Synthesis of Protected Carbohydrate Derivatives through Homologation of Threose and Erythrose Derivatives with Chiral γ-Alkoxy Allylic Stannanes

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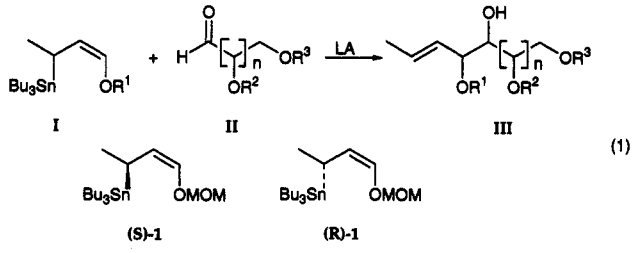
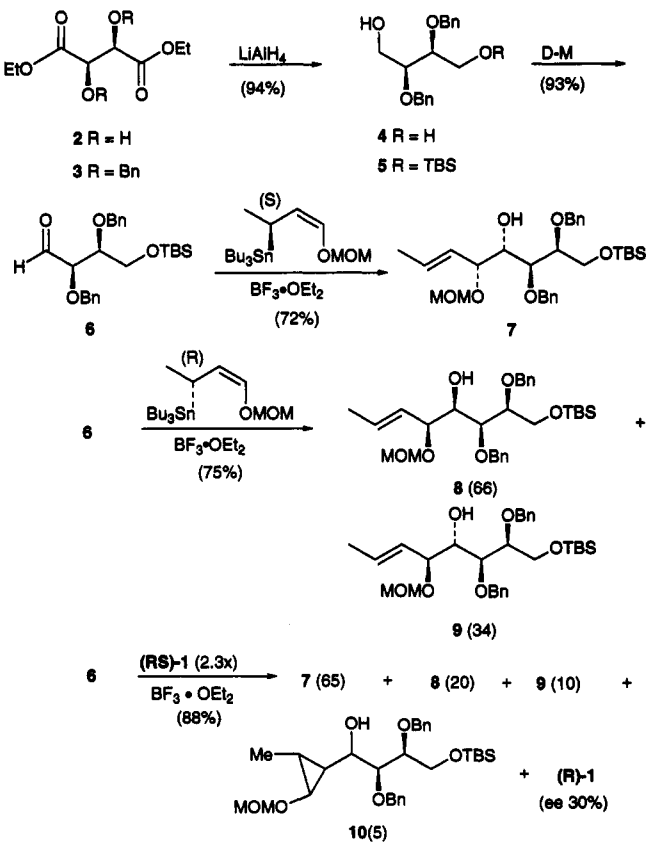
Additions of the γ-alkoxy allylic stannanes (*S*)-1 and (*R*)-1 and the racemate (*RS*)-1 to the threose and erythrose aldehyde derivatives **6** and **15** in the presence of BF_3·OEt_2 or $MgBr_2$·OEt_2 were examined in order to establish stereochemical preferences. It was found that (*S*)-1 and aldehyde **6** afforded the *syn,anti,syn* adduct **7** in the BF_3-promoted reaction, while (*R*)-1 and **6** gave the *syn,syn,syn* adduct **8** under $MgBr_2$ conditions. Likewise, (*S*)-1 and aldehyde **15** yielded the *syn,anti,anti* adduct **16** with BF_3, whereas (*R*)-1 and **15** led to the *syn,syn,anti* adduct **17** with $MgBr_2$. The $MgBr_2$-promoted reactions showed sufficient rate differences between the matched and mismatched stannanes to allow the use of racemic stannane (*RS*)-1 in just over 2-fold excess, whereupon the matched adducts **8** and **17** were favored by greater than 9:1 over the mismatched adducts. The major adducts **7**, **8**, **16**, and **17** were converted to the hexose derivatives **21**, **30/31**, **34**, and **39** by ozonolysis, selective deprotection, and refunctionalization. Adducts **16** and **17** were dihydroxylated with OsO_4–NMO to the deoxyoctose precursors **40/41** and **42/43**.

An increasing awareness of the vital role played by carbohydrates in biological processes has stimulated interest in the synthesis of mono- and oligosaccharides.[1] Several years ago, we described methodology for chain homologation of representative protected polyhydroxylated aldehydes, including pentabenzyl glucose, in which the chiral γ-OMOM allylic stannanes **I** were matched to the aldehyde partner **II** (eq 1).[2] Through use of BF_3·OEt_2



or $MgBr_2$·OEt_2 as Lewis acid (LA) promoters, we were able to secure products resulting from both Felkin–Ahn and chelation-controlled additions.[2] The present study on additions of alkoxystannanes (*S*)-1 and (*R*)-1 and the racemate (*RS*)-1 to threose and erythrose related aldehydes **6** and **15** was undertaken in order to evaluate the potential of the methodology for the stereoselective synthesis of C6 and C8 polyol precursors of carbohydrates.[3]

Additions of Stannanes (*S*)-1 and (*R*)-1 to Aldehydes 6 and 15. The protected threose **6** was prepared from (*R,R*)-diethyl tartrate **2** by reduction of the dibenzyl ether **3** with $LiAlH_4$ followed by monosilylation of the resulting diol **4** and Dess–Martin periodinane oxidation of the derived alcohol **5**.[4] Addition of the matched alkoxy allylic stannane (*S*)-1 in a BF_3-promoted reaction afforded the *syn,anti* adduct **7** in 72% yield.[2] The enantiomeric stannane (*R*)-1 led to a 2:1 mixture of the *syn,syn* and *anti,anti* products **8** and **9** in 75% yield.



When aldehyde **6** was allowed to react with an excess of racemic stannane (*RS*)-1, the *syn,anti*; *syn,syn*, and

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(1) *Cf.* (a) Danishefsky, S. J.; DeNinno, M. P. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 15. (b) Roush, W. R. In *Trends in Carbohydrate Synthesis*; Horton, D., Hawkins, L. D., McGarvey, G. J., Eds.; ACS Symposium Series 386; American Chemical Society: Washington, DC, 1989; p 242.

(2) Marshall, J. A.; Luke, G. P. *J. Org. Chem.* **1991**, *56*, 483. For a review of this area, see: Marshall, J. A. *Chemtracts—Org. Chem.* **1992**, 75.

(3) Nonoxygenated allyltin derivatives have also been employed for homologation of carbohydrates: (a) Jarosz, S.; Fraser-Reid, B. *J. Org. Chem.* **1989**, *54*, 4011. (b) Kim, E.; Gordon, D. M.; Schmid, W.; Whitesides, G. M. *J. Org. Chem.* **1993**, *58*, 5500.

(4) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155.

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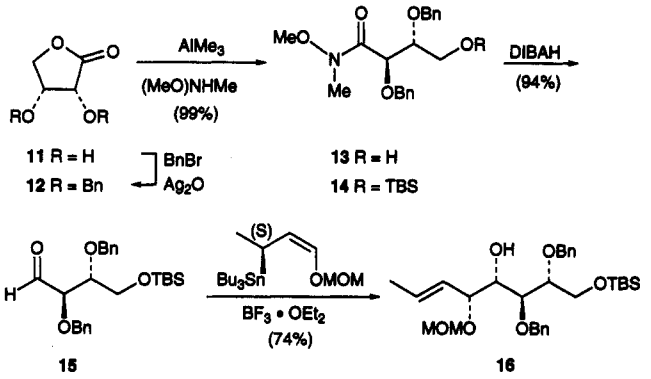
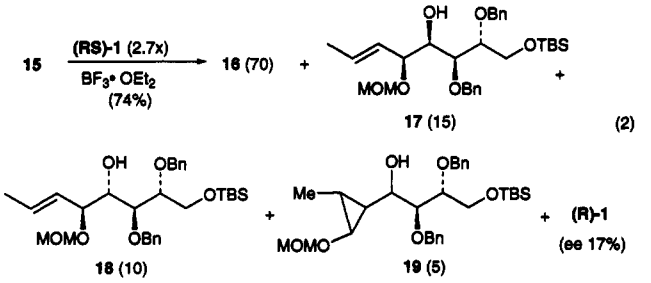
anti,anti adducts **7**, **8**, and **9** were obtained as a 65:20:10 mixture, along with a small amount of a product tentatively identified as cyclopropane **10** (5%). As expected, the recovered stannane **1** was enriched in the (*R*) enantiomer, consistent with a faster reaction between the matched stannane (*S*)-**1** and aldehyde **6**.

In order to probe the possible influence of configuration at the β-position of aldehydes such as **II** on the stereoselectivity of the addition reaction, we prepared the erythrose derivative **15**. This was achieved starting from D-erythronolactone **11** through benzylation[5] and conversion to the Weinreb amide **13** and then silylation and reduction with DIBAH.[6] Addition of stannane (*S*)-**1** in the presence of $BF_3{\cdot}OEt_2$ afforded the matched *syn,anti* adduct **16** in 74% yield as the sole product.



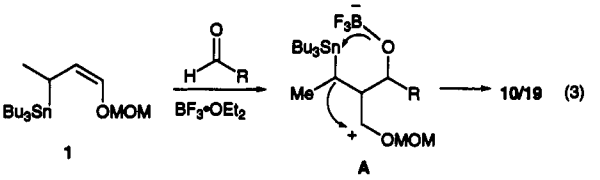
Reaction of aldehyde **15** with excess racemic stannane (*RS*)-**1** proceeded in 74% yield and afforded a 70:15:10 mixture of *syn,anti*, *syn,syn*, and *anti,anti* products **16**, **17**, and **18**, the first from the matched and the next two from the less favorable mismatched pairing of stannanes (*S*)-**1** and (*R*)-**1**, along with a trace of product tentatively identified as cyclopropane **19** (*ca.* 5%) (eq 2). The latter



(2)

two adducts could not be separated, so the structural assignment to **18** is made by analogy with the findings for aldehyde **6**. The formation of cyclopropane products from other stannanes and aldehydes is currently under investigation, and these findings will be disclosed in due course.

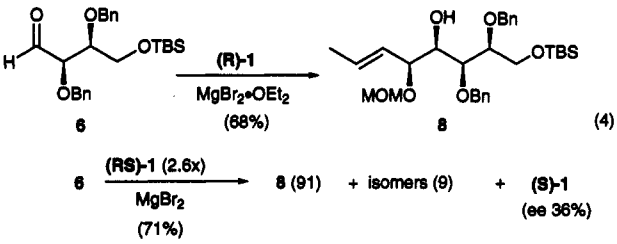
Cyclopropanes **10** and **19** could arise by enol ether-directed attack on the aldehyde and subsequent 1,3-elimination (eq 3).[7] To our knowledge, this type of product



(3)

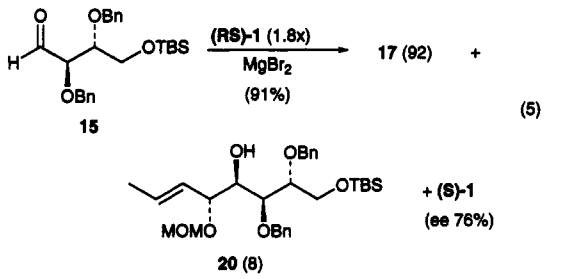
has not been previously identified in allylic stannane additions. The structures of the cyclopropanes were surmised from the ^1H NMR spectra of the mixtures. We could not purify these materials and were therefore unable to assign stereochemistry.

Employing stannane (*R*)-**1** in the matched $MgBr_2$-catalyzed addition, we obtained the *syn,syn* adduct **8** from aldehyde **6** in 68% yield.[2] Addition of excess (*RS*)-**1** led to a 91:9 mixture of the *syn,syn* adduct **8** and several other inseparable diastereomers (eq 4). In this case, the recovered stannane **1** was mainly the (*S*) enantiomer.



(4)

The $MgBr_2$-promoted addition of excess racemic alkoxy allylic stannane (*RS*)-**1** to aldehyde **15** led to a 92:8 mixture of *syn,syn* and *anti,syn* adducts **17** and **20** in 91% yield (eq 5). The minor adduct **20** is presumed to arise from

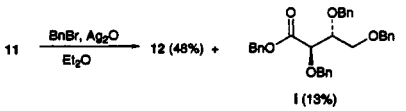


(5)

stannane (*S*)-**1**, the mismatched reagent.[2] As expected, the recovered stannane was enriched in the (*S*) enantiomer. When a 1.8-fold excess of (*RS*)-**1** was employed in this addition 94% of the aldehyde was consumed and we recovered stannane (*S*)-**1** of 76% ee.

Thus, we are able to efficiently prepare the *syn,anti,syn* and *syn,syn,syn* adducts **7** and **8** from the threose derivative **6** and the *syn,anti,anti* and *syn,syn,anti* adducts **16** and **17** from the erythrose analogue **15**. The β stereocenter of these aldehydes appears to exert little influence on the addition reactions.[8] In the case of the $MgBr_2$-promoted reactions, the rate difference between the matched and mismatched partners is sufficient to allow use of the racemic stannane to access the *syn,syn* adducts **8** and **17** (eqs 4 and 5).

(5) In addition to lactone **12** (38% yield), we isolated the perbenzylated ester **i** and the two possible monobenzylated lactones from this reaction. When the reaction was carried out in THF we obtained an appreciable amount of the monobenzyl ether of 1,4-butanediol.

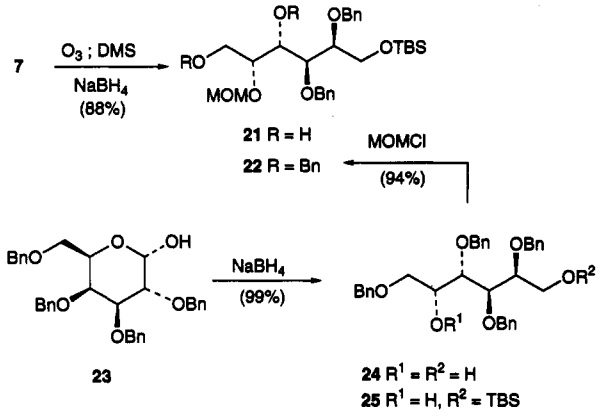


(6) (a) Basha, A.; Lipton, M.; Weinreb, S. M. *Tetrahedron Lett.* **1977**, 4171. (b) Nahm, S.; Weinreb, S. M. *Tetrahedron Lett.* **1981**, *22*, 3815.

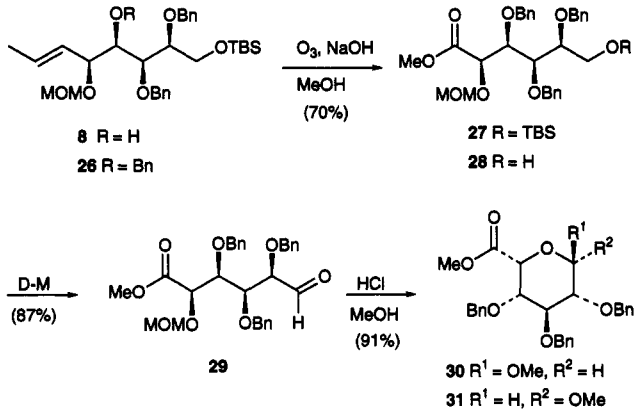
(7) *Cf.* (a) Davis, D. D.; Johnson, H. T. *J. Am. Chem. Soc.* **1974**, *96*, 7576. (b) Fleming, I.; Rowley, M. *Tetrahedron* **1986**, *42*, 3181.

(8) For examples in which diastereoselectivity is sensitive to β- and γ-stereocenters in such aldehydes, see: (a) Marshall, J. A.; Yashunsky, D. V. *J. Org. Chem.* **1991**, *56*, 5493. (b) Burgess, K.; Chaplin, D. A. *Tetrahedron Lett.* **1992**, *33*, 6077.

Stereochemistry of the Adducts: Syntheses of Hexose Derivatives. The *syn,anti,syn* adduct **7** was converted to diol **21** by ozonolysis and *in situ* reduction with $NaBH_4$. Subsequent benzylation with BnBr in the presence of Ag_2O led to the benzyl ether **22** in 83% yield. An authentic sample of ether **22** was prepared from 2,3,4,6-tetra-*O*-benzyl-α-D-galactose (**23**)[9] by a sequence involving reduction with $NaBH_4$, selective silylation of the primary alcohol with TBSCl, and subsequent etherification of the secondary alcohol with MOMCl.

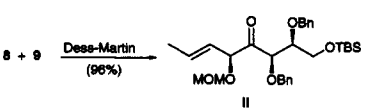


The *syn,syn,syn* adduct, alcohol **8**, afforded the ester **27** upon benzylation followed by ozonolysis in MeOH–CH_2Cl_2 and NaOH.[10] Desilylation and then Dess–Martin oxidation[4] led to the aldehyde **29**, which gave rise to a separable mixture of methyl glycosides **30** and **31** upon treatment with methanolic HCl. These anomers have been prepared previously from *myo*-inositol.[11] Their ^1H NMR spectra and optical rotations are in excellent agreement with the reported values.

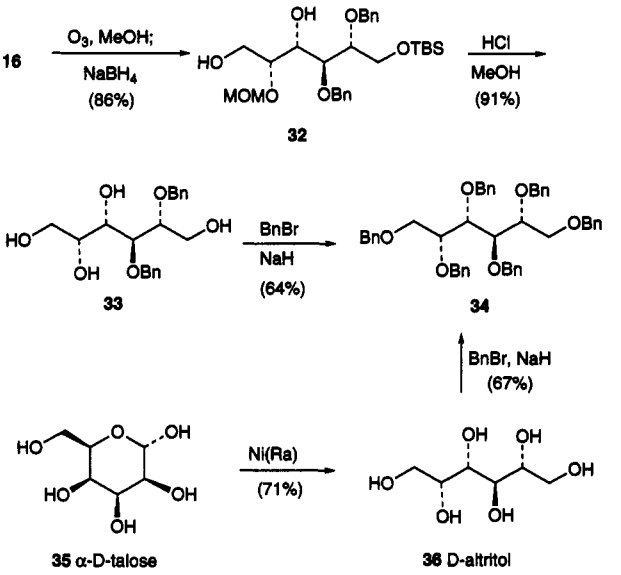


The minor adduct **9** from the BF_3-promoted mismatched pairing of aldehyde **6** with stannane (*R*)-**1** is assigned by analogy and from mechanistic considerations.[2,12]

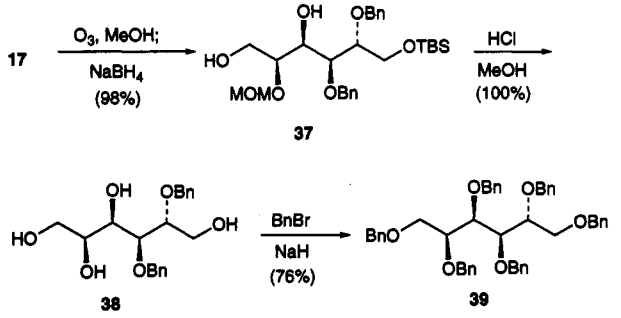
(9) Austin, P. W.; Hardy, F. E.; Buchanan, J. G.; Baddiley, J. *J. Chem. Soc.* **1965**, 1419.
(10) Marshall, J. A.; Garofalo, A. W. *J. Org. Chem.* **1993**, *58*, 3675.
(11) Chida, N.; Yamada, E.; Ogawa, S. *J. Carbohydr. Chem.* **1988**, *7*, 555.
(12) Support for this assignment was provided by oxidation of the mixture with the Dess–Martin periodinane reagent[4] whereupon a single ketone **ii** was secured in 96% yield.



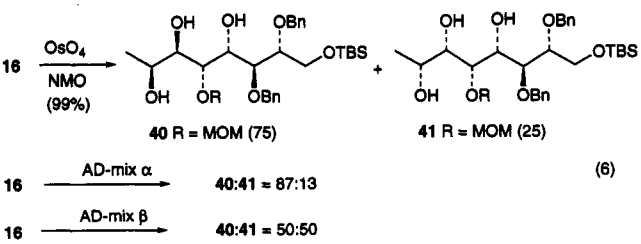
The *syn,anti,anti* adduct **16** was converted to diol **32** by ozonolysis and *in situ* reduction. Treatment with methanolic HCl led to the tetrol **33** which was directly benzylated affording the perbenzyl ether **34**. An authentic sample of this ether was prepared from α-D-talose (**35**)[13] via D-altritol (**36**).



The *syn,syn,anti* adduct **17** was subjected to the analogous sequence of ozonolysis, reduction, deprotection, and benzylation, affording the perbenzyl derivative **39** of D-sorbitol.[13]



Synthesis of ω-Deoxyoctose Derivatives. With a view toward application of the foregoing methodology to the synthesis of higher carbohydrate homologues, we briefly examined the dihydroxylation of adducts **16** and **17**. Application of the OsO_4–NMO protocol on adduct **16** afforded a 75:25 mixture of triols **40** and **41** (eq 6).[14]

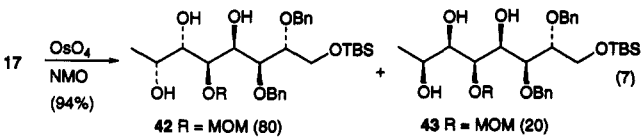


It is assumed that the major product of this mixture arises from *anti* attack relative to the adjacent OMOM substituent, and the stereochemistry is assigned accord-

(13) Aldrich Chemical Co., Milwaukee, WI.
(14) VanRheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973.

ingly.[15] Support for this assignment was obtained from dihydroxylation experiments with the Sharpless AD-mix-α and -β reagents.[16] With the former, the ratio of *anti* to *syn* dihydroxylation products **40**:**41** increased to 87:13, while the latter reagent led to a decreased ratio of 50:50, as expected for matched and mismatched reactions.

Adduct **17** afforded an 80:20 mixture of triols **42** and **43** with catalytic OsO_4–NMO (eq 7). Attempts to increase



this ratio through use of AD-mix-β were unsuccessful. The reaction was less than 10% complete after 7 days. It is known that allylic oxygen substituents retard the rate of asymmetric dihydroxylations.[17] Presumably, steric factors which hinder the incorporation of olefin **17** into the active site of the AD-mix reagent are largely responsible for the lack of reactivity. Improved selectivity might be possible through use of a vicinal TBS array.[15c,18] This possibility was not pursued.

The foregoing study shows that high levels of stereoselectivity can be achieved through matching of substrate and reagent chirality in additions of γ-alkoxy allylic stannanes to tetrose derivatives. The resulting adducts are potential intermediates for carbohydrate synthesis. Through proper choice of protecting groups, either end of hexitol derivatives such as **21**, **32**, and **37** could serve as the aldehyde carbon (C1), as illustrated in Figure 1, thus increasing the versatility of the methodology. These studies are currently ongoing.

Experimental Section[19]

2,3-Di-*O*-benzyl-4-*O*-(*tert*-butyldimethylsilyl)-L-threitol (5). To a solution of 2,3-*O*-dibenzyl-L-threitol (**4**)[20] (7.16 g, 23.7 mmol) in THF (140 mL) was added n-BuLi (2.5 M, 10.0 mL, 25.0 mmol) dropwise at 0 °C. The resulting solution was stirred at 0 °C for 45 min, whereupon TBSCl (3.93 g, 26.1 mmol) in THF (40 mL) was added. After being stirred at 0 °C for 1 h, the reaction was quenched with saturated aqueous $NaHCO_3$. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined extracts were dried over $MgSO_4$ and concentrated. The crude material was purified by flash chromatography (25% ethyl acetate–hexanes) on silica gel to give TBS ether **5** (9.38 g, 95%) as a colorless oil: $[\alpha]^{27}_D$ +14.7 (*c* 0.95, $CHCl_3$); IR (film) ν 3455, 3030, 1094 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33–7.26 (m, 10 H), 4.71, 4.61 (ABq, J = 11.8 Hz, 2 H), 4.65, 4.60 (ABq, J = 11.7 Hz, 2 H), 3.79–3.62 (m, 6 H), 2.37 (dd, J = 7.3, 5.2 Hz, 1 H), 0.88 (s, 9 H), 0.033 (s, 6 H). Anal. Calcd for $C_{24}H_{36}O_4Si$: C, 69.19; H, 8.71. Found: C, 69.29; H, 8.74.

2,3-Di-*O*-benzyl-4-*O*-(*tert*-butyldimethylsilyl)-L-threose (6). To a solution of alcohol **5** (159.1 mg, 0.382 mmol) in dry CH_2Cl_2 (2.5 mL) at room temperature was added the Dess–Martin reagent[4] (202 mg, 0.477 mmol) in one portion. After 20 min, the reaction mixture was diluted with ether and poured into a vigorously stirring solution of $Na_2S_2O_3$ in saturated aqueous $NaHCO_3$. After the layers became clear (~10 min), they were separated and the ether layer was washed with saturated aqueous $NaHCO_3$. The combined aqueous washes were reextracted twice with ether, and the combined ether extracts were dried over $MgSO_4$ and concentrated. Flash chromatography on silica gel (10–15% ethyl acetate–hexanes) afforded aldehyde **6** (147.6 mg, 93%): $[\alpha]^{27}_D$ +38.1 (*c* 1.08, $CHCl_3$); IR (film) ν 3031, 1734, 1095 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), δ 9.69 (d, J = 1.2 Hz, 1 H), 7.33–7.25 (m, 10 H), 4.73, 4.59 (ABq, J = 11.9 Hz, 2 H), 4.59, 4.53 (ABq, J = 11.8 Hz, 2 H, 3.96 (dd, J = 3.6, 1.2 Hz, 1 H), 3.83–3.68 (m, 3 H), 0.85 (s, 9 H), 0.005 (s, 6 H). Anal. Calcd for $C_{24}H_{34}O_4Si$: C, 69.53; H, 8.27. Found: C, 69.50; H, 8.27.

(2*S*,3*R*,4*S*,5*R*,6*E*)-2,3-Bis(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]-5-(methoxymethoxy)-6-octen-4-ol (7). To a solution of stannane (*S*)-1[21] (83.0 mg, 0.205 mmol) and aldehyde **6** (79.4 mg, 0.191 mmol) in dry CH_2Cl_2 (0.5 mL) at −78 °C was added, dropwise, BF_3-Et_2O (31 μL, 0.248 mmol). After 40 min at −78 °C, the reaction was quenched with saturated aqueous $NaHCO_3$ and allowed to warm to room temperature. The mixture was then diluted with ether and additional $NaHCO_3$. After the layers were separated, the aqueous layer was reextracted twice with ether. The combined ether extracts were dried over $MgSO_4$ and concentrated. Flash chromatography on silica gel (15–20% ethyl acetate–hexanes) afforded alcohol **7** (72.8 mg, 72%; 81% corrected for 8.9 mg of recovered **6**): $[\alpha]^{27}_D$ −38.1 (*c* 1.24, $CHCl_3$); IR (film) ν 3499, 3030, 1095 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 7.36–7.26 (m, 10 H), 5.70 (dq, J = 15.5, 6.4 Hz, 1 H), 5.52 (ddq, J = 15.5, 8.3, 1.5 Hz, 1 H), 4.73 and 4.54, 4.72 and 4.66, 4.63 and 4.59 (ABq's, J = 6.7, 11.7, 10.4 Hz, 6 H), 4.22 (d, J = 8.0 Hz, 1 H), 3.86–3.76 (m, 5 H), 3.37 (s, 3 H), 3.06 (d, J = 6.3 Hz, 1 H), 1.69 (dd, J = 6.3, 1.4 Hz, 3 H), 0.87 (s, 9 H), 0.003 (s, 6 H). Anal. Calcd for $C_{30}H_{46}O_6Si$: C, 67.89; H, 8.74. Found: C, 67.95; H, 8.75.

(2*S*,3*R*,4*R*,5*S*,6*E*)-2,3-Bis(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]-5-(methoxymethoxy)-6-octen-4-ol (8) and

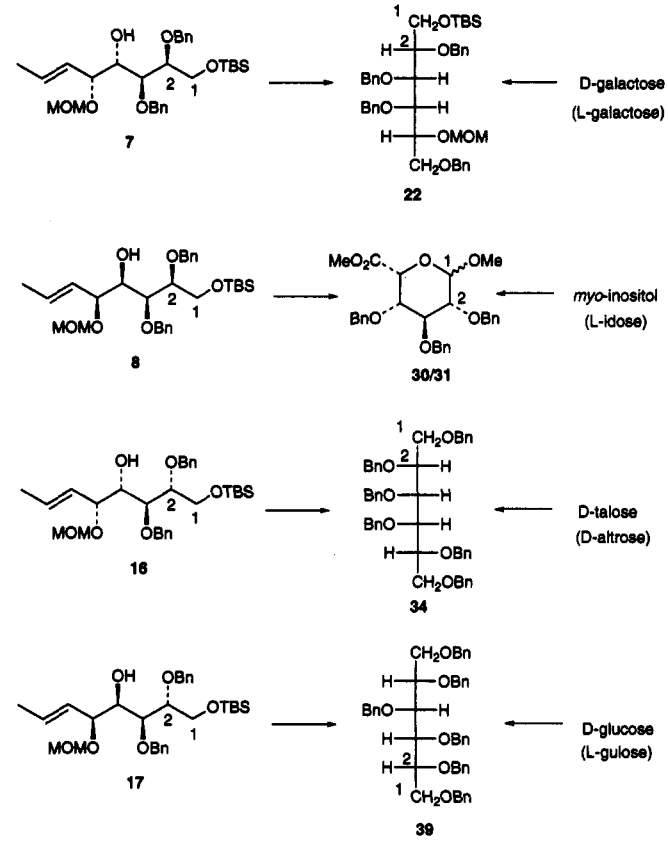


Figure 1. Correlation of synthetic intermediates **7**, **8**, **16**, and **17** with carbohydrates.

(15) *Cf.* (a) Stork, G.; Kahn, M. *Tetrahedron Lett.* **1983**, *24*, 3951. (b) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron* **1984**, *40*, 2247. (c) Saito, S.; Morikawa, Y.; Moriwake, T. *J. Org. Chem.* **1990**, *55*, 5424.

(16) Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K.-S.; Kwong, H.-L.; Morikawa, K.; Wang, Z.-M.; Xu, D.; Zhang, X.-L. *J. Org. Chem.* **1992**, *57*, 2768.

(17) Xu, D.; Crispino, G. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 7570. Sinha, S. C.; Keinan, E. *J. Org. Chem.* **1994**, *59*, 949.

(18) Marshall, J. A.; Beaudoin, S.; Lewinski, K. *J. Org. Chem.* **1993**, *58*, 5876.

(19) For typical experimental protocols and parameters see ref 21.

(20) Nemoto, H.; Takamatsu, S.; Yamamoto, Y. *J. Org. Chem.* **1991**, *56*, 1321.

(21) Marshall, J. A.; Welmaker, G. S.; Gung, B. W. *J. Am. Chem. Soc.* **1991**, *113*, 647.

(2*S*,3*R*,4*S*,5*S*,6*E*)-2,3-Bis(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]-5-(methoxymethoxy)-6-octen-4-ol (9). The procedure described for alcohol 7 was followed with stannane (*R*)-1[21] (65 mg, 0.16 mmol), aldehyde 6 (74 mg, 0.18 mmol), and BF_3·Et_2O (26 μL, 0.21 mmol) in CH_2Cl_2 (0.5 mL; 3 h). Flash chromatography (15–20% ethyl acetate–hexanes) afforded adducts 8 (42 mg, 49%) and 9 (22 mg, 26%) as colorless oils.

8: $[\alpha]^{25}_D$ +42.4 (*c* 0.80, $CHCl_3$); IR (film) ν 3488, 1097 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32–7.25 (m, 10 H), 5.49 (dq, *J* = 15.4, 6.4 Hz, 1 H), 5.21 (ddq, *J* = 15.4, 8.6, 1.6 Hz, 1 H), 4.78 and 4.48, 4.71 and 4.58, 4.69 and 4.53 (ABq's, *J* = 11.4, 11.8, 6.6 Hz, 6 H), 4.05 (t, *J* = 8.0 Hz, 1 H), 3.90–3.69 (m, 5 H), 3.35 (s, 3 H), 2.71 (d, *J* = 4.9 Hz, 1 H), 1.64 (dd, *J* = 6.4, 1.6 Hz, 3 H), 0.89 (s, 9 H), 0.052 (s, 3 H), 0.042 (s, 3 H). Anal. Calcd for $C_{30}H_{46}O_6Si$: C, 67.89; H, 8.74. Found: C, 68.03; H, 8.76.

9: $[\alpha]^{25}_D$ +57.7 (*c* 0.65, $CHCl_3$); IR (film) ν 3466, 1102 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32–7.25 (m, 10 H), 5.57 (dq, *J* = 15.5, 6.1 Hz, 1 H), 5.48 (ddq, *J* = 15.5, 8.1, 1.3 Hz, 1 H), 4.74 and 4.64, 4.68 and 4.51, 4.52 and 4.50 (ABq's, *J* = 11.9, 6.7, 11.5 Hz, 6 H), 4.13 (dd, *J* = 8.2, 3.9 Hz, 1 H), 4.00 (dd, *J* = 8.0, 4.4 Hz, 1 H), 3.90–3.77 (m, 3 H), 3.59 (dd, *J* = 7.8, 2.8 Hz, 1 H), 3.32 (s, 3 H), 3.17 (d, *J* = 4.5 Hz, 1 H), 1.70 (dd, *J* = 6.1, 1.2 Hz, 3 H), 0.87 (s, 9 H), 0.015 (s, 6 H). Anal. Calcd for $C_{30}H_{46}O_6Si$: C, 67.89; H, 8.74. Found: C, 67.98; H 8.77.

BF_3·Et_2O-Promoted Addition of Stannane (*RS*)-1 to Aldehyde 6. The procedure described for alcohol 7 was followed with racemic stannane (*RS*)-1 (220 mg, 0.55 mmol), aldehyde 6 (103 mg, 0.25 mmol), and BF_3·Et_2O (40 μL, 0.32 mmol) in CH_2Cl_2 (1.0 mL; 2 h). Flash chromatography (5–10–15–20% ethyl acetate–hexanes) afforded enantioenriched stannane (*R*)-1 (111 mg, 93%, $[\alpha]^{25}_D$ −39.9 (*c* 1.61, CH_2Cl_2), 30% ee), adduct 7 (65 mg, 50%), a mixture of 7 and 9 (18 mg, 14%; ratio 1:1 by ^1H NMR analysis), and a mixture of 8 and cyclopropane 10 (32 mg, 24%; ratio 4:1 by ^1H NMR analysis) as colorless oils.

10: partial ^1H NMR (300 MHz, $CDCl_3$) δ 3.40 (s), 1.09 (d, *J* = 6.2 Hz), 0.80 (m).

$MgBr_2$·Et_2O-Promoted Addition of Stannane (*R*)-1 to Aldehyde 6: (2*S*,3*R*,4*R*,5*S*,6*E*)-2,3-Bis(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]-5-(methoxymethoxy)-6-octen-4-ol (8). To a suspension of $MgBr_2$·Et_2O (92 mg, 0.357 mmol) in CH_2Cl_2 (1.0 mL) at −23 °C was added a solution of aldehyde 6 (135 mg, 0.324 mmol) in CH_2Cl_2 (1.5 mL). After 45 min, a solution of stannane (*R*)-1 (162 mg, 0.400 mmol) in CH_2Cl_2 (1.0 mL) was slowly added to the reaction mixture at −23 °C. The reaction was allowed to slowly warm to room temperature, and after 4.25 h it was quenched by the addition of saturated aqueous $NaHCO_3$. The mixture was diluted with ether and water. The layers were separated, and the aqueous layer was reextracted three times with ether. The combined ether extracts were dried over $MgSO_4$ and concentrated. Flash chromatography on silica gel (15–20% ethyl acetate–hexanes) afforded adduct 8 (116 mg, 68%, or 99% based on 43 mg of recovered 6) as a colorless oil.

$MgBr_2$·Et_2O-Promoted Addition of Stannane (*RS*)-1 to Aldehyde 6. The procedure described for adduct 8 was followed with racemic stannane (*RS*)-1 (244 mg, 0.607 mmol), aldehyde 6 (101 mg, 0.243 mmol), and $MgBr_2$·Et_2O (98 mg, 0.380 mmol) in CH_2Cl_2 (3.0 mL; 20 h at −10 °C). Flash chromatography (5–10–15–20% ethyl acetate–hexanes) afforded enantioenriched stannane (*S*)-1 (102 mg, 72%, $[\alpha]^{25}_D$ +50.5 (*c* 1.72, CH_2Cl_2), 36% ee), adduct 8 (84 mg, 65%, or 71% corrected for recovered aldehyde 6 (8 mg), and a mixture of minor diastereomers (8 mg, 6%) as colorless oils.

(2*R*,3*R*)-2,3-Bis(benzyloxy)-4-hydroxybutanoic Acid 1,4-Lactone (2,3-*O*-Dibenzyl-D-erythronolactone) (12). To a stirred solution of lactone 8[22] (400 mg, 3.39 mmol) and benzyl bromide (1.1 mL, 9.25 mmol) in ether (20 mL) was added freshly prepared, dry silver oxide (2.62 g, 11.29 mmol) in three portions over a period of 20 min in the dark. The reaction is slightly exothermic; no external heating was applied. The mixture was stirred for 20 h at room temperature and filtered. The filtrate was concentrated under reduced pressure, and the crude oil was purified by flash chromatography on silica gel (15–50% ethyl acetate–hexanes) affording benzyl ester i (220 mg, 13%), desired dibenzyl ether 12 (490 mg, 48%), and a mixture of monobenzyl ethers (210 mg, 30%) as white solids.

12: mp 89–90 °C (hexanes); R_f 0.42 (35% ethyl acetate–hexanes); $[\alpha]^{25}_D$ +5.9 (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) ν 3020, 1792, 1157 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.37–7.32 (m, 10 H), 4.94, 4.81 (ABq, *J* = 12.2 Hz, 2 H), 4.72, 4.62 (ABq, *J* = 12.0 Hz, 2 H), 4.33 (m, 1 H), 4.19–4.11 (m, 3 H) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.4, 137.2, 136.7, 128.6–127.9 (six lines), 74.2, 74.0, 72.5, 72.1, 69.6. Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.45; H, 6.09. Found: C, 72.38; H, 6.13.

i: R_f 0.86 (35% ethyl acetate–hexanes); IR ($CHCl_3$) ν 3017, 1744, 1223 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.37–7.22 (m, 20 H), 5.16 (s, 2 H), 4.68 and 4.45, 4.60 and 4.57 (ABq's, *J* = 11.5 Hz, 4 H), 4.46 (s, 2 H), 4.23 (d, *J* = 5.2 Hz, 1 H), 3.98 (dd, *J* = 10.2, 5.3 Hz, 1 H), 3.70 (dd, *J* = 10.3, 4.8 Hz, 1 H), 3.64 (dd, *J* = 10.3, 5.4 Hz, 1 H).

Monobenzyl ethers: R_f 0.13 and 0.15 (35% ethyl acetate–hexanes); IR ($CHCl_3$) ν 3559, 3018, 1790, 1224 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.37–7.29 (m, 5 H), 5.03 and 4.83, 4.72 and 4.44 (ABq's, *J* = 11.8, 11.3 Hz, 2 H), 4.36–4.14 (m, 4 H).

(2*R*,3*R*)-2,3-Bis(benzyloxy)-4-hydroxy-*N*-methoxy-*N*-methylbutanamide (13). To a stirred suspenson of *N*,*O*-dimethylhydroxylamine hydrochloride (314 mg, 3.22 mmol) in CH_2Cl_2 (6 mL) at 0 °C was slowly added (*caution*: gas evolution) 2.0 M $AlMe_3$ in hexanes (1.6 mL, 3.22 mmol). After the addition was complete, the clear solution was stirred at room temperature for 15 min and then recooled to 0 °C, and the solution of lactone 12 (480 mg, 1.61 mmol) in CH_2Cl_2 (6 mL) was added. After 20 min, 0.5 M aqueous HCl was added. Extraction with CH_2Cl_2 afforded crude amide 13 (575 mg, 99%) as a colorless liquid. Flash chromatography on silica gel caused partial hydrolysis and relactonization to 12. Therefore, this product was characterized and used without further purification: $[\alpha]^{25}_D$ +29.6 (*c* 0.5, $CHCl_3$); IR (film) ν 3446, 2937, 1664, 1116 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.33–7.26 (m, 10 H), 4.66, 4.45 (ABq, *J* = 11.8 Hz, 2 H), 4.63 (m, 1 H), 4.53 (s, 2 H), 3.86–3.73 (m, 3 H), 3.48 (s, 3 H), 3.18 (s, 3 H), 2.04 (br m, 1 H, disappears on exchange with D_2O). Anal. Calcd for $C_{20}H_{25}NO_5$: C, 66.84; H, 7.01; N, 3.90. Found: C, 66.71; H, 6.97; N, 3.81.

(2*R*,3*R*)-2,3-Bis(benzyloxy)-4-[(*tert*-butyldimethylsilyl)oxy]-*N*-methoxy-*N*-methylbutanamide (14). To a stirred solution of amide 13 (568 mg, 1.58 mmol) in DMF (6 mL) at 0 °C was added imidazole (258 mg, 3.80 mmol) followed by TBSCl (286 mg, 1.89 mmol). After 1 h, water was added and the product was isolated by extraction with Et_2O. Purification by flash chromatography (35% ethyl acetate–hexanes) afforded ether 14 (735 mg, 98%) as a colorless liquid: $[\alpha]^{25}_D$ +13.7 (*c* 0.7, $CHCl_3$); IR (film) ν 3036, 1671, 1101 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.32–7.24 (m, 10 H), 4.64, 4.48 (ABq, *J* = 11.4 Hz, 2 H), 4.61, 4.45 (ABq, *J* = 11.9 Hz, 2 H), 4.62 (m, 1 H), 3.90 (m, 1 H), 3.81 (m, 2 H) 3.46 (s, 3 H), 3.15 (s, 3 H), 0.88 (s, 9 H), 0.34 (s, 3 H), 0.31 (s, 3 H). Anal. Calcd for $C_{26}H_{39}NO_5Si$: C, 65.93; H, 8.30; N, 2.96. Found: C, 65.72; H, 8.25; N, 2.94.

2,3-Di-*O*-benzyl-4-*O*-(*tert*-butyldimethylsilyl)-D-erythrose (15). To a stirred solution of amide 14 (634 mg, 1.34 mmol) in THF (12 mL) at −78 °C was slowly (over 5 min) added 1.5 M DIBALH in toluene (1.8 mL, 2.68 mmol). After 30 min a saturated solution of Rochelle's salt was added, the cold bath was removed, and stirring was continued until two distinct phases were apparent. Extraction with ether and purification by flash cromatography (10% ethyl acetate–hexanes) afforded aldehyde 15 (523 mg, 94%) as a colorless liquid: $[\alpha]^{25}_D$ +3.9 (*c* 1.0, $CHCl_3$); IR (film) ν 1733, 1103 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 9.63 (d, *J* = 1.5 Hz, 1 H), 7.34–7.28 (m, 10 H), 4.71, 4.67 (ABq, *J* = 12.0 Hz, 2 H), 4.58, 4.59 (ABq, *J* = 12.3 Hz, 2 H), 4.04 (dd, *J* = 2.7, 1.5 Hz, 1 H), 3.81 (m, 2 H), 3.77 (dd, *J* = 13.5, 8.8 Hz, 1 H), 0.85 (s, 9 H), 0.014 (s, 3 H), 0.006 (s, 3 H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 202.4, 138.3, 137.9, 128.9–127.8 (five lines), 83.1, 81.6, 73.4, 72.8, 61.5, 26.3, 18.7, −5.1, −5.2. Anal. Calcd for $C_{24}H_{34}O_4Si$: C, 69.53; H, 8.27. Found: C, 69.57; H, 8.29.

(2*R*,3*R*,4*S*,5*R*,6*E*)-2,3-Bis(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]-5-(methoxymethoxy)-6-octen-4-ol (16). The procedure described for adduct 7 was followed with stannane (*S*)-1 (130 mg, 0.322 mmol), aldehyde 15 (103 mg, 0.248 mmol), and BF_3·Et_2O (40 μL, 0.32 mmol) in CH_2Cl_2 (1.0 mL; 2 h). Flash chromatography (15–20% ethyl acetate–hexanes) afforded al-

(22) Dunigan, J.; Weigel, L. O. *J. Org. Chem.* **1991**, *56*, 6225.

cohol 16 (98 mg, 74%) as a colorless liquid: $[\alpha]^{25}_D$ -42.3 (c 0.80, $CHCl_3$); IR (film) ν 3480, 2933, 1097 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36–7.26 (m, 10 H), 5.67 (dq, J = 15.5, 6.4 Hz, 1 H), 5.44 (ddq, J = 15.4, 8.4, 1.6 Hz, 1 H), 4.75 and 4.56, 4.73 and 4.63, 4.69 and 4.50 (ABq's, J = 11.2, 11.8, 6.6 Hz, 6 H), 4.24 (dd, J = 8.4, 3.9 Hz, 1 H), 3.96–3.91 (m, 2 H), 3.83–3.79 (m, 2 H), 3.71 (ddd, J = 9.5, 5.6, 3.9 Hz, 1 H), 3.33 (s, 3 H), 2.84 (d, J = 5.6 Hz, 1 H), 1.67 (dd, J = 6.4, 1.5 Hz, 3 H), 0.88 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 138.8, 138.7, 131.0, 128.3–127.4 (seven lines), 93.7, 80.8, 78.6, 76.8, 74.5, 73.2, 72.8, 62.7, 55.9, 25.9, 18.3, 17.9, -5.4. Anal. Calcd for $C_{30}H_{46}O_6Si$: C, 67.89; H, 8.74. Found: C, 67.99; H, 8.78.

BF_3·Et_2O-Promoted Addition of Stannane (*RS*)-1 to Aldehyde 15. The procedure described for adduct 7 was followed with racemic stannane (*RS*)-1 (258 mg, 0.641 mmol), aldehyde 15 (103 mg, 0.248 mmol), and BF_3·Et_2O (40 μL, 0.322 mmol) in CH_2Cl_2 (1.0 mL; 2.5 h). Flash chromatography (5–10–15–20% ethyl acetate–hexanes) afforded enantioenriched stannane (*R*)-1 (127 mg, 85%, $[\alpha]^{25}_D$ -23.0 (c 1.30, CH_2Cl_2), 17% ee), adduct 16 (60 mg, 46%), a mixture of 16 and 18 (16 mg, 12%, ratio 1:1 by ^1H NMR analysis), and a mixture of 17 and cyclopropane 19 (21 mg, 16%; ratio of 2:1 by ^1H NMR analysis) as colorless oils.

18: ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.27 (m, 10 H), 5.53 (dq, J = 15.5, 6.0 Hz, 1 H), 5.49 (ddq, J = 15.5, 8.1, 1.0 Hz, 1 H), 4.76–4.41 (m, 6 H), 4.22 (dd, J = 8.2, 3.2 Hz, 1 H), 3.98–3.63 (m, 5 H), 3.31 (s, 3 H), 2.80 (br s, 1 H), 1.69 (dd, J = 5.9, 0.9 Hz, 3 H), 0.89 (s, 9 H), 0.054 (s, 3 H), 0.050 (s, 3 H).

19: partial ^1H NMR (300 MHz, $CDCl_3$) δ 3.38 (s), 1.08 (d, J = 6.2 Hz), 0.85 (m).

$MgBr_2$·Et_2O-Promoted Addition of Stannane (*RS*)-1 to Aldehyde 15: (2*R*,3*R*,4*R*,5*S*,6*E*)-2,3-Bis(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]-5-(methoxymethoxy)-6-octen-4-ol (17) and (2*R*,3*R*,4*R*,5*R*,6*E*)-2,3-Bis(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]-5-(methoxymethoxy)-6-octen-4-ol (20). The procedure described for adduct 8 was followed with racemic stannane (*RS*)-1 (258 mg, 0.642 mmol), aldehyde 15 (142 mg, 0.342 mmol), and $MgBr_2$·Et_2O (160 mg, 0.621 mmol) in CH_2Cl_2 (5.0 mL; 30 h at -10 °C). Flash chromatography (5–10–15–20% ethyl acetate–hexanes) afforded enantioenriched stannane (*S*)-1 (98 mg, 85%, $[\alpha]^{25}_D$ +103 (c 1.50, CH_2Cl_2), 76% ee), adducts 17 (150 mg, 83%, or 89% corrected for 9 mg of recovered aldehyde 15), and 20 (15 mg, 8%) as colorless oils.

17: $[\alpha]^{25}_D$ +34.3 (c 0.50, $CHCl_3$); IR (film) ν 3508, 2933, 1097 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.25 (m, 10 H), 5.60 (dq, J = 15.4, 6.5 Hz, 1 H), 5.27 (ddq, J = 15.4, 8.7, 1.6 Hz, 1 H), 4.75–4.49 (m, 6 H), 4.13 (dd (apparent t), J = 8.4, 8.0 Hz, 1 H), 3.92–3.71 (m, 5 H), 3.36 (s, 3 H), 3.05 (br s, 1 H), 1.66 (dd, J = 6.4, 1.5 Hz, 3 H), 0.88 (s, 9 H), 0.035 (s, 3 H), 0.032 (s, 3 H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 138.9, 138.8, 132,6, 128.8–128.0 (seven lines), 94.0, 80.7, 78.7, 77.2, 73.7, 73.5, 73.4, 62.7, 55.9, 26.3, 18.7, 18.3, -4.9, -5.0. Anal. Calcd for $C_{30}H_{46}O_6Si$: C, 67.89; H, 8.74. Found: C, 67.83; H, 8.76.

20: $[\alpha]^{25}_D$ -36.4 (c 1.0, $CHCl_3$); IR (film) ν 3507, 2934, 1093 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.26 (m, 10 H), 5.73 (dq, J = 15.4, 6.4 Hz, 1 H), 5.43 (ddq, J = 15.4, 8.4, 1.6 Hz, 1 H), 4.75–4.46 (m, 6 H), 4.07 (dd (apparent t), J = 8.0, 7.2 Hz, 1 H), 3.92–3.71 (m, 5 H), 3.32 (s, 3 H), 2.99 (d, J = 6.2 Hz, 1 H), 1.73 (dd, J = 6.4, 1.5 Hz, 3 H), 0.89 (s, 9 H), 0.043 (s, 3 H), 0.040 (s, 3 H). Anal. Calcd for $C_{30}H_{46}O_6Si$: C, 67.89; H, 8.74. Found: C, 67.81; H, 8.78.

4,5-Di-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-2-*O*-(methoxymethyl)-L-galactitol (21). Ozone was bubbled through a solution of homoallylic alcohol 7 (137 mg, 0.258 mmol) in methanol (5 mL) at -78 °C. When the solution turned blue (3–4 min) the O_3 flow was replaced by N_2. After the excess O_3 was removed (~2 min) the reaction was quenched at -78 °C with ~1 mL of Me_2S, and the mixture was allowed to warm to room temperature. After 1.5 h, excess $NaBH_4$ was added to the mixture. The reduction was complete within 5 min, whereupon the mixture was diluted with satuated aqueous $NaHCO_3$, ether, and water. The layers were separated, and the aqueous layer was reextracted twice with ether. The combined ether extracts were dried over $MgSO_4$ and concentrated. Flash chromatography on silica gel (40–50% ethyl acetate–hexanes) afforded diol 21 (118 mg, 88%) as a colorless oil: $[\alpha]^{28}_D$ +1.27 (c 0.63, $CHCl_3$); IR (film) ν 3456, 1098 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.26 (m, 10 H), 4.74 and 4.64, 4.69 and 4.46, 4.60 and 4.45 (ABq's, J = 11.8; 6.9; 11.2 Hz, 6 H), 3.84–3.75 (m, 8 H), 3.41 (s, 3 H), 3.30–3.28 (m, 2 H), 0.88 (s, 9 H), 0.0359 (s, 6 H). Anal. Calcd for $C_{28}H_{44}O_7Si$: C, 64.58; H, 8.52. Found: C, 64.40; H, 8.56.

1,3,4,5-Tetra-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-2-*O*-(methoxymethyl)-L-galactitol (22). A. From Diol 21. To a solution of diol 21 (39.5 mg, 0.076 mmol) in DMF (0.3 mL) at room temperature was added benzyl bromide (90 μL, 0.759 mmol) followed by freshly prepared Ag_2O (175 mg, 0.759 mmol). After 14 h, the mixture was diluted with a small amount of ether and then filtered through a 3-mm plug of silica gel. The filtrate was concentrated, and the resulting DMF solution was partitioned between hexanes and water. The layers were separated, and the hexane layer was washed with water and brine. The combined aqueous washes were reextracted twice with hexanes, and the combined hexane extracts were dried over $MgSO_4$ and concentrated. Flash chromatography on silica gel (10–15% ethyl acetate–hexanes) afforded ether 22 (44 mg, 83%) as a colorless oil: R_f 0.28 (10% ethyl acetate–hexanes); $[\alpha]^{28}_D$ +8.38 (c 1.54, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.30–7.22 (m, 20 H), 4.72–4.41 (m, 10 H), 4.07–4.01, 3.99–3.89, 3.80–3.75 (m's, 6 H), 3.67, 3.60 (ABX, J_{AB} = 9.8, J_{AX} = 4.9, J_{BX} = 5.3 Hz, 2 H), 3.32 (s, 3 H), 0.856 (s, 9 H), -0.01 (s, 6 H); IR (film) ν 2928, 1102 cm^{-1}. Anal. Calcd for $C_{42}H_{56}O_7Si$: C, 71.96; H, 8.05. Found: C, 71.88; H, 8.06.

B. From Alcohol 25. To a solution of alcohol 25 (183 mg, 0.278 mmol) in CH_2Cl_2 (2.0 mL) at 0 °C was added (i-Pr)$_2$NEt (150 μL) followed by MOMCl (30 μL, 0.417 mmol). After 1 h, the mixture was allowed to warm to room temperature; after a total of 24 h, it was diluted with ether and 5% aqueous HCl. The layers were separated, and the ether layer was washed with 5% aqueous HCl, water, and saturated aqueous $NaHCO_3$. The aqueous washes were reextracted once with ether. The combined ether extracts were dried over $MgSO_4$ and concentrated. Flash chromatography on silica gel (10–15% ethyl acetate–hexanes) afforded fully protected galactol 22 (183 mg, 94%) as a colorless oil: R_f 0.28 (10% ethyl acetate–hexanes); $[\alpha]^{26}_D$ +8.74 (c 1.19, $CHCl_3$). The IR and ^1H NMR spectra are identical to those of ether 22 prepared from diol 21.

1,3,4,5-Tetra-*O*-benzyl-L-galactitol (24). To a solution of 2,3,4,6-tetra-*O*-benzyl-D-galactose (23)[9] (780 mg, 1.44 mmol) in EtOH (8 mL) was added excess $NaBH_4$. After being stirred overnight, the reaction mixture was diluted with ether and then poured into water. The layers were separated, and the ether layer was washed twice with water and once with brine. The combined aqueous washes were reextracted three times with ether. The combined ether extracts were dried over $MgSO_4$ and concentrated. Flash chromatography on silica gel (35% ethyl acetate–hexanes) afforded diol 24 (773 mg, 99%) as a colorless oil: $[\alpha]^{28}_D$ -8.2 (c 0.93, $CHCl_3$); IR (film) ν 3448, 3030, 2868, 1098 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33–7.21 (m, 20 H), 4.76–4.38 (m, 8 H), 4.02 (m, 1 H), 3.87–3.48 (m, 7 H), 3.24 (d, J = 4.7 Hz, 1 H), 2.25 (dd, J = 7.0, 5.1 Hz, 1 H).

1,3,4,5-Tetra-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-L-galactitol (25). To a solution of diol 24 (291 mg, 0.536 mmol) in CH_2Cl_2 (2.5 mL) at 0 °C was added TBSCl (84.8 mg, 0.562 mmol), followed by a few crystals of DMAP and finally Et_3N (0.15 mL). The mixture was allowed to warm to room temperature and, after 5.5 h, diluted with water and ether. The layers were separated, and the ether layer was washed with saturated aqueous $CuSO_4$ and brine. The combined washes were reextracted once with ether. The combined ether extracts were dried over $MgSO_4$ and concentrated. Flash chromatography on silica gel (15–20% ethyl acetate–hexanes) afforded TBS ether 25 (227 mg, 64%; 95% corrected for 94.0 mg of recovered alcohol 24) as a colorless oil: $[\alpha]^{28}_D$ -10.7 (c 1.51 $CHCl_3$); IR (film) ν 3487, 3030, 1091 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31–7.19 (m, 20 H), 4.74 and 4.68, 4.72 and 4.57, 4.51 and 4.39, 4.47 and 4.40 (ABq's, J = 11.3, 11.8, 11.5, 11.9 Hz, 8 H), 4.07 (m, 1 H), 3.94, 3.83 (ABX, J_{AB} = 5.5, J_{AX} = 4.1, J_{BX} = 1.8 Hz, 2 H), 3.75–3.70; 3.52–3.49 (m, 5 H), 3.15 (d, J = 5.2 Hz, OH), 0.87 (s, 9 H), 0.004 (s, 3 H), -0.001 (s, 3 H). Anal. Calcd for $C_{40}H_{52}O_6Si$: C, 73.13; H, 7.98. Found: C, 72.96; H, 7.94.

(2*S*,3*R*,4*R*,5*S*,6*E*)-2,3,4-Tris(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]-5-(methoxymethoxy)-6-octene (26). To a suspension of NaH (38 mg, 1.59 mmol) in DMF (2 mL) was added

a solution of alcohol 8 (280 mg, 0.53 mmol at room temperature. After 10 min, the mixture was cooled to 0 °C, and benzyl bromide (107 μL, 0.90 mmol) was added. After 2 h, the reaction was quenched carefully (*caution*: gas evolution) with water and extracted twice with CH_2Cl_2. The combined extracts were washed with water and brine, dried over $MgSO_4$, and concentrated. Purification by flash chromatography (10% ethyl acetate–hexanes) afforded tribenzyl ether **26** (285 mg, 87%) as a colorless oil: $[\alpha]^{25}_D$ +61.9 (*c* 1.2, $CHCl_3$); IR (film) ν 2929, 1097 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.31–7.25 (m, 15 H), 5.42 (dq, J = 15.5, 6.3 Hz, 1 H), 5.31 (ddq, J = 15.5, 7.9, 1.2 Hz, 1 H), 4.80–4.46 (m, 8 H), 4.03 (dd, J = 8.2, 3.9 Hz, 1 H), 3.92 (dd, J = 6.8, 3.2 Hz, 1 H), 3.78 (dd, J = 6.7, 4.1 Hz, 1 H), 3.71–3.67 (m, 3 H), 3.30 (s, 3 H), 1.60 (dd, J = 6.3, 1.2 Hz, 3 H), 0.85 (s, 9 H), –0.021 (s, 3 H), –0.031 (s, 3 H). Anal. Calcd for $C_{37}H_{52}O_6Si$: C, 71.57; H, 8.44. Found: C, 71.53; H 8.37.

Methyl (2*R*,3*S*,4*R*,5*S*)-3,4,5-Tris(benzyloxy)-6-[(*tert*-butyldimethylsilyl)oxy]-2-(methoxymethoxy)hexanoate (27). A solution of olefin **26** (210 mg, 0.420 mmol) in CH_2Cl_2 (3.5 mL) and 2.5 M methanolic NaOH (0.94 mL) was stirred at –78 °C as ozone was passed through the solution. After 30 min, the initially yellow reaction mixture acquired the blue characteristic color of ozone, and a yellow precipitate had formed. ^1H NMR analysis of a sample of the reaction mixture showed consumption of the olefin and formation of ester **27**. However, the aldehyde was also detected, indicating incomplete reaction. Additional 2.5 M methanolic NaOH (0.30 mL) was added, whereupon the reaction mixture again turned yellow. Admission of ozone was continued at –78 °C until the solution again turned blue. Water was added, and the mixture was allowed to warm to room temperature and extracted with ether. The combined organic extracts were dried over $MgSO_4$ and concentrated. ^1H NMR analysis of the crude product showed the presence of aldehyde. Both compounds have R_f 0.36 (20% ethyl acetate–hexanes) and cannot be separated by flash chromatography. To a solution of this crude product in methanol (4 mL) was added an excess of $NaBH_4$ at room temperature. After 5 min, the workup described for diol **21** was followed. Purification by flash cromatography (20% ethyl acetate–hexanes) afforded ester **27** (152 mg, 70%) as a colorless oil: $[\alpha]^{25}_D$ +37.0 (*c* 1.0, $CHCl_3$); IR (film) ν 2952, 1756, 1098 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.33–7.23 (m, 15 H), 4.78 and 4.76 (AB, J = 11.1 Hz, 2 H), 4.65–4.54 (m, 6 H), 4.29 (dd, J = 8.2, 3.0 Hz, 1 H), 4.01–3.96 (m, 2 H), 3.77 (dd, J = 9.9, 5.7 Hz, 1 H), 3.69–3.59 (m, 2 H), 3.52 (s, 3 H), 3.32 (s, 3 H), 0.84 (s, 9 H), –0.012 (s, 3 H), –0.030 (s, 3 H). Anal. Calcd for $C_{36}H_{50}O_6Si$: C, 67.68; H, 7.89. Found: C, 67.55; H 7.89.

Methyl (2*R*,3*S*,4*R*,5*S*)-3,4,5-Tris(benzyloxy)-6-hydroxy-2-(methoxymethoxy)hexanoate (28). To a stirred solution of TBS ether **27** (135 mg, 0.211 mmol) in 1.0 M acetic acid in THF (1.5 mL) was added *n*-Bu_4NF (1.0 M in THF, 1.5 mL) at room temperature. After 20 h, saturated aqueous $NaHCO_3$ was added, and the product was isolated by extraction with CH_2Cl_2. The combined extracts were washed with water and brine, dried over $MgSO_4$, and concentrated. Purification by flash chromatography (35–50% ethyl acetate–hexanes) afforded alcohol **28** (109 mg, 98%) as a colorless oil: $[\alpha]^{25}_D$ +39.0 (*c* 1.0, $CHCl_3$); IR (film) ν 3518, 2952, 1755, 1056 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.34–7.26 (m, 15 H), 4.77–4.55 (m, 8 H), 4.23–4.17 (m, 2 H), 3.91 (dd, J = 6.4, 4.4 Hz, 1 H), 3.80–3.64 (m, 3 H), 3.52 (s, 3 H), 3.34 (s, 3 H), 1.86 (br t, 1 H). Anal. Calcd for $C_{30}H_{36}O_6$: C, 68.69; H, 6.92. Found: C, 68.83; H 6.94.

Methyl (2*R*,3*S*,4*S*,5*R*)-3,4,5-Tris(benzyloxy)-2-(methoxymethoxy)-6-oxohexanoate (29). To a solution of alcohol **28** (84 mg, 0.16 mmol) in CH_2Cl_2 (1.5 mL) at room temperature was added the Dess–Martin reagent[4] (94 mg, 0.22 mmol) in one portion. After 20 min, the reaction mixture was concentrated under reduced pressure. Purification by flash chromatography (25–35% ethyl acetate–hexanes) afforded aldehyde **29** (74 mg, 89%) as a colorless oil: $[\alpha]^{25}_D$ +43.0 (*c* 0.4, $CHCl_3$); IR (film) ν 1732, 1046 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 9.66 (s, 1 H), 7.32–7.24 (m, 15 H), 4.83–4.45 (m, 8 H), 4.18 (dd, J = 6.0, 4.3 Hz, 1 H), 4.10–4.03 (m, 2 H), 3.91 (d, J = 4.2 Hz, 1 H), 3.56 (s, 3 H), 3.29 (s, 3 H).

Methyl (Methyl 2,3,4-tri-*O*-benzyl-α-L-idopyranoside)-uronate (30) and Its β-Anomer (31). Aldehyde **29** (35 mg, 0.067 mmol) was dissolved in 1 mL of 1% methanolic HCl (prepared from 12 M HCl and MeOH), and the mixture was heated under reflux for 1.5 h. The reaction mixture was neutralized with anhydrous $NaHCO_3$ at 0 °C, filtered, and concentrated under reduced pressure. Purification by flash chromatography (20–50% ethyl acetate–hexanes) afforded α-methyl pyranoside **30** (20 mg, 61%) and its β-anomer **31** (10 mg, 30%) as colorless oils.

30: R_f 0.60 (35% ethyl acetate–hexanes); $[\alpha]^{26}_D$ –33.8 (*c* 1.0, $CHCl_3$) (lit.[11] $[\alpha]^{27}_D$ –29); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.34–7.22 (m, 15 H), 4.99 (d, J = 4.7 Hz, 1 H), 4.71–4.50 (m, 7 H), 3.87–3.80 (m, 2 H), 3.70 (s, 3 H), 3.46 (s 3H), 3.41 (dd, J = 5.9, 5.4 Hz, 1 H).

31: R_f 0.38 (35% ethyl acetate–hexanes); $[\alpha]^{26}_D$ +48.2 (*c* 1.0, $CHCl_3$) (lit.[11] $[\alpha]^{27}_D$ +44); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.32–7.20 (m, 15 H), 4.76–4.45 (m, 6 H), 4.54 (d, J = 2.5 Hz, 1 H), 4.28 (d, J = 3.7 Hz, 1 H), 4.02 (t, J = 5.5 Hz, 1 H), 3.72 (s, 3 H), 3.67 (dd, J = 5.3, 3.7 Hz, 1 H), 3.46 (s overlap m, 4 H).

6-*O*-(*tert*-Butyldimethylsilyl)-4,5-di-*O*-benzyl-2-*O*-(methoxymethyl)-D-altritol (32). Ozone was bubbled through a solution of homoallylic alcohol **16** (200 mg, 0.377 mmol) in methanol (5 mL) at –78 °C. When the solution turned blue in color (5–6 min), the O_3 flow was replaced by N_2. After the excess O_3 was removed (~2 min), excess $NaBH_4$ was added to the mixture and the mixture was allowed to warm to room temperature. The reduction was complete within 10 min at room temperature, whereupon the mixture was diluted with satuated aqueous $NaHCO_3$, ether, and water. The layers were separated, and the aqueous layer was reextracted twice with CH_2Cl_2. The combined ether extracts were washed with water and brine, dried over $MgSO_4$, and concentrated. Flash chromatography on silica gel (40–50% ethyl acetate–hexanes) afforded diol **32** (168 mg, 86%) as a colorless oil: $[\alpha]^{25}_D$ –10.4 (*c* 0.75, $CHCl_3$); IR (film) ν 3444, 1094 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.26 (m, 10 H), 4.80–4.41 (m, 6 H), 3.97–3.67 (m, 8 H), 3.40 (s, 3 H), 3.15 (br m, 2 H, disappears on exchange with D_2O), 0.88 (s, 9 H), 0.056 (s, 6 H). Anal. Calcd for $C_{28}H_{44}O_7Si$: C, 64.58; H, 8.52. Found: C, 64.49; H, 8.48.

4,5-Di-*O*-benzyl-D-altritol (33). Diol **32** (49 mg, 0.067 mmol) was dissolved in 1 mL of 1% methanolic HCl (prepared from 12 M HCl and MeOH), and the mixture was heated under reflux for 20 min. The reaction mixture was neutralized with anhydrous $NaHCO_3$ at 0 °C, filtered, and concentrated under reduced pressure. Purification by flash chromatography (50% ethyl acetate–hexanes, 5:5:1 hexanes–ethyl acetate–methanol) afforded tetrol **33** (31 mg, 91%) as a colorless oil: $[\alpha]^{25}_D$ –22.4 (*c* 0.5, $CHCl_3$); IR (film) ν 3374, 1067 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.28 (m, 10 H), 4.73, 4.70 (ABq, J = 11.0 Hz, 2 H), 4.67, 4.61 (ABq, J = 11.6 Hz, 2 H), 3.91–3.72 (m, 8 H). Anal. Calcd for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23. Found: C, 66.07; H, 7.25.

1,2,3,4,5,6-Hexa-*O*-benzyl-D-altritol (34). A. From Tetrol 33. To a solution of alcohol **33** (14 mg, 0.039 mmol) in DMF (0.3 mL) was added at room temperature NaH (6 mg, 0.232 mmol) followed by benzyl bromide (23 μL, 0.193 mmol) and finally *n*-Bu_4NI (3 mg). After 3 h, the reaction was quenched carefully (*caution*: gas evolution) with water and extracted twice with CH_2Cl_2. Combined extracts were washed with water and brine, dried over $MgSO_4$, and concentrated. Purification by flash chromatography (10% ethyl acetate–hexanes) afforded perbenzyl-D-altritol (**34**) (18 mg, 64%) as a colorless oil: $[\alpha]^{25}_D$ –1.2 (*c* 1.0, $CHCl_3$); IR (film) ν 3030, 1097 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.30–7.19 (m, 30 H), 4.71–4.43 (m, 12 H), 4.03–3.92 (m, 4 H), 3.79 (dd, J = 10.5, 3.1 Hz, 1 H), 3.70 (dd, J = 10.5, 5.7 Hz, 1 H), 3.60 (d, J = 4.8 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 139.4–138.7 (six lines), 128.7–127.7 (17 lines), 79.9, 79.3, 79.2, 74.7, 73.7–73.3 (four lines), 72.9, 71.0, 70.6. Anal. Calcd for $C_{48}H_{50}O_6$: C, 79.75; H, 6.97. Found: C, 79.74; H, 7.00.

B. From α-D-(+)-Talose. α-D-(+)-Talose (100 mg, 0.556 mmol) and freshly prepared Raney nickel (1 g) were refluxed in 70% aqueous ethanol (10 mL) for 1 h.[23] The nickel was removed by filtration, and the filtrate was concentrated under reduced pressure to give D-altritol (**36**) (72 mg, 71%) as a colorless syrup. Benzylation of crude **36** with NaH (109 mg, 4.55 mmol), benzyl bromide (450 μL, 3.79 mmol), and *n*-Bu_4NI (70 mg) in DMF (2

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mL) at room temperature for 20 h afforded, after flash chromatography (10% ethyl acetate–hexanes), perbenzyl-D-altritol (34) (175 mg, 67%) as a colorless oil: $[\alpha]^{25}_D$ -1.7 (c 1.0, $CHCl_3$); the IR and ^1H NMR spectra are identical to those of ether 34 prepared from tetrol 33.

4,5-Di-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-2-*O*-(methoxymethyl)-D-sorbitol (37). The procedure described for 32 was followed with homoallylic alcohol 17 (100 mg, 0.188 mmol). Flash chromatography (50% ethyl acetate–hexanes) afforded diol 37 (96 mg, 98%) as a colorless oil: $[\alpha]^{25}_D$ -35.7 (c 1.14, $CHCl_3$); IR (film) ν 3456, 1102 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33–7.27 (m, 10 H), 4.77–4.55 (m, 6 H), 3.89–3.61 (m, 8 H), 3.40 (s, 3 H), 3.27, 3.05 (d, br m, 2 H, disappear on exchange with D_2O), 0.89 (s, 9 H), 0.044 (s, 6 H). Anal. Calcd for $C_{28}H_{44}O_7Si$: C, 64.58; H, 8.52. Found: C, 64.46; H, 8.56.

4,5-Di-*O*-benzyl-D-sorbitol (38). The procedure described for tetrol 33 was followed with MOM ether 37 (68 mg, 0.131 mmol). Flash chromatography (50% ethyl acetate–hexanes, 5:5:1 hexanes–ethyl acetate–methanol) afforded tetrol 38 (47 mg, 100%) as a colorless oil: $[\alpha]^{25}_D$ -19.9 (c 1.43, $CHCl_3$); IR (film) ν 3395, 1056 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32–7.29 (m, 10 H), 4.77, 4.59 (ABq, J = 11.2 Hz, 2 H), 4.64 (s, 2 H), 3.89–3.60 (m, 8 H), 3.18, 3.09, 2.30 (br m, 4 H, disappear on exchange with D_2O). Anal. Calcd for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23. Found: C, 66.13; H, 7.24.

1,2,3,4,5,6-Hexa-*O*-benzyl-D-sorbitol (39). A. From Tetrol 38. The procedure described for ether 34 was followed with tetrol 38 (35 mg, 0.097 mmol), NaH (14 mg, 0.583 mmol), benzyl bromide (58 μL, 0.487 mmol), and n-Bu_4NI (7 mg) in DMF (0.4 mL). Flash chromatography (10% ethyl acetate–hexanes) afforded fully benzylated D-sorbitol 39 (53 mg, 76%) as a colorless oil: $[\alpha]^{25}_D$ +4.4 (c 1.0, $CHCl_3$); IR (film) ν 3028, 1097 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29–7.22 (m, 30 H), 4.71–4.34 (m, 12 H), 3.96 (t, J = 4.6 Hz, 1 H), 3.86–3.83 (m, 4 H), 3.69 (dd, J = 11.6, 6.6 Hz, 1 H), 3.57 (dd, J = 10.4, 3.2 Hz, 1 H), 3.49 (dd, J = 10.3, 4.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 139.2–138.8 (six lines), 128.7–127.7 (17 lines), 79.9–79.2 (four lines), 75.2, 74.4, 73.7, 73.6, 73.3, 72.4, 70.9, 70.4. Anal. Calcd for $C_{48}H_{50}O_6$: C, 79.75; H, 6.97. Found: C, 79.64; H, 6.99.

B. From D-Sorbitol. Benzylation of D-sorbitol (424 mg, 2.33 mmol) with NaH (0.75 g, 31.4 mmol), benzyl bromide (2.5 mL, 21.0 mmol), and n-Bu_4NI (150 mg) in DMF (10 mL) at room temperature for 20 h afforded, after flash chromatography (10% ethyl acetate–hexanes), perbenzyl-D-sorbitol (39) (1.30 g, 77%) as a colorless oil: $[\alpha]^{25}_D$ +3.9 (c 1.0, $CHCl_3$); the IR and ^1H NMR spectra are identical to those of ether 39 prepared from tetrol 38.

Dihydroxylation of Adduct 16. A. With Catalytic OsO_4. To a stirred solution of olefin 16 (33 mg, 0.062 mmol) in a 9:1 mixture of acetone–water (0.5 mL) at room temperature were added N-methylmorpholine N-oxide (14 mg, 0.120 mmol) and an aqueous solution of osmium tetraoxide (0.1 M, 50 μL, 0.005 mmol). After 20 h, saturated aqueous $NaHSO_3$ was added. After the mixture was stirred for 30 min, the products were extracted with ether twice, washed with water and brine, dried over $MgSO_4$, and concentrated. Flash chromatography on silica gel (50% ethyl acetate–hexanes) afforded a mixture of triols 40 and 41 (35 mg, 100%, ratio 75:25 by ^1H NMR analysis) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.27 (m, 10 H), 4.80–4.43 (m, 6 H), 4.00–3.74 (m, 8 H), 3.38, 3.34 (two s, 3 H, ratio 75:25), 1.17, 1.15 (two d, J = 6.5 Hz, 3 H), 0.89 (s, 9 H), 0.063 (s, 3 H), 0.054 (s, 3 H).

B. With AD-Mix-α. To a stirred two-phase solution of AD-mix-α[16] (87 mg) in a 1:1 mixture of t-BuOH–water (0.5 mL) at room temperature was added methanesulfonamide (6 mg, 0.063 mmol). The mixture was cooled to 0 °C, and olefin 16 (10 mg, 0.019 mmol) in t-BuOH (0.3 mL) was added. The mixture was vigorously stirred for 10 h at 0 °C, whereupon TLC analysis showed no reaction. After 3 days of stirring at room temperature, the mixture was quenched with saturated aqueous $NaHSO_3$ and stirred for 30 min. The products were extracted with CH_2Cl_2 twice, washed with water and brine, dried over $MgSO_4$, and concentrated. Flash chromatography on silica gel (50% ethyl acetate–hexanes) afforded a mixture of triols 40 and 41 (1.5 mg, 14%, ratio 87:13 by ^1H NMR analysis) as a colorless oil, along with recovered olefin 16 (7 mg, 70%).

C. With AD-Mix-β. The procedure described above was followed with olefin 16 (22 mg, 0.041 mmol), methanesulfonamide (6 mg, 0.063 mmol), and AD-mix-β[16] (87 mg). Flash chromatography (50% ethyl acetate–hexanes) afforded a mixture of triols 40 and 41 (3 mg, 11%, ratio 50:50 by ^1H NMR analysis) as a colorless oil, along with recovered olefin 16 (18 mg, 82%).

Dihydroxylation of Adduct 17 with Catalytic OsO_4. The procedure described for osmylation of 16 was followed with olefin 17 (55 mg, 0.104 mmol), N-methylmorpholine N-oxide (24 mg, 0.207 mmol), and an aqueous solution of osmium tetraoxide (0.1 M, 100 μL, 0.01 mmol) in a 9:1 mixture of acetone–water (0.5 mL). Flash chromatography on silica gel (50% ethyl acetate–hexanes) afforded a mixture of triols 42 and 43 (54 mg, 93%, ratio 80:20 by ^1H NMR and ^{13}C NMR analysis) as a colorless oil: ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.27 (m, 10 H), 4.78–4.52 (m, 6 H), 4.05–3.37 (m, 8 H), 3.361, 3.356 (two s, 3 H, ratio 80:20), 1.13 (d, J = 6.5 Hz, 3 H), 0.89 (s, 9 H), 0.054, 0.049 (two s, 6 H).

42: partial ^{13}C NMR (75 MHz, $CDCl_3$) δ 98.1, 81.1, 79.4, 76.9, 74.5, 73.3, 72.9, 71.9, 66.7, 61.9, 56.2.

43: partial ^{13}C NMR (75 MHz, $CDCl_3$) δ 98.5, 81.6, 80.9, 73.8, 73.2, 70.1, 62.2, 56.1.

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Supplementary Material Available: ^1H NMR spectra of key intermediates (16 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.