.62 (3 H, s), 1.64 (1 H, dd, *J* = 2.3, 14.9 Hz), 1.78 (1 H, dddd, *J* = 2.3, 4.1, 10.5, 10.7 Hz), 1.92 (1 H, dd, *J* = 4.3, 14.8 Hz), 2.32 (1 H, dd, *J* = 12.0, 13.9 Hz), 3.27 (1 H, dd, *J* = 9.1, 10.4 Hz), 3.36 (1 H, dd, *J* = 6.0, 9.1 Hz), 3.44 (3 H, s), 3.48 (1 H, dd, *J* = 3.5, 9.2 Hz), 3.51–3.57 (2 H), 3.68 (1 H, br d, *J* = 2.9 Hz), 3.70 (1 H, ddd, *J* = 1.5, 9.2, 10.6 Hz), 3.83 (1 H, dd, *J* = 1.5, 10.6 Hz), 3.85–3.92 (2 H). ^{13}C NMR ($CDCl_3$): δ 9.61. HRMS (FAB, NaI): calcd for $C_{50}H_{58}O_9S$ (M + Na) 857.3699, found 857.3702. $[\alpha]_D$: +82.5° (*c* 1.63, $CHCl_3$). **C.3′ Axial (Gulo) Isomer 12.** IR (neat): 3454 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.20 (1 H, br d, *J* = 15.9 Hz), 1.64 (1 H, dd, *J* = 2.2, 14.9 Hz), 1.73 (3 H, s), 1.78 (1 H, dddd, *J* = 2.2, 4.3, 10.5, 10.5 Hz), 1.84 (1 H, dd, *J* = 4.3, 14.9 Hz), 2.68 (1 H, dd, *J* = 4.2, 15.9 Hz), 3.33 (1 H, dd, *J* = 9.0, 11.4 Hz), 3.35 (1 H, br s), 3.43 (3 H, s), 3.47 (1 H, dd, *J* = 3.5, 9.2 Hz), 3.69 (1 H, ddd, *J* = 1.6, 9.1, 10.5 Hz), 3.79 (1 H, br d, *J* = 10.5 Hz), 3.86 (1 H, m), 3.88 (1 H, dd, *J* = 1.6, 10.5 Hz), 4.13 (1 H, br dd, *J* = 6.0, 6.3 Hz), 4.66 (1 H, d, *J* = 3.5 Hz). ^{13}C NMR ($CDCl_3$): δ 9.92. HRMS (FAB, NaI): calcd for $C_{50}H_{58}O_9S$ (M + Na) 857.3699, found 857.3739. $[\alpha]_D$: +76.2° (*c* 0.94, $CHCl_3$).

2′-Deoxy Disaccharides 13 and 14. A stirred solution of the galacto thioketal 11 (1.11 g, 1.35 mmol), AIBN (85 mg), and tributyltin hydride (5 mL) in toluene (10 mL) was heated rapidly to 110 °C and stirred for 30 min. The reaction mixture was cooled to room temperature, applied to a silica gel column, and eluted with 25% ethyl acetate/hexanes. A second silica gel chromatography (flash silica, 25% ethyl acetate/hexanes) yielded the galacto disaccharide 13 as a clear colorless oil (1.02 g, 1.31 mmol, 97% yield). The gulo thioketal 12 (47 mg, 0.057 mmol) was converted to the gulo disaccharide 14 (39 mg, 0.050 mmol, 88% yield; clear colorless oil) by the same procedure. **C.3′ Equatorial (Galacto) Isomer 13.** IR (neat): 3453 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.30 (1 H, ddd, *J* = 11.7, 11.7, 11.8 Hz), 1.52 (1 H, br dd, *J* = 4.6, 12.1 Hz), 1.61 (2 H, m), 1.67 (1 H, d, *J* = 10.1 Hz), 1.93 (1 H, m), 3.31 (3 H, s), 3.51 (1 H, dd, *J* = 5.7, 9.0 Hz), 3.56 (1 H, dd, *J* = 8.0, 9.0 Hz), 3.58 (1 H, dd, *J* = 3.5, 9.1 Hz), 3.74 (1 H, dd, *J* = 8.4, 9.4 Hz), 3.83 (1 H, ddd, *J* = 2.3, 3.4, 11.0 Hz), 4.69 (1 H, d, *J* = 3.5 Hz). ^{13}C NMR ($CDCl_3$): δ 33.38. HRMS (FAB, NaI): calcd for $C_{49}H_{56}O_9$ (M + Na) 811.3822, found 811.3860. $[\alpha]_D$: +10.1° (*c* 1.20, $CHCl_3$). **C.3′ Axial (Gulo) Isomer 14.** IR (neat): 3458 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.28 (1 H, br d, *J* = 13.9 Hz), 1.58–1.61 (2 H), 1.66 (1 H, ddd, *J* = 2.7, 9.4, 13.9 Hz), 1.99 (1 H, dddd, *J* = 4.3, 4.3, 10.7, 10.7 Hz), 3.22 (1 H, dd, *J* = 1.5, 1.6 Hz), 3.29 (3 H, s), 3.48 (1 H, dd, *J* = 6.7, 9.5 Hz), 3.52 (1 H, dd, *J* = 6.3, 9.5 Hz), 3.58 (1 H, dd, *J* = 3.5, 9.1 Hz), 3.63 (1 H, dd, *J* = 1.9, 10.8 Hz), 3.71 (1 H, dd, *J* = 4.1, 10.8 Hz), 3.78–3.84 (2 H), 3.78–3.89 (2 H), 3.93 (1 H, m), 4.69 (1 H, d, *J* = 3.4 Hz). ^{13}C NMR ($CDCl_3$): δ 33.37. HRMS (FAB, NaI): calcd for $C_{49}H_{56}O_9$ (M + Na) 811.3822, found 811.3865. $[\alpha]_D$: +2.4° (*c* 0.62, $CHCl_3$).

2′-Deoxy Disaccharide Ketone 15. The galacto disaccharide 13 (244 mg, 0.309 mmol) was oxidized to the ketone 15 (clear colorless oil, 206.6 mg, 0.262 mmol, 85% yield) by the usual Swern procedure. The gulo disaccharide 14 (39 mg, 0.050 mmol) was converted to the identical ketone (38 mg, 0.049 mmol, 98% yield) by the same procedure. IR (neat): 1722 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.64 (1 H, ddd, *J* = 4.3, 4.3, 14.7 Hz), 1.69 (1 H, ddd, *J* = 4.7, 7.7, 14.7 Hz), 1.98 (1 H, m), 2.08 (1 H, br d, *J* = 13.4 Hz), 2.55 (1 H, dd, *J* = 11.6, 13.4 Hz), 3.29 (3 H, s), 3.52 (1 H, ddd, *J* = 1.5, 5.7, 6.7 Hz), 3.66 (1 H, dd, *J* = 4.0, 10.9 Hz), 3.72 (1 H, dd, *J* = 9.3, 10.5 Hz), 3.82 (1 H, ddd, *J* = 1.9, 3.6, 11.0 Hz), 4.68 (1 H, d, *J* = 3.5 Hz). ^{13}C NMR ($CDCl_3$): δ 206.29. HRMS (FAB, NaI): calcd for $C_{49}H_{54}O_9$ (M + Na) 809.3665, found 809.3631. $[\alpha]_D$: −6.0° (*c* 1.19, $CHCl_3$).

(Tribenzyl-α-L-fucosyl)allene (16). A stirred solution of 2,3,4-*O*-tribenzyl-L-fucose (18.12 g, 41.7 mmol) and triethylamine (15 mL) in ether (200 mL) at 0 °C under argon was treated with *p*-nitrobenzoyl chloride (10 g, 54 mmol). The reaction mixture was stirred at room temperature overnight. The reaction was quenched with water and stirred for several hours. Aqueous workup (CH_2Cl_2) gave the crude *p*-nitrobenzoate which was azeotroped with toluene and used without further purification. A stirred solution of the crude *p*-nitrobenzoate and propargyltrimethylsilane (20 mL) in acetonitrile (600 mL) at 0 °C under argon was treated with TMSOTf (10.0 mL, 51.7 mmol). The reaction mixture was stirred at room temperature overnight. Aqueous workup (CH_2Cl_2) and silica gel chromatography (flash silica, 5%, 10% ethyl acetate/hexanes) yielded the allene 16 as a white crystalline solid (10.17 g, 22.3 mmol, 54% yield). An analytical sample was obtained by recrystallization from methanol/water; white prisms, mp 84–85 °C. IR (neat): 1955 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.18 (3 H, d, *J* = 6.4 Hz), 3.68 (1 H, dd, *J* = 1.7, 2.8 Hz), 3.74 (1 H, dd, *J* = 2.8, 9.1 Hz), 3.93 (1 H, dq, *J* = 1.7, 6.4 Hz), 4.13 (1 H, dd, *J* = 5.4, 9.1 Hz), 5.42 (1 H, ddd, *J* = 5.6, 6.6, 6.7 Hz). ^{13}C NMR ($CDCl_3$): δ 208.77. MS (FAB, NaI): 479 amu (M + Na). $[\alpha]_D$: −87.2° (*c* 1.24, $CHCl_3$). Anal. Calcd for $C_{30}H_{32}O_4$: C, 78.91; H, 7.06. Found: C, 78.67; H, 7.06.

(Tribenzyl-α-L-fucosyl)methanol (17). A stirred solution of the allene 16 (2.1 g, 4.6 mmol) and sodium acetate (200 mg) in methanol/methylene chloride (3:1, 120 mL) was cooled to −78 °C under nitrogen. Ozone was bubbled through the reaction mixture for 6 min, at which time a blue color was observed. Nitrogen was bubbled through the solution for 3 min, and dimethyl sulfide (4 mL) was added dropwise. The reaction was stirred for 5 min, treated with sodium borohydride (3.4 g), and warmed carefully to 0 °C. Aqueous workup (CH_2Cl_2) and silica gel chromatography (flash silica, 30%, 40% ethyl acetate/hexanes)

yielded the primary alcohol **17** as a white crystalline solid (1.15 g, 2.56 mmol, 56% yield). An analytical sample was obtained by recrystallization from ether/hexanes; white needles, mp 51–52 °C. IR (neat): 3438 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.31 (3 H, d, J = 6.6 Hz), 1.96 (1 H, dd, J = 3.6, 8.6 Hz), 3.69 (1 H, ddd, J = 4.7, 8.6, 11.6 Hz), 3.90 (1 H, dd, J = 4.2, 6.0 Hz), 4.01 (1 H, m), 4.12 (1 H, ddd, J = 4.6, 4.7, 7.7 Hz). ^{13}C NMR ($CDCl_3$): δ 15.32. MS (FAB, NaI): 471 amu (M + Na). $[\alpha]_D$: −18.3° (c 1.55, $CHCl_3$). Anal. Calcd for $C_{28}H_{32}O_5$: C, 74.97; H, 7.19. Found: C, 74.99; H, 7.21.

Trisaccharide Aldol Products 19 and 20. The primary alcohol **17** (recrystallized from ethyl acetate/hexanes, 70 mg, 0.151 mmol) was oxidized by the usual Swern procedure. Silica gel chromatography (nonflash silica, 15%, 20% ethyl acetate/hexanes) yielded the aldehyde as a clear colorless oil. A stirred solution of HMDS (43 μL, 0.205 mmol) in toluene (0.5 mL) at −78 °C under argon was treated with n-BuLi (2.3 M in hexanes, 83 μL, 0.192 mmol). The reaction mixture was stirred at −78 °C for 5 min and 0 °C for 15 min. The mixture was cooled to −78 °C, and a solution of the ketone **15** (50 mg, 0.064 mmol) was added dropwise, followed by TMEDA (100 μL). The reaction mixture was stirred at −78 °C for 35 min. A solution of $MgBr_2$ (0.25 M in THF, 0.77 mL, 0.192 mmol) was added, and the mixture was stirred for 5 min. A solution of the aldehyde (55 mg, 0.122 mmol) was added dropwise. The reaction was stirred for 20 min at −78 °C and quenched with saturated NH_4Cl. Aqueous workup (EtOAc) and size exclusion chromatography (JAI LC-908, chloroform) yielded a mixture of the aldol products **19** and **20** as a clear colorless oil (2:1 mixture of diasteriomers, 52.1 mg, 67% yield). The aldol products were carried on as a mixture for preparative purposes. The diasteriomers could be separated by preparative TLC (20% ethyl acetate/hexanes) for analytical purposes. **C.α′ *S* Isomer 19.** IR (neat): 3540, 1704 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.30 (3 H, d, J = 6.9 Hz), 1.83–1.95 (2 H), 2.26 (1 H, m), 2.57 (1 H, d, J = 11.6 Hz), 3.33 (3 H, s), 3.37 (1 H, dd, J = 2.0, 9.9 Hz), 3.55 (1 H, dd, J = 3.5, 9.1 Hz), 3.77–3.79 (2 H), 3.97 (1 H, ddd, J = 1.8, 9.4, 11.6 Hz), 4.06 (1 H, dq, J = 6.9, 6.9 Hz), 4.27 (1 H, dd, J = 1.1, 9.4 Hz). ^{13}C NMR ($CDCl_3$): δ 214.17. HRMS (FAB, NaI): calcd for $C_{77}H_{84}O_{14}$ (M + Na) 1255.5760, found 1255.5830. $[\alpha]_D$: −5.0° (c 1.33, $CHCl_3$). **C.α′ *R* Isomer 20.** IR (neat): 3495, 1719 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.24 (3 H, d, J = 6.8 Hz), 1.84 (1 H, br dd, J = 9.0, 13.8 Hz), 2.23 (1 H, m), 2.36 (1 H, br dd, J = 6.7, 13.8 Hz), 3.04 (1 H, d, J = 1.9 Hz), 3.11 (1 H, dd, J = 5.9, 9.4 Hz), 3.35 (3 H, s), 3.55 (1 H, dd, J = 3.5, 9.2 Hz), 4.05 (1 H, dd, J = 3.5, 3.9 Hz), 4.16 (1 H, dq, J = 5.0, 6.8 Hz), 4.43 (1 H, m), 4.67 (1, H, d, J = 3.5 Hz). ^{13}C NMR ($CDCl_3$): δ 208.94. HRMS (FAB, NaI): calcd for $C_{77}H_{84}O_{14}$ (M + Na) 1255.5760, found 1255.5830. $[\alpha]_D$: −15.4° (c 1.13, $CHCl_3$).

Trisaccharide Enones 21 and 22. A stirred solution of the mixture of aldol products **19**, **20** (31.1 mg, 0.025 mmol), and triethylamine (0.4 mL) in ether (3 mL) at 0 °C under argon was treated with methanesulfonyl chloride (100 μL, 1.29 mmol). The reaction mixture was stirred at 0 °C for 30 min. The reaction was quenched with distilled water and stirred for 1 h. Aqueous workup gave the crude mesylate which was taken up in THF (2.5 mL) and cooled to −78 °C. Ammonia (2.5 mL) was condensed into the solution. The mixture was stirred without cooling for 30 min and concentrated in vacuo. Silica gel chromatography (flash silica, 25% ethyl acetate/hexanes) yielded a mixture of the enones **21** and **22** as a clear colorless oil (25.4 mg, 0.021 mmol, 84% yield). **Enone 21.** ^1H NMR ($CDCl_3$): δ 1.20 (3 H, d, J = 6.3 Hz), 1.64–1.69 (2 H), 2.14 (1 H, m), 3.30 (3 H, s), 3.57 (1 H, dd, J = 5.6, 9.4 Hz), 3.76 (1 H, d, J = 2.3 Hz), 3.80 (1 H, dd, J = 9.3, 9.5 Hz), 3.81 (1 H, m), 3.89 (1 H, ddd, J = 2.3, 5.3, 7.5 Hz), 3.95 (1 H, br d, J = 9.0 Hz), 4.46 (1 H, m), 6.75 (1 H, dd, J = 1.9, 6.0 Hz). **Enone 22.** ^1H NMR ($CDCl_3$): δ 1.23 (3 H, d, J = 6.7 Hz), 1.82 (1 H, ddd, J = 2.8, 10.3, 14.7 Hz), 2.05 (1 H, ddd, J = 2.3, 5.5, 14.7 Hz), 2.22 (1 H, m), 3.28 (3 H, s), 3.69–3.74 (2 H), 3.75–3.81 (2 H), 3.92–3.99 (2 H), 4.05 (1 H, dd, J = 3.4, 6.0 Hz), 4.07 (1 H, br d, J = 10.0 Hz), 5.16 (1 H, dd, J = 3.1, 8.3 Hz), 6.06 (1 H, dd, J = 1.7, 8.4 Hz).

Trisaccharide Ketone 23. A stirred solution of tributyltin hydride (0.5 mL) and AIBN (10 mg) in benzene (15 mL) was heated to reflux. A solution of the mixture of enones **21** and **22** (20 mg, 0.0166 mmol) in benzene (1.5 mL) was added dropwise, and the reaction mixture was stirred at reflux for 10 min. The reaction was cooled to room temperature, applied to a silica gel column, and eluted with 25% ethyl acetate/hexanes. Preparative TLC (flash silica, 20% ethyl acetate/hexanes) yielded the trisaccharide ketone **23** as a clear colorless oil (17.1 mg, 0.0140 mmol, 85% yield). IR (neat): 1716 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.08 (3 H, d, J = 6.3 Hz), 1.54 (1 H, br dd, J = 11.0, 13.0 Hz), 1.73 (1 H, br dd, J = 10.8, 14.5 Hz), 1.82 (1 H, br dd, J = 11, 13 Hz) 1.98 (1 H, br dd, J = 3.7, 14.5 Hz), 2.20 (1 H, m), 3.12 (1 H, ddd, J = 1.0, 10.0, 11.0 Hz), 3.27 (3 H, s), 3.34 (1 H, br dd, J = 10.0, 10.3 Hz), 3.80 (1 H, s), 3.89 (1 H, m), 3.94 (1 H, br d, J = 10.9 Hz), 4.29 (1 H, m). ^{13}C NMR ($CDCl_3$): δ 210.21. HRMS (FAB, NaI): calcd for $C_{77}H_{84}O_{13}$ (M + Na) 1239.5810, found 1239.5820. $[\alpha]_D$: −33.0° (c 1.62, $CHCl_3$).

Heptabenzyl Trisaccharide 24. A stirred solution of the trisaccharide ketone **23** (11.2 mg, 9.3 μmol) in methanol (3.0 mL) at 0 °C under argon was treated with sodium borohydride (10 mg, 0.026 mmol). The reaction mixture was stirred at 0 °C for 30 min. Aqueous workup and preparative TLC (30% ethyl acetate/hexanes) yielded the trisaccharide alcohol **24** as a clear colorless oil (11.1 mg, 9.2 mmol, 99% yield). IR (neat): 3481 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.11 (3 H, d, J = 6.4 Hz), 1.44–1.54 (2 H), 1.60–1.70 (2 H), 1.88 (1 H, br dd, J = 5.9, 13.9 Hz), 2.05 (1 H, m), 2.55 (1 H, d, J = 9.4 Hz), 3.14 (1 H, br dd, J = 9.8, 9.9 Hz), 3.30 (3 H, s), 3.42 (1 H, ddd, J = 3.2, 9.4, 10.5 Hz), 3.46 (1 H, dd, J = 5.5, 8.0 Hz), 3.52 (1 H, dd, J = 5.5, 8.9 Hz), 3.68 (1 H, br q, J = 6.4 Hz), 3.72 (1 H, br d, J = 3.2 Hz), 3.76 (1 H, dd, J = 9.2, 10.7 Hz), 3.86 (1 H, br dd, J = 5.3, 8.9 Hz), 3.96 (1 H, ddd, J = 2.7, 3.0, 10.9 Hz), 4.25 (1 H, ddd, J = 4.5, 5.3, 9.5 Hz). For ^1H NMR in C_6D_6, see supplementary material. ^{13}C NMR ($CDCl_3$): δ 16.10. HRMS (FAB, NaI): calcd for $C_{77}H_{86}O_{13}$ (M + Na) 1241.5970, found 1241.5930. $[\alpha]_D$: −20.1° (c 1.14, $CHCl_3$).

Trisaccharide Polyol 2. A stirred solution of the protected trisaccharide **24** (10.6 mg, 8.7 μmol) in methanol (5 mL) was hydrogenated over Pearlman's catalyst (11 mg) at 1 atm for 24 h. The reaction mixture was filtered through Celite and concentrated in vacuo to yield the trisaccharide polyol **2** as a clear colorless oil (4.84 mg). An analytical sample was obtained by chromatography on TSK G3000S polystyrene gel. IR (Neat): 3354, 2930, 1070 cm^{-1}. ^1H NMR (2.5% CD_3OD/C_5D_5N): δ 1.57 (3 H, d, J = 6.5 Hz), 1.98 (1 H, ddd, J = 4.0, 9.5, 15.1 Hz), 2.26 (1 H, dddd, J = 3.7, 4.0, 10.9, 10.9 Hz), 2.37 (1 H, ddd, J = 4.7, 5.5, 14.7 Hz), 2.46 (1 H, dddd, J = 2.3, 5.5, 9.9, 10.1 Hz), 2.53 (1 H, ddd, J = 2.3, 9.8, 14.7 Hz), 2.78 (1 H, br dd, J = 3.7, 15.1 Hz), 3.45 (3 H, s), 3.75 (1 H, br dd, J = 4.1, 7.6 Hz), 3.89 (1 H, br dd, J = 9.5, 10.1 Hz), 3.99 (1 H, dd, J = 2.9, 9.9 Hz), 3.99 (1 H, dd, J = 3.6, 9.3 Hz), 4.06 (1 H, dd, J = 5.7, 11.6 Hz), 4.11 (1 H, dd, J = 4.1, 11.5 Hz), 4.18 (1 H, br d, J = 2.9 Hz), 4.19 (1 H, dd, J = 2.2, 2.4 Hz), 4.36 (1 H, dd, J = 2.4, 8.7 Hz), 4.37–4.42 (3 H), 4.42 (1 H, dd, J = 7.6, 11.5 Hz), 4.44 (1 H, dq, J = 2.2, 6.5 Hz), 4.66 (1 H, dd, J = 5.2, 8.7 Hz), 4.96 (1 H, ddd, J = 4.7, 5.2, 9.8 Hz), 5.11 (1 H, d, J = 3.6 Hz). ^{13}C NMR (CD_3OD): δ 16.60, 24.98, 30.70, 40.79, 42.35, 55.35, 63.59, 64.15, 69.30, 69.94, 70.25, 71.54, 72.01, 72.56, 73.73, 74.58, 75.24, 76.13, 78.27, 80.26, 101.39. HRMS (FAB, neg): calcd for $C_{21}H_{33}O_{13}$ (M − H) 497.2234, found 497.2242. $[\alpha]_D$: +14.1° (c 0.31, CH_3OH).

Heptabenzyl 3′-Deoxy Trisaccharide 27. A stirred solution of the trisaccharide alcohol **24** (12.8 mg, 11.6 μmol) in dry THF (1.5 mL) at 0 °C under argon was treated with NaH (50% oil dispersion, 25 mg, 0.5 mmol). The reaction mixture was stirred for 15 min. Carbon disulfide (25 μL, 0.42 mmol) was added, and the mixture was stirred for 1 h. The reaction was treated with methyl iodide (50 μL, 0.80 mmol), stirred for 1 h, and quenched with saturated NH_4Cl. Aqueous workup (ether) yielded the crude xanthate which was azeotroped with toluene and used without further purification. A solution of the xanthate (11.6 μmol), tributyltin hydride (250 μL, 0.93 mmol), and AIBN (cat.) in toluene (1.5 mL) under argon was heated rapidly to reflux. The solution was stirred for 10 min and cooled to room temperature. The mixture was applied to a flash silica gel column and eluted with toluene followed by ether to yield an oil. Preparative TLC (0.5 mm, 25% ethyl acetate/hexanes) yielded the 3′-deoxy trisaccharide **27** as a clear colorless oil (10.0 mg, 9.2 μmol, 80% yield). IR (neat): 2865 cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.85–1.00 (2 H), 1.13 (3 H, d, J = 6.3 Hz), 1.50 (1 H, ddd, J = 2.4, 10.5, 14.8 Hz), 1.73 (1 H, m), 1.86 (1 H, ddd, J = 3.0, 11.4, 14.6 Hz), 2.05 (1 H, br dd, J = 5.0, 14.8 Hz), 2.17 (1 H, m), 2.36 (1 H, ddd, J = 3.0, 3.1, 14.0

Hz), 3.21 (1 H, br dd, J = 10.5, 9.5 Hz), 3.26 (3 H, s), 3.72 (1 H, dd, J = 4.0, 10.8 Hz), 3.82 (1 H, dd, J = 9.3, 10.4 Hz), 3.91 (1 H, m), 4.02–4.09 (2 H). ^{1}H NMR (C_6D_6): see supplementary material. ^{13}C NMR ($CDCl_3$): δ 31.38. HRMS (FAB, NaI): calcd for $C_{77}H_{86}O_{12}$ (M + Na) 1225.6020, found 1225.5950. $[\alpha]_D$: −38.6° (c 1.39, $CHCl_3$).

3′-Deoxy Trisaccharide Polyol 4. The protected 3′-deoxy trisaccharide **27** (13.0 mg, 10.8 μmol) was deprotected by the same procedure as the 3-hydroxy compound **24** to yield the trisaccharide polyol **4** as a clear colorless oil (6.46 mg). An analytical sample was obtained by chromatography on TSK G3000S polystyrene gel. IR (neat): 3330, 2926, 1451, 1070 cm^{-1}. ^{1}H NMR (CD_3OD): δ 1.13 (1 H, ddd, J = 3.0, 11.0, 14.5 Hz), 1.22 (3 H, d, J = 6.5 Hz), 1.32 (1 H, ddd, J = 2.8, 11.0, 13.8 Hz), 1.61 (1 H, ddd, J = 3.6, 9.4, 15.1 Hz), 1.72 (1 H, dddd, J = 3.6, 4.0, 10.7, 10.8 Hz), 1.78 (1 H, m), 1.93 (1 H, ddd, J = 2.6, 12.1, 14.5 Hz), 2.05 (1 H, br dd, J = 4.0, 15.1 Hz), 2.17 (1 H, ddd, J = 3.6, 3.7, 13.8 Hz), 3.27 (1 H, br dd, J = 9.1, 9.4 Hz), 3.38 (3 H, s), 3.38 (1 H), 3.57 (1 H, dd, J = 4.1, 11.7 Hz), 3.60–3.69 (6 H), 3.74 (1 H, br s), 3.76–3.82 (2 H), 3.88 (1 H, dd, J = 5.7, 8.9 Hz), 3.89 (1 H, dd, J = 1.9, 11.7 Hz), 4.01 (1 H, ddd, J = 3.0, 5.7, 12.1 Hz), 4.68 (1 H, d, J = 3.7 Hz). ^{13}C NMR (CD_3OD): δ 16.67, 27.41, 30.89, 31.74, 37.56, 42.11, 55.36, 64.06, 64.19, 66.10, 68.48, 69.93, 71.66, 72.05, 72.53, 72.86, 73.90, 75.23, 81.04, 81.56, 101.42. HRMS (FAB, neg): calcd for $C_{28}H_{38}O_{12}$ (M − H) 481.2285, found 481.2275. $[\alpha]_D$: −12.3° (c 0.37, CH_3OH).

5-Deshydroxymethyl Methyl Ketone 32. The 5-deshydroxymethyl primary alcohol **25** (1.35 g, 3.63 mmol) was converted to the methyl ketone **32** (1.17 g, 3.05 mmol, 84% yield; amorphous white solid) by the same procedure as the parent 5-hydroxymethyl compound. IR (neat): 1715 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.04 (3 H, s), 2.07 (1 H, dd, J = 8.6, 16.8 Hz), 2.30 (1 H, m), 2.65 (1 H, dd, J = 4.3, 16.8 Hz), 3.33 (1 H, dd, J = 11.3, 11.3 Hz), 3.37 (3 H, s), 3.51–3.58 (2 H), 4.63 (1 H, d, J = 3.1 Hz). ^{13}C NMR ($CDCl_3$): δ 206.96. HRMS (FAB, NaI): calcd for $C_{23}H_{28}O_5$ (M + Na) 407.1835, found 407.1819. $[\alpha]_D$: +10.2° (c 2.02, $CHCl_3$).

5-Deshydroxymethyl Monocyclic Aldol Products 33 and 34. A stirred solution of HMDS (305 μL, 1.44 mmol) in toluene (2 mL) at −78 °C under argon was treated with n-BuLi (2.49 M in hexanes, 550 μL, 1.37 mmol). The reaction mixture was stirred at −78 °C for 5 min and 0 °C for 15 min. The mixture was cooled to −78 °C, and a solution of the ketone **32** (502.0 mg, 1.31 mmol) in toluene (3 mL) was added dropwise. The reaction mixture was stirred at −78 °C for 20 min. A solution of the aldehyde (1.9 mmol) in toluene (3.25 mL) was added dropwise. The reaction was stirred for 20 min and quenched with saturated NH_4Cl. The mixture was diluted with ethyl acetate and washed with saturated NH_4Cl and brine. The organic layer was dried over $MgSO_4$ and concentrated in vacuo. Size exclusion chromatography (JAI LC-908, $CHCl_3$) yielded a mixture of the aldol products **33** and **34** as a clear colorless oil (755.6 mg, 0.946 mmol, 72% yield). The diasteriomers could be separated by silica gel chromatography (flash silica, 20% ethyl acetate/hexanes). **Erythro Diasteriomer 33.** IR (neat): 3464, 1709 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.05 (3 H, s), 0.06 (3 H, s), 0.87 (9 H, s), 2.07 (1 H, dd, J = 9.1, 17.2 Hz), 2.28 (1 H, m), 2.44 (1 H, dd, J = 8.7, 16.0 Hz), 2.63 (1 H, dd, J = 3.1, 16.0 Hz), 2.68 (1 H, dd, J = 3.7, 17.2 Hz), 3.28 (1 H, dd, J = 11.3, 11.3 Hz), 3.35 (1 H), 3.36 (3 H, s), 3.65 (1 H, d, J = 2.6 Hz), 3.69 (1 H, dd, J = 4.0, 9.8 Hz), 4.09 (1 H, ddd, J = 3.9, 4.0, 6.4 Hz); 4.19 (1 H, m). ^{13}C NMR ($CDCl_3$): δ 209.00. HRMS (FAB, NaI): calcd for $C_{47}H_{62}O_9Si$ (M + Na) 821.4061, found 821.4029. $[\alpha]_D$: +20.9° (c 2.05, $CHCl_3$). **Threo Diasteriomer 34.** IR (neat): 3497, 1711 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.03 (3 H, s), 0.04 (3 H, s), 0.87 (9 H, s), 1.97 (1 H, dd, J = 8.9, 16.9 Hz), 2.25 (1 H, m), 2.34 (1 H, dd, J = 3.9, 16.2 Hz), 2.55 (1 H, dd, J = 8.9, 16.2 Hz), 2.62 (1 H, dd, J = 4.1, 16.9 Hz), 2.90 (1 H, d, J = 5.2 Hz), 3.24–3.30 (2 H), 3.37 (3 H, s), 3.61 (1 H, dd, J = 3.8, 10.2 Hz), 4.03 (1 H, ddd, J = 3.9, 5.3, 5.4 Hz), 4.19 (1 H, m), 4.62 (1 H, d, J = 3.1 Hz). ^{13}C NMR ($CDCl_3$): δ 208.18. HRMS (FAB, NaI): calcd for $C_{47}H_{62}O_9Si$ (M + Na) 821.4061, found 821.4034. $[\alpha]_D$: +14.2° (c 0.93, $CHCl_3$).

5-Deshydroxymethyl Disaccharide Thioketals 35 and 36. The 5-deshydroxymethyl erythro aldol product **33** (180.2 mg, 0.228 mmol) was converted to the galacto thioketal **35** (128.7 mg, 0.180 mmol, 79% yield; clear colorless oil) by the same procedure as the parent 5-hydroxymethyl compound. The 5-deshydroxymethyl threo aldol product **34** (170.5 mg, 0.216 mmol) was converted to the gulo thioketal **36** (120.0 mg, 0.168 mmol, 78% yield; clear colorless oil) by the same procedure. **C.3′ Equatorial (Galacto) Isomer 35.** IR (neat): 3457 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.65–1.71 (2 H), 1.73 (1 H, d, J = 10.5 Hz), 1.83 (3 H, s), 3.34 (1 H, dd, J = 11.4, 11.4 Hz), 3.38 (3 H, s), 3.48 (1 H, dd, J = 9.3, 9.9 Hz), 3.52 (1 H, dd, J = 3.3, 9.3 Hz), 3.57 (1 H, dd, J = 6.2, 9.3 Hz), 3.66 (1 H, dd, J = 7.3, 9.3 Hz), 3.73 (1 H, m), 3.88 (1 H, dd, J = 5.2, 11.5 Hz), 4.03 (1 H, m), 4.06 (1 H, dd, J = 6.5, 7.0 Hz). ^{13}C NMR ($CDCl_3$): δ 9.61. HRMS (FAB, NaI): calcd for $C_{42}H_{50}O_8S$ (M + Na) 737.3124, found 737.3098. $[\alpha]_D$: +67.5° (c 0.87, $CHCl_3$). **C.3′ Axial (Gulo) Isomer 36.** IR (neat): 3453 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.57 (1 H, dd, J = 1.1, 15.3 Hz), 1.64 (1 H, dd, J = 9.4, 14.7 Hz), 1.93 (3 H, s), 2.01–2.10 (2 H), 2.48 (1 H, dd, J = 4.1, 15.3 Hz), 3.34 (1 H, dd, J = 11.4, 11.4 Hz), 3.37 (1 H, br s), 3.38 (3 H, s), 3.47 (1 H, dd, J = 9.3, 9.8 Hz), 3.51 (1 H, dd, J = 3.2, 9.3 Hz), 3.57 (1 H, dd, J = 5.2, 9.9 Hz), 3.63 (1 H, dd, J = 6.7, 9.9 Hz), 3.89 (1 H, dd, J = 5.2, 11.4 Hz), 3.93 (1 H, d, J = 10.9 Hz), 3.99 (1 H, m), 4.21 (1 H, ddd, J = 1.1, 5.4, 6.5 Hz). ^{13}C NMR ($CDCl_3$): δ 9.97. HRMS (FAB, NaI): calcd for $C_{42}H_{50}O_8S$ (M + Na) 737.3124, found 737.3088. $[\alpha]_D$: +50.8° (c 1.00, $CHCl_3$).

5-(Deshydroxymethyl)-2′-deoxy Disaccharides 37 and 38. The 5-deshydroxymethyl galacto thioketal **35** (120.0 mg, 0.168 mmol) was converted to the galacto disaccharide **37** (88.9 mg, 0.133 mmol, 79% yield; clear colorless oil) by the same procedure as the parent 5-hydroxymethyl compound. The 5-deshydroxymethyl gulo thioketal **36** (100.0 mg, 0.140 mmol) was converted to the gulo disaccharide **38** (78.8 mg, 0.118 mmol, 84% yield; clear colorless oil) by the same procedure. **C.3′ Equatorial (Galacto) Isomer 37.** IR (neat): 3460 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.26 (1 H, ddd, J = 4.5, 8.1, 14.2 Hz), 1.47 (1 H, ddd, J = 11.8, 11.8, 11.8 Hz), 1.61 (1 H, br dd, J = 4.5, 12.0 Hz), 1.78 (1 H, d, J = 10.3 Hz), 1.87 (1 H, ddd, J = 4.2, 8.1, 14.2 Hz), 2.00 (1 H, m), 3.31 (1 H, m), 3.36 (3 H, s), 3.41–3.47 (2 H), 3.50–3.65 (6 H), 3.71 (1 H, br d, J = 3.0 Hz), 4.61 (1 H, d, J = 3.5 Hz). ^{13}C NMR ($CDCl_3$): δ 34.08. HRMS (FAB, NaI): calcd for $C_{41}H_{48}O_8$ (M + Na) 691.3247, found 691.3234. $[\alpha]_D$: +17.6° (c 1.77, $CHCl_3$). **C.3′ Axial (Gulo) Isomer 38.** IR (neat): 3462 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.24 (1 H, ddd, J = 4.2, 8.2, 14.2 Hz), 1.33 (1 H, d, J = 3.0 Hz), 1.41 (1 H, br d, J = 4.3 Hz), 1.78 (1 H, ddd, J = 2.8, 11.4, 14.2 Hz), 1.86 (1 H, ddd, J = 4.4, 8.5, 14.3 Hz), 2.03 (1 H, m), 3.26 (1 H, br s), 3.35 (3 H, s), 3.46 (1 H, dd, J = 11.5, 11.5 Hz), 3.51 (1 H, dd, J = 3.3, 9.1 Hz), 3.61 (1 H, dd, J = 5.1, 11.5 Hz), 3.75 (1 H, m), 3.92 (1 H, ddd, J = 1.0, 6.4, 6.5 Hz), 4.01 (1 H, m), 4.61 (1 H, d, J = 3.3 Hz). ^{13}C NMR ($CDCl_3$): δ 34.26. HRMS (FAB, NaI): calcd for $C_{41}H_{48}O_8$ (M + Na) 691.3247, found 691.3226. $[\alpha]_D$: +8.5° (c 1.92, $CHCl_3$).

5-(Deshydroxymethyl)-2′-deoxy Disaccharide Ketone 39. The 5-deshydroxymethyl galacto disaccharide **37** (71.1 mg, 0.106 mmol) was converted to the disaccharide ketone **39** (64.6 mg, 0.097 mmol, 91% yield; clear colorless oil) by the same procedure as the parent 5-hydroxymethyl compound. The 5-deshydroxymethyl gulo disaccharide **38** (59.5 mg, 0.0890 mmol) was converted to the identical ketone (52.8 mg, 0.792 mmol, 89% yield; clear colorless oil) by the same procedures. IR (neat): 1723 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.34 (1 H, ddd, J = 4.1, 8.3, 14.4 Hz), 1.94 (1 H, ddd, J = 4.1, 8.0, 14.4 Hz), 2.03 (1 H, m), 2.15 (1 H, br d, J = 13.2 Hz), 2.76 (1 H, dd, J = 11.8, 13.2 Hz), 3.35 (3 H, s), 3.44 (1 H, dd, J = 11.5, 11.5 Hz), 3.52 (1 H, dd, J = 3.1, 9.0 Hz), 3.67–3.70 (2 H), 4.62 (1 H, d, J = 3.0 Hz). ^{13}C NMR ($CDCl_3$): δ 206.79. HRMS (FAB, NaI): calcd for $C_{41}H_{46}O_8$ (M + Na) 689.3090, found 689.3105. $[\alpha]_D$: +3.1° (c 1.40, $CHCl_3$).

5-Deshydroxymethyl Trisaccharide Aldol Products 40 and 41. The 5-deshydroxymethyl disaccharide ketone **39** (26 mg, 0.039 mmol) was converted to the aldol products **40** and **41** (4:1 mixture of diasteriomers, 29.1 mg, 0.0261 mmol, 67% yield; clear colorless oil) by the same procedure as the parent 5-hydroxymethyl compound. **C.α′ *S* Isomer 40.** IR (neat): 3541, 1707 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.29 (3 H, d, J = 6.8 Hz), 1.58 (1 H, ddd, J = 1.5, 11.5, 13.0 Hz), 2.13 (1 H, ddd, J = 2.4, 10.0, 13.0 Hz), 2.19 (1 H, m), 2.62 (1 H, d, J = 10.9 Hz), 3.37 (1 H), 3.38 (3 H, s), 3.47 (1 H, dd, J = 11.5, 11.6 Hz), 3.51 (1 H, dd, J = 3.3, 9.3 Hz), 3.55 (1 H, dd, J = 9.3, 9.7 Hz), 3.64–3.67 (2 H), 3.68–3.75 (2 H), 3.85 (1 H, dd, J = 3.1, 5.5 Hz), 3.88 (1 H, dd, J = 1.5, 5.5 Hz), 3.96 (1 H, ddd, J = 1.6, 9.4, 10.8 Hz), 4.05 (1 H, dq, J = 6.8, 6.8 Hz), 4.61

(1 H, d, J = 3.3 Hz). ^{13}C NMR ($CDCl_3$): δ 213.59. HRMS (FAB, NaI): calcd for $C_{69}H_{76}O_{13}$ (M + Na) 1135.5180, found 1135.5230. $[\alpha]_D$: −9.1° (c 0.98, $CHCl_3$). **C.α′ *R* Isomer 41.** IR (neat): 3483, 1716 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.24 (3 H, d, J = 6.7 Hz), 1.85 (1 H, ddd, J = 1.5, 11.2, 14.1 Hz), 2.13 (1 H, ddd, J = 2.9, 9.9, 14.1 Hz), 2.22 (1 H, m), 3.09 (1 H, dd, J = 5.7, 9.4 Hz), 3.19 (1 H, d, J = 2.8 Hz), 3.35 (3 H, s), 3.43 (1 H, dd, J = 11.5, 11.5 Hz), 3.50 (1 H, dd, J = 3.3, 9.2 Hz), 3.55 (1 H, dd, J = 9.2, 9.8 Hz), 3.75 (1 H, ddd, J = 1.9, 6.0, 6.0 Hz), 3.77 (1 H, dd, J = 3.1, 4.5 Hz), 3.82 (1 H, d, J = 1.9 Hz), 3.83 (1 H, dd, J = 3.4, 5.6 Hz), 3.91 (1 H, dd, J = 3.1, 5.6 Hz), 4.05 (1 H, dd, J = 3.4, 4.0 Hz), 4.16 (1 H, dq, J = 4.5, 6.7 Hz). ^{13}C NMR ($CDCl_3$): δ 209.17. HRMS (FAB, NaI): calcd for $C_{69}H_{76}O_{13}$ (M + Na) 1135.5180, found 1135.5240. $[\alpha]_D$: −20.9° (c 1.08, $CHCl_3$).

5-Deshydroxymethyl Trisaccharide Ketone 43. The mixture of 5-deshydroxymethyl trisaccharide aldol products **40** and **41** (29.1 mg, 0.0261 mmol) was converted to the enones **42a,b** (22.2 mg, 0.0203 mmol, 78% yield; clear colorless oil) by the same procedure as the parent 5-hydroxymethyl compound. A mixture of 5-deshydroxymethyl trisaccharide enones **42a,b** (14 mg, 0.0128 mmol) was converted to the trisaccharide ketone **43** (10.2 mg, 9.3 μmol, 73% yield; clear colorless oil) by the same procedure as the parent 5-hydroxymethyl compound. **Enones 42a, 42b.** See supplementary material. **Ketone 43.** IR (neat): 1718 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.02 (3 H, d, J = 6.3 Hz), 1.45–1.55 (2 H), 1.86 (1 H, br dd, J = 11.7, 12.0 Hz), 2.02–2.11 (2 H), 3.29 (1 H, ddd, J = 1.5, 10.1, 11.5 Hz), 3.36 (1 H, ddd, J = 2.5, 6.9, 10.2 Hz), 3.39 (3 H, s), 3.77 (1 H, br s), 3.87 (1 H, dd, J = 5.0, 11.6 Hz), 4.04 (1 H, br dd, J = 5.6, 8.0 Hz), 4.32 (1 H, ddd, J = 2.3, 5.4, 11.7 Hz). ^{13}C NMR ($CDCl_3$): δ 211.00. HRMS (FAB, NaI): calcd for $C_{69}H_{76}O_{12}$ (M + Na) 1119.5230, found 1119.5260. $[\alpha]_D$: −24.5° (c 1.50, $CHCl_3$).

Heptabenzyl 5-Deshydroxymethyl Trisaccharide 26. The 5-deshydroxymethyl trisaccharide ketone **43** (15.0 mg, 0.0137 mmol) was converted to the trisaccharide alcohol **26** (12.8 mg, 0.0116 mmol, 85% yield; clear colorless oil) by the same procedure as the parent 5-hydroxymethyl compound. IR (neat): 3458 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.15 (3 H, d, J = 6.5 Hz), 1.36 (1 H, ddd, J = 2.3, 10.6, 14.2 Hz), 1.48 (1 H, ddd, J = 3.2, 7.1, 15.4 Hz), 1.75–1.83 (2 H), 1.92 (1 H, ddd, J = 2.8, 9.4, 14.2 Hz), 2.11 (1 H, m), 2.50 (1 H, d, J = 9.3 Hz), 3.13 (1 H, ddd, J = 2.3, 9.4, 9.4 Hz), 3.37 (3 H, s), 3.37 (1 H, dd, J = 11.5, 11.5 Hz), 3.64 (1 H, dd, J = 2.8, 8.2 Hz), 3.69 (1 H, dd, J = 5.1, 9.4 Hz), 3.72 (1 H, br d, J = 2.9 Hz), 3.82 (1 H, dq, J = 2.1, 6.5 Hz), 3.85 (1 H, m), 4.31 (1 H, ddd, J = 3.2, 4.0, 10.2 Hz). ^{1}H NMR (C_6D_6): see supplementary material. ^{13}C NMR ($CDCl_3$): δ 16.01. HRMS (FAB, NaI): calcd for $C_{69}H_{78}O_{12}$ (M + Na) 1121.5390, found 1121.5440. $[\alpha]_D$: −13.6° (c 1.22, $CHCl_3$).

5-Deshydroxymethyl Trisaccharide Polyol 3. The protected trisaccharide **26** (3.0 mg, 2.7 μmol) was deprotected by the same procedure as compound **2**, to yield the trisaccharide polyol **3** as a clear colorless oil (2.45 mg). An analytical sample was obtained by chromatography on TSK G3000S polystyrene gel. IR (neat): 3326, 2921, 2852, 1582, 1413, 1321, 1073, 1045 cm^{-1}. ^{1}H NMR (D_2O): δ 1.08 (3 H, d, J = 6.4 Hz), 1.46 (1 H, ddd, J = 1.0, 9.8, 14.9 Hz), 1.55–1.63 (2 H), 1.67 (1 H, ddd, J = 2.9, 10.5, 14.9 Hz), 1.73 (1 H, ddd, J = 1.0, 10.6, 13.3 Hz), 1.94 (1 H, m), 3.22 (1 H, ddd, J = 1.0, 10.5, 10.0 Hz), 3.36–3.45 (4 H), 3.53–3.62 (7 H) 3.81 (1 H, dd, J = 6.2, 9.7 Hz), 3.87 (1 H, br q, J = 6.4 Hz), 4.07 (1 H, m), 4.69 (1 H, d, J = 3.3 Hz). ^{13}C NMR (CD_3OD): δ 16.55, 24.57, 32.34, 40.58, 40.72, 55.48, 63.25, 69.41, 69.86, 70.31, 72.44, 73.22, 74.25, 75.19, 75.68, 77.89, 79.96, 102.03. MS (FAB, neg): 467 amu (M − H, rel intensity 9%). HRMS (FAB, NaI): calcd for $C_{20}H_{36}O_{12}$ (M − H) 467.2129, found 467.2116. $[\alpha]_D$: 0° (c 0.11, $CHCl_3$).

Heptabenzyl 3′-Deoxy-5-deshydroxymethyl Trisaccharide 28. The 5-deshydroxymethyl trisaccharide alcohol **26** (12.8 mg, 0.0116 mmol) was converted to the 3′ deoxy trisaccharide **28** (10.0 mg, 9.2 μmol, 80% yield; clear colorless oil) by the same procedure as the parent 5-hydroxymethyl compound. IR (neat): 2929 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.87–0.94 (2 H), 1.12 (3 H, d, J = 6.4 Hz), 1.39 (1 H, ddd, J = 2.4, 10.4, 14.2 Hz), 1.72–1.82 (2 H), 1.92 (1 H, ddd, J = 2.9, 9.0, 14.2 Hz), 2.09 (1 H, m), 2.36 (1 H, ddd, J = 2.8, 2.9, 14.1 Hz), 3.06 (1 H, ddd, J = 2.4, 9.0, 9.5 Hz), 3.37 (3 H, s), 3.41 (1 H, dd, J = 11.5, 11.5 Hz), 3.63 (1 H, dd, J = 6.3, 9.6 Hz), 3.73 (1 H, m), 3.74 (1 H, dd, J = 3.2, 11.5 Hz), 3.95 (1 H, m), 4.08 (1 H, ddd, J = 2.9, 5.1, 11.9 Hz). ^{1}H NMR (C_6D_6): see supplementary material. ^{13}C NMR ($CDCl_3$): δ 31.01. HRMS (FAB, NaI): calcd for $C_{69}H_{78}O_{11}$ (M + Na) 1105.5440, found 1105.5450. $[\alpha]_D$: −33.0° (c 0.94, $CHCl_3$).

3′-Deoxy-5-deshydroxymethyl Trisaccharide Polyol 5. The protected trisaccharide **28** (9.1 mg, 8.4 μmol) was deprotected by the same procedure as compound **2** to yield the trisaccharide polyol **5** as a clear colorless oil (5.0 mg). An analytical sample was obtained by chromatography on TSK G3000S polystyrene gel. IR (neat): 3358, 2929, 1653, 1364, 1191, 1067, 1042, 675 cm^{-1}. ^{1}H NMR (33% CD_3OD/D_2O): δ 1.14 (1 H, ddd, J = 3.0, 10.9, 14.8 Hz), 1.20 (3 H, d, J = 6.5 Hz), 1.42 (1 H, ddd, J = 2.7, 11.8, 14.3 Hz), 1.57 (1 H, ddd, J = 2.0, 9.6, 14.5 Hz), 1.71 (1 H, m), 1.78 (1 H, ddd, J = 3.2, 10.2, 14.5 Hz), 1.85 (1 H, ddd, J = 2.8, 12.1, 14.8 Hz), 2.02 (1 H, m), 2.12 (1 H, ddd, J = 3.4, 3.6, 14.3 Hz), 3.24 (1 H, ddd, J = 2.0, 10.1, 10.1 Hz), 3.38 (3 H, s), 3.45–3.52 (4 H), 3.63 (1 H, dd, J = 4.4, 11.7 Hz), 3.67 (1 H, dd, J = 7.7, 11.7 Hz), 3.69–3.75 (3 H), 3.83 (1 H, br q, J = 6.5 Hz), 3.84 (1 H, br s), 3.93 (1 H, dd, J = 6.2, 9.3 Hz), 4.07 (1 H, ddd, J = 3.0, 6.2, 12.1 Hz), 4.76 (1 H, d, J = 3.1 Hz). ^{13}C NMR ($CDCl_3$): δ 16.57, 27.12, 31.55, 32.40, 37.31, 40.39, 55.47, 63.48, 63.82, 66.18, 68.86, 70.04, 72.18, 72.74, 73.33, 75.25, 81.11, 81.32, 102.03. HRMS (FAB, NaI): calcd for $C_{20}H_{36}O_{11}$ (M + Na) 451.2179, found 451.2191. $[\alpha]_D$: −21.4° (c 0.25, $CHCl_3$).

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Supplementary Material Available: Complete spectroscopic data (IR, ^{1}H NMR, ^{13}C NMR, MS, HRMS, and ^{1}H NMR spectra) for all compounds (55 pages). This material is contained in many 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.