Preferred Conformation of C-Glycosides. 8. Synthesis of 1,4-Linked Carbon Disaccharides†,‡

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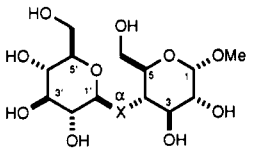
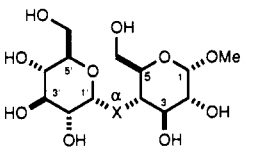
Three general synthetic routes to 1,4-linked carbon disaccharides (e.g., **3**, **4**, **15–17**, **21–23**, **44**, and **45**) are presented. Control of the stereochemistry at C.1′, C.2′, C.5′, and C.4, the incorporation of deuterium labels at the C.α position, and structural modifications of the right-hand ring are addressed.

Introduction

In order to investigate the conformational properties[1] of the carbon analogues of 1,4-linked disaccharides, it was necessary to develop a general synthesis of *C*-1,4-disaccharides, such as the carbon analogue **3** of cellobioside (**1**) and the carbon analogue **4** of maltoside (**2**). To fulfill our requirements, the synthetic plan must address (a) the issue of stereochemical control at C.1′, (b) the stereospecific incorporation of deuterium labels at the C.α position, and (c) the preparation of structurally modified derivatives, in particular at C.3 and C.5.[2]



1: X=O
3: X=CH_2



2: X=O
4: X=CH_2

With this in mind, we developed three synthetic approaches, routes A, B, and C (Scheme I). The key intermediates II, III, and IV required for these synthetic studies diverge from a precursor of structure type I. The first two approaches, routes A and B, involve nucleophilic attack on a pyranose oxonium ion. In connection with the chemical studies of the marine natural product palytoxin,[3] we showed that the stereochemical course of such a nucleophilic attack can be rationalized in terms of stereoelectronic and steric effects.[4] On the basis of this rationale, the addition of a hydride nucleophile to the oxonium II′ at C.1′ is expected to yield predominantly the equatorial *C*-glycoside V(*S*). On the other hand, the attack of a carbon nucleophile on the oxonium III′ at C.5′ is expected to yield V(*R*).

The key step in route C is an intramolecular epoxide opening, i.e., IV to V. The acid-catalyzed intramolecular epoxide opening is known to be effective for the construction of tetrahydrofuran[5] and tetrahydropyran[6] ring systems. The stereochemistry at C.1′ and C.5′ of the starting material dictates the stereochemical course of the cyclization. Thus, substrates IV(*S*) and IV(*R*) lead to V(*S*) and V(*R*), respectively.

We planned to synthesize the intermediate of structure type I by osmylation of the olefin VI or VII (Scheme II). An empirical rule concerning the stereochemical outcome of the osmylation of allylic alcohols and ethers was formulated in these laboratories.[7] On the basis of this rule, we anticipated the major product in the osmylation of VI to be I(*R*) with the C.1′ stereochemistry required for the synthesis of II, III(*R*), and IV(*R*). On the other hand, osmylation of VII should produce predominantly I(*S*), which has the C.1′ stereochemistry corresponding to IV(*S*). The C.2′ stereochemistry of I(*S*) and I(*R*) does not correspond to the C.2′ stereochemistry of **3** and **4**, but we hoped to invert this stereocenter into the corresponding C.2-gluco configuration at a later stage of the synthesis.

The *cis*- and *trans*-olefins VI and VII should be obtainable by olefination of a suitably functionalized C.4-substituted pyranoside with a derivative of a pentose aldehyde. A literature search for a suitable starting material suggested that the known C.4-allylglucoside **5**[8] would fulfill our needs.

Results and Discussion

The Synthesis of Intermediate I. Using a sequence of standard reactions, the phosphonium salt **6** was synthesized from **5** in 60% overall yield. The aldehyde **7** was prepared in 67% yield, following the procedure known for its antipode.[9] Wittig olefination of the ylide generated from **6** and the aldehyde **7** provided the olefin **8** in 82% yield. The olefinic vicinal coupling constant (J = 11.1 Hz) in deuteriobenzene established its cis geometry.

Stoichiometric osmylation of the olefin **8** (OsO_4/Py/THF/−35 °C) afforded a 6:1 mixture of diol **9** (60% yield) and its diastereomer (11% yield). Catalytic osmylation [OsO_4 (cat.)/*N*-methylmorpholine *N*-oxide (NMMO)[10]/1,4-diazabicyclo[2,2,2]octane (DABCO),[11] acetone/water, 5 °C] proceeded with comparable selectivity, giving **9** and

† Preliminary results of a part of this work have been published: Babirad, S. A.; Wang, Y.; Kishi, Y. *J. Org. Chem.* **1987**, *52*, 1370. For Part 7 of this series, see: Goekjian, P. G.; Wu, T.-C.; Kang, H.-Y.; Kishi, Y. *J. Org. Chem.* **1991**, *56*, 6422.

‡ Taken in part from Wang, Y. Ph.D. Dissertation, Harvard University, 1990.

(1) (a) Wu, T.-C.; Goekjian, P. G.; Kishi, Y. *J. Org. Chem.* **1987**, *52*, 4819. Goekjian, P. G.; Wu, T.-C.; Kishi, Y. *J. Org. Chem.* **1991**, *56*, 6412. (b) Goekjian, P. G.; Wu, T.-C.; Kang, H.-Y.; Kishi, Y. *J. Org. Chem.* **1987**, *52*, 4823. Goekjian, P. G.; Wu, T.-C.; Kang, H.-Y.; Kishi, Y. *J. Org. Chem.* **1991**, *56*, 6422.

(2) (a) Babirad, S. A.; Wang, Y.; Goekjian, P. G.; Kishi, Y. *J. Org. Chem.* **1987**, *52*, 4825. (b) Wang, Y.; Goekjian, P. G.; Ryckman, D. M.; Kishi, Y. *J. Org. Chem.* **1988**, *53*, 4151. (c) Miller, W. H.; Ryckman, D. M.; Goekjian, P. G.; Wang, Y.; Kishi, Y. *J. Org. Chem.* **1988**, *53*, 5580.

(3) (a) For the gross structure of palytoxin, see the references cited in ref 13 of Part 6 of this series. (b) For the stereochemistry assignment of palytoxin, see the references cited in ref 14 of Part 6 of this series. (c) For a total synthesis of palytoxin carboxylic acid and amide, see the references cited in ref 15 of Part 6 of this series.

(4) (a) Lewis, M. D.; Cha, J. K.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 4976. (b) Tino, J. A.; Lewis, M. D.; Kishi, Y. *Heterocycles*, **1987**, *25*, 97. (c) Babirad, S. A.; Wang, Y.; Kishi, Y. *J. Org. Chem.* **1987**, *52*, 1370.

(5) For example, see a review: Boivin, T. L. B. *Tetrahedron* **1987**, *43*, 3309.

(6) For example, see: Nicolaou, K. C.; Papahatjis, D. P.; Claremon, D. A.; Dolle, R. E. *J. Am. Chem. Soc.* **1981**, *103*, 6967.

(7) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron* **1984**, *40*, 2247 and references cited therein.

(8) Kelly, A. G.; Roberts, J. S. *J. Chem. Soc., Chem. Commun.* **1980**, 228.

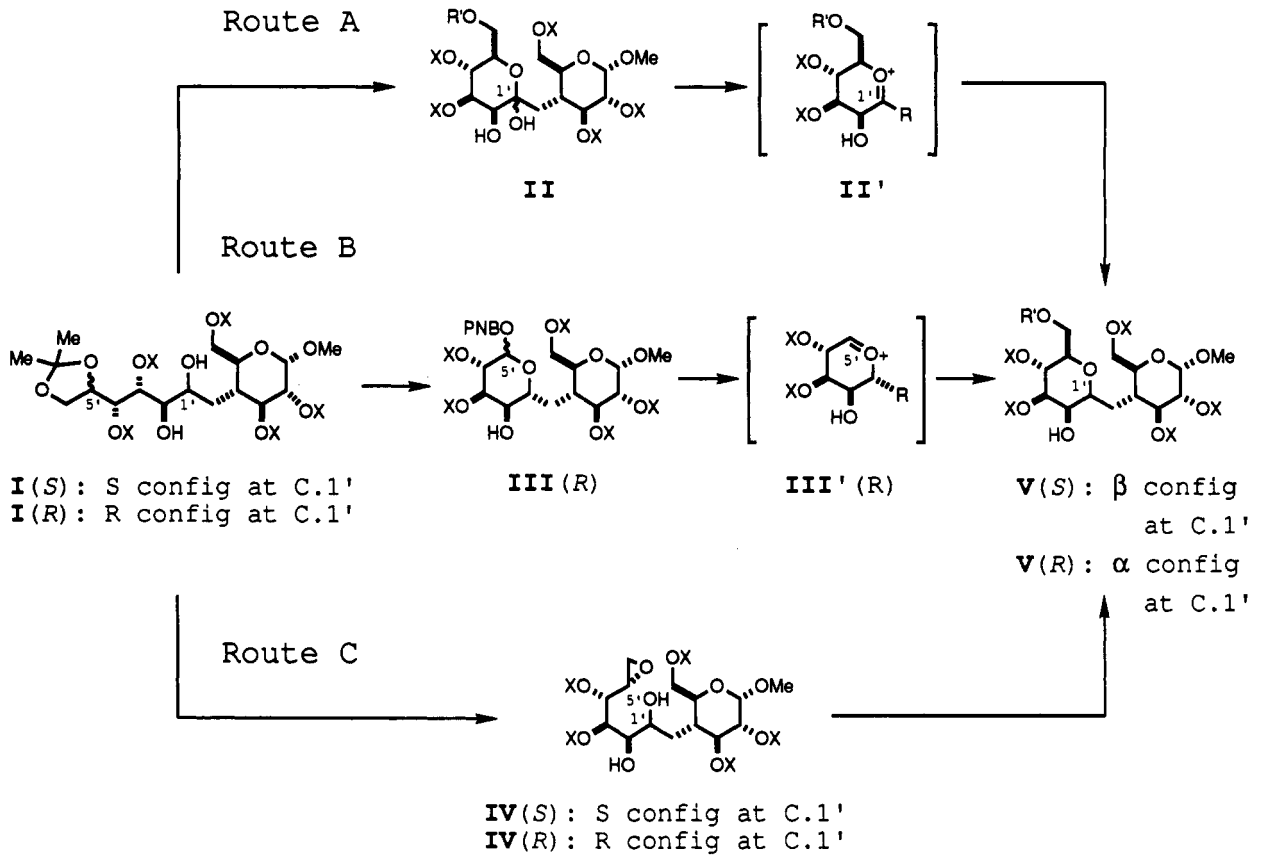
(9) Just, G.; Potvin, P. *Can. J. Chem.* **1980**, *58*, 2173.

(10) VanRheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973.

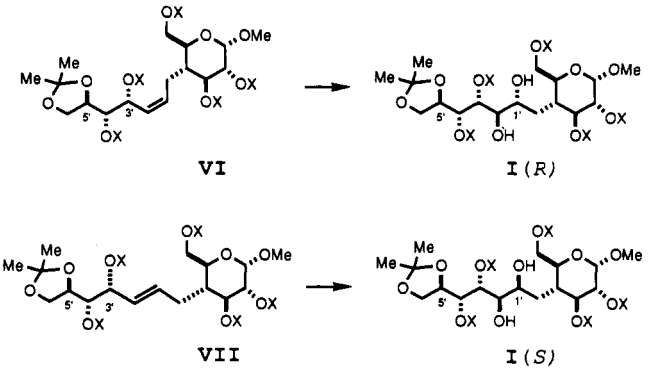
(11) It is worthwhile to note that catalytic osmylation did not proceed in the absence of DABCO.

0022-3263/92/1957-0468$03.00/0

Scheme I



Scheme II

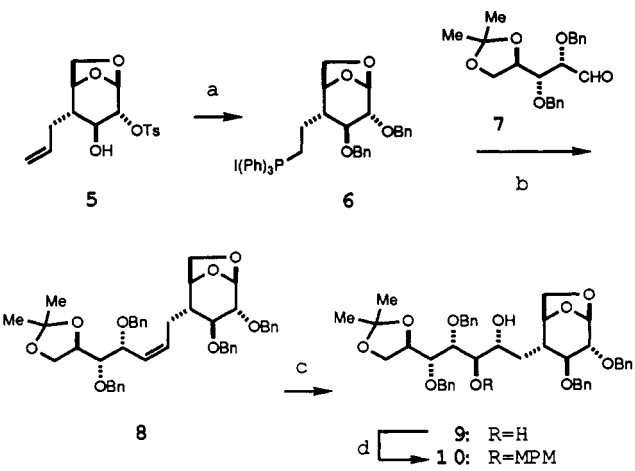


its diastereomer in 55% and 16% yield, respectively. The stereochemistry of **9** was tentatively assigned on the basis of the empirical rule[7] and was confirmed at a later stage of the synthesis.

Using a recently developed asymmetric process[12] employing a chiral diamine[12f] (OsO_4/*N*,*N*'-bis(mesitylmethyl)-(*R*,*R*')-1,2-diphenyl-1,2-diaminoethane/CH_2Cl_2/−80 °C/1 day), the selectivity of the osmylation was boosted to a 58:1 ratio of **9** (80% yield) to its diastereomer. As expected, osmylation in the presence of the antipode of the diaminoethane was found to be extremely sluggish (less than 5% conversion at −50 °C for 1 week), and the selectivity dropped to 4.6 to 1.[13]

One important practical aspect of the asymmetric osmylation is the remarkable enhancement of the reaction rate in the presence of the chiral diamine. Osmylation proceeded smoothly even at −80 °C, suggesting the possibility of improving the stereoselectivity of the osmylation

Scheme III[a]

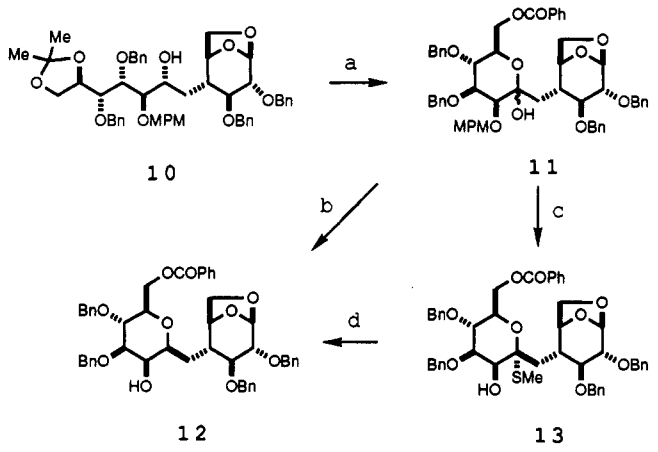


[a] Reagents and conditions: (a) (i) Na–Hg, MeOH; (ii) BnBr, NaH, *n*-$Bu_4N^+I^-$ (cat.), THF/DMF (2:1); (iii) OsO_4 (cat.), NMMO, acetone/H_2O (4:1); (iv) $NaIO_4$, MeOH/H_2O (1:1); (v) $NaBH_4$, MeOH/Et_2O (1:2); (vi) MsCl, Et_3N, Et_2O; (vii) NaI, $NaHCO_3$, acetone; (viii) PPh_3, DMF, 110 °C; (b) *n*-BuLi, THF, −78 to 0 °C; (c) OsO_4, *N*,*N*'-bis(mesitylmethyl)-(*R*,*R*')-1,2-diphenyl-1,2-diaminoethane, CH_2Cl_2, −80 °C; (d) MPM–Br, NaH, THF.

(12) For asymmetric osmylation, see: (a) Hentges, S. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 4263. For the latest paper on this subject from this group, see: Shibata, T.; Gilheany, D. G.; Blackburn, B. K.; Sharpless, K. B. *Tetrahedron Lett.* **1990**, *31*, 3817. (b) Yamada, T.; Narasaka, K. *Chem. Lett.* **1986**, 131. (c) Tokles, M.; Snyder, J. K. *Tetrahedron Lett.* **1986**, *27*, 3951. (d) Tomioka, K.; Nakajima, M.; Koga, K. *J. Am. Chem. Soc.* **1987**, *109*, 6213. Tomioka, K.; Nakajima, M.; Koga, K. *Tetrahedron Lett.* **1990**, *31*, 1741. (e) Hirama, M.; Oishi, T.; Itô, S. *J. Chem. Soc., Chem. Commun.* **1989**, 665. Oishi, T.; Hirama, M. *J. Org. Chem.* **1989**, *54*, 5834. (f) Corey, E. J.; Jardin, P. D.; Virgil, S.; Yuen P.-W.; Connell, R. D. *J. Am. Chem. Soc.* **1989**, *111*, 9243.

(13) For a recent review on double stereodifferentiation, see: Masamune, S.; Choy, W.; Petersen, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1.

Scheme IV[a]



[a] Reagents and conditions: (a) (i) Swern oxidation; (ii) 4 N HCl/THF; (iii) PhCOCl, pyridine; (b) *n*-Pr_3SiH, $BF_3{\cdot}Et_2O$, CH_3CN, −20 °C; (c) MeSH, $BF_3{\cdot}Et_2O$, CH_2Cl_2, 0 °C; (d) *n*-Bu_3SnH, AIBN, PhMe, 110 °C.

without recourse to a chiral auxiliary. Indeed, osmylation of **8** using the achiral *N,N'*-bis(mesitylmethyl)-1,2-diaminoethane (−80 °C/2 days) gave a respectable 18:1 selectivity of **9** (66% yield) to its diastereomer.

Monoprotection of **9** was accomplished by treatment with *p*-methoxybenzyl bromide and sodium hydride in THF to provide the C.2′ mono-*p*-methoxybenzyl (MPM) ether **10** in 69% yield.[14] The observed regioselectivity seems to be general for this type arrangement of functional groups and is useful from a preparative point of view. The origin of the selectivity may be attributed to an electronic effect of the electronegative oxygen at the C.3′ position.[16] An additional example was found in a later stage of this study (vide infra).

Route A. The MPM ether **10** was converted into the hemiketal **11** in three steps in 69% overall yield (Scheme IV). Upon treatment with tri-*n*-propylsilane and boron trifluoride etherate in acetonitrile at −20 °C, **11** gave the β(equatorial) isomer **12** in 82% yield along with a small amount of the α(axial) isomer (stereoselectivity ca. 7:1). The structure of the silane was found to have a strong influence on the stereoselectivity of the reduction. Under identical conditions, triethylsilane produced a 3:1 ratio of β/α isomers, but the selectivity with phenyldimethylsilane dropped to 3:2. Furthermore, the selectivity of the silane reduction is delicately substrate dependent. For example, reduction of the 3-deoxy hemiketal **56** with phenyldimethylsilane gave exclusively the unexpected α(axial) product **55** (vide infra).

An alternative method of reduction was investigated. It is known that monothioketals are reduced by trialkyltin hydrides, usually with excellent stereoselectivity.[17] The hemiketal **11** was transformed to the methyl monothioketal **13** by treatment with methyl mercaptan and boron trifluoride etherate at 0 °C (94% yield). Compound **13** was subjected to radical reduction (*n*-Bu_3SnH/AIBN/110 °C) to give exclusively the β isomer **12**. The observed stereospecificity appears to be very general, and the two-step transformation is attractive for preparative purposes.

Inversion of the C.2′ stereocenter of **12** was accomplished by Swern oxidation,[18] followed by reduction with borane–triethylamine complex,[19] in good overall yield (Scheme V). The stereoselectivity of the reduction was at least 8:1. Saponification of the benzoyl group of **12** and **14**, followed by hydrogenolysis of the benzyl groups, gave the 1,6-anhydropolyols **15** and **17**, respectively. Acid methanolysis[20] of **15** and **17** furnished the desired methyl glucosides **16** and **3** in 90% yield, respectively, as a 5:1 mixture of methyl α- and β-glycosides, which were readily separated as the peracetates.

Route B. Using a sequence of standard reactions, the secondary alcohol **10** was converted into the pyranosyl-*p*-nitrobenzoates **18A** (70% overall) and **18B** (25% overall) (Scheme VI).[21] Treatment of the major *p*-nitrobenzoate with propargyltrimethylsilane[22] and trimethylsilyl triflate in acetonitrile at −20 °C yielded the expected product **19** (70% yield) along with a small amount of the C.5′ stereoisomer (stereoselectivity ca. 10:1). Under the same conditions, the minor *p*-nitrobenzoate **18B** was recovered unchanged. Under more forcing conditions, the 1,6-anhydro moiety of **18B** was found to participate in the C-glycosidation, giving the desired product **19** only in low yield. It was therefore more practical to recycle the minor *p*-nitrobenzoate into the major *p*-nitrobenzoate. Ozonolysis of **19**, followed by reduction then benzoylation, provided the alcohol **20** in 92% yield.

Inversion of the C.2′ stereocenter of **20** was again accomplished by Swern oxidation and diborane reduction (stereoselectivity: >10:1) in 80% overall yield (Scheme VII). Using the same sequence of reactions as before, these intermediates were converted to *C*-disaccharides **21–23**, and **4**, respectively.

Route C. An intermediate such as **10** provides an obvious route to the epoxide required to test the feasibility of route C. However, the C.5′ stereochemistry necessary for the synthesis of *C*-maltoside **4** via this route is opposite to that of **10**. We envisioned that this could be accomplished by following the same route as before with aldehyde **24**.

The aldehyde **24** was prepared from L-xylose, using six standard synthetic steps. Wittig reaction of the ylide generated from **6** with **24** gave the *cis*-olefin **25** in 76% yield (Scheme VIII). Osmylation, followed by MPM monoprotection then acetonide hydrolysis, furnished the triol. Treatment of the resultant triol with sodium hydride and tosylimidazole[23] gave the expected epoxide **26A**. Upon treatment with a mild acid (PPTS[24] in methylene chloride), however, the epoxide **26A** yielded a 2:1 mixture of pyranoside and furanoside. Formation of the furanoside appeared to be due to the instability of the MPM protecting group under acidic conditions. In order to suppress

(14) The regiochemistry of **10** was determined based on the analysis of the ^1H NMR of the corresponding acetate. A small amount of di-MPM ether and undesired mono-MPM ether were found as by-products, and they were recycled by removal of the MPM group with ceric ammonium nitrate (CAN)[15] and then resubjected to the same reaction conditions.

(15) Johansson, R.; Samuelsson, B. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2371.

(16) Scattered examples for this type of selectivity are known in the literature; for example, see: Norrman, B. *Acta Chem. Scand.* **1968**, *22*, 1381.

(17) Nicolaou, K. C.; McGarry, D. G.; Somers, P. K.; Veale, C. A.; Furst, G. T. *J. Am. Chem. Soc.* **1987**, *109*, 2504.

(18) (a) Omura, K.; Swern, D. *Tetrahedron*, **1978**, *34*, 1651. (b) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.

(19) Jones, W. M. *J. Am. Chem. Soc.* **1960**, *82*, 2528.

(20) (a) Fisher, E. *Ber. Dtsch. Chem. Ges.* **1889**, *26*, 2400. (b) Prystas, M.; Sorm, F. *Collect. Czech. Chem. Commun.* **1971**, *36*, 1448.

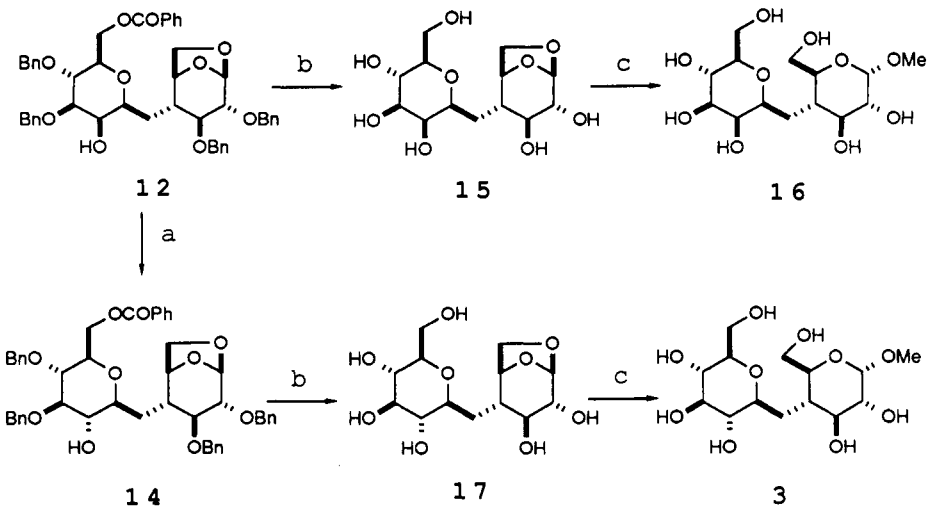
(21) We were unable to establish the stereochemistry of **18A** and **18B** firmly, based on the ^1H NMR spectra. However, the reactivity difference observed in the C-alkylation suggested the stereochemistry of **18A** (the major product) to be β and the stereochemistry of **18B** (the minor product) to be α.

(22) Masson, J. C.; Le Quan, M.; Cadiot, P. *Bull. Soc. Chim. Fr.* **1967**, 777.

(23) (a) Staab, H. A. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 351. (b) Hicks, D. R.; Fraser-Reid, B. *Synthesis* **1974**, 203.

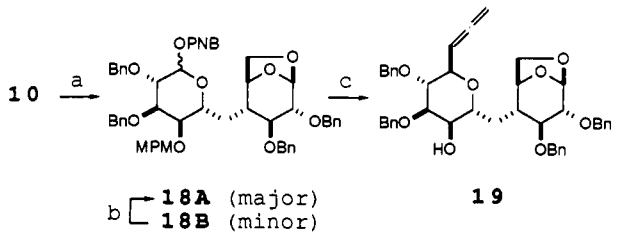
(24) Miyashita, M.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772.

Scheme V[a]



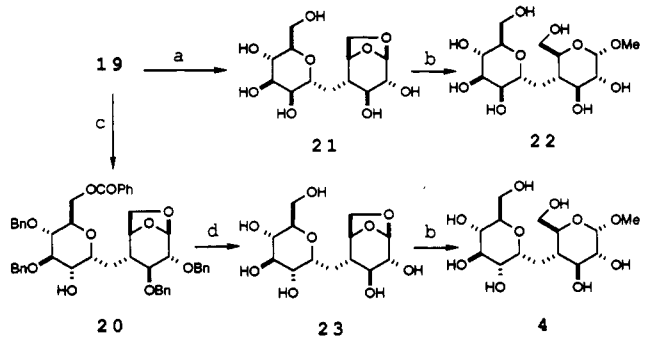
[a] Reagents and conditions: (a) (i) Swern oxidation; (ii) BH_3·Et_3N, THF; (b) (i) NaOMe, MeOH; (ii) H_2, $Pd(OH)_2/C$, MeOH; (c) MeOH, HCl, 90 °C.

Scheme VI[a]



[a] Reagents and conditions: (a) (i) $AcOH/H_2O$ (3:2), 40 °C; (ii) $Pb(OAc)_4$, PhH, 0 °C; (iii) PNB–Cl, Py, CH_2Cl_2; (b) (i) K_2CO_3, MeOH; (ii) PNB–Cl, Py, CH_2Cl_2; (c) propargyl–TMS, TMSOTf, CH_3CN.

Scheme VII[a]

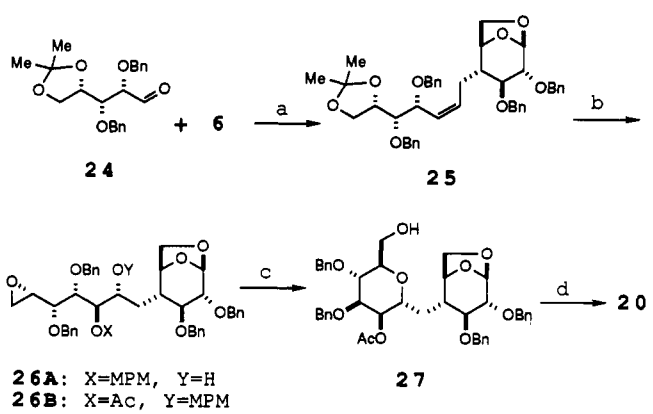


[a] Reagents and conditions: (a) (i) O_3, MeOH, −78 °C, followed by Me_2S then $NaBH_4$ workup; (ii) H_2, $Pd(OH)_2/C$, MeOH; (b) MeOH, HCl, 90 °C; (c) (i) same as (a) (i); (ii) PhCOCl, Py; (iii) Swern oxidation; (iv) BH_3·THF, THF; (d) (i) NaOMe, MeOH; (ii) same as (a) (ii).

formation of the furanoside, the C.2′ acetate **26B** was tested. Upon CAN deprotection[15] of the MPM group then *p*-toluenesulfonic acid (*p*-TsOH) treatment, **26B** gave the desired pyranoside **27** in 96% yield. The resultant pyranoside was transformed to and correlated with the *C*-disaccharide **20** obtained via route B.

The synthesis of *C*-cellobiose **3** via route C requires the *trans*-olefin **29**. The *trans*-olefin was prepared by Julia reaction (Scheme IX).[25] The sulfone **28**, synthesized from **5** in 60% overall yield, was reacted with the aldehyde **24**

Scheme VIII[a]



[a] Reagents and conditions: (a) *n*-BuLi, THF, −78 to 0 °C; (b) (i) OsO_4, *N,N′*-bis(mesitylmethyl)-(*R,R*)-1,2-diphenyl-1,2-diaminoethane, CH_2Cl_2, −80 °C; (ii) $MeOPhCH(OMe)_2$, PPTS, PhH, 80 °C; (iii) $NaBH_3CN$,[15] CF_3CO_2H, molecular sieves (3 Å), DMF; (iv) Ac_2O, Py; (v) 3 N HCl, THF; (vi) *p*-TsCl, Py; (vii) NaH, THF; (c) (i) CAN, CH_3CN/H_2O (10:1); (ii) *p*-TsOH, CH_2Cl_2; (d) (i) K_2CO_3, MeOH; (ii) PhCOCl, Py.

under modified Julia conditions.[26] to yield a mixture of all four possible adducts. Treatment of the resultant mixture with 4% sodium amalgam yielded the *trans*-olefin **29** in 47% overall yield along with some of the *cis*-olefin **25** (trans:cis = 5:1). Following the same sequence of reactions as before, the *trans*-olefin **29** was converted into the epoxide **30A** in six steps (51% overall yield).

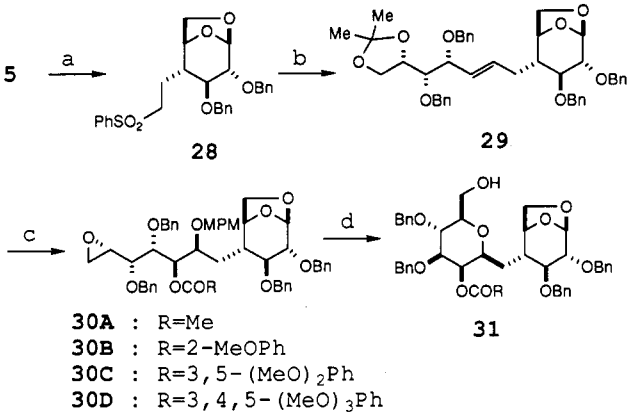
Unlike the erythro series, *p*-TsOH treatment of **30A** yielded exclusively the furanoside. The difference in reactivity between the erythro and the threo series may be attributed to more facile migration of the acyl group in the latter series. To prevent acyl migration, epoxides **30B–D** bearing representative electron-rich acyl groups were tested. The epoxide **30B** gave a ca. 2:1 ratio of pyranoside/furanoside under the same acidic conditions. The epoxide **30C** improved the ratio up to ca. 5:1, and the epoxide **30D** gave exclusively the desired pyranoside product **31** [R = 3, 4, 5-$(MeO)_3$Ph] in 85% yield. Com-

(25) For a review on Julia reaction, see: Magnus, P. D. *Tetrahedron* 1977, *33*, 2019.

(26) Achmatowicz, B.; Baranowska, E.; Daniewski, A. R.; Pankowski, J.; Wicha, J. *Tetrahedron Lett.* 1985, *26*, 5597.

(27) Horita, K.; Yoshioka, T.; Tanaka, T.; Oikawa, Y.; Yonemitsu, O. *Tetrahedron* 1986, *42*, 3021 and references cited therein.

Scheme IX[a]

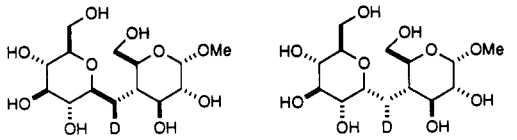


[a] Reagents and conditions: (a) (i–v) same as (a) (i–v) in Scheme III; (vi) PhSSPh, *n*-Bu_3P, THF; (vii) MCPBA, CH_2Cl_2; (b) (i) **28** was treated with *n*-BuLi (THF, 0 °C), with $BF_3{\cdot}Et_2O$ (−78 °C), then with **24** (−78 to 0 °C); (ii) Na–Hg, MeOH, 0 °C; (c) (i) OsO_4, *N*,*N*′-bis(mesitylmethyl)-(*R*,*R*)-1,2-diphenyl-1,2-diaminoethane, CH_2Cl_2, −80 °C; (ii) $MeOPhCH(OMe)_2$, PPTS, PhH, 80 °C; (iii) $NaBH_3CN$, CF_3CO_2H, molecular sieves (3 Å), DMF; (iv) RCOCl, DMAP; (v) 3 N HCl, THF; (vi) *p*-TsCl, Py; (vii) NaH, THF; (d) (i) DDQ,[27] pH 7 buffer, CH_2Cl_2; (ii) *p*-TsOH, CH_2Cl_2.

pound **31** was then transformed into the final product **3** as described before.

In summary, three complementary routes have been developed to synthesize 1,4-linked carbon disaccharides. Route A provides access to equatorial β(1,4)-linked *C*-disaccharides. Route B gives access to axial α(1,4)-linked *C*-disaccharides. Route C provides access to both α(1,4)- and β(1,4)-linked *C*-disaccharides.

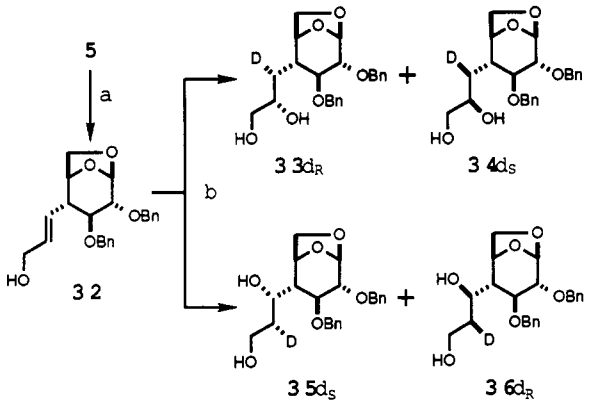
C. α-Deuterated Analogues. Conclusive assignment of the C.α methylene protons responsible for the individual resonances in the ^1H NMR spectrum was crucial for conformational analysis of the 1,4-linked carbon disaccharides.[1,2] For this reason, it was necessary to synthesize the specifically monodeuterated compounds **3**-d_R and **4**-d_S.



The synthesis must meet two requirements: (a) these substances must be stereochemically homogeneous, and (b) the absolute configuration of the carbon–deuterium bond must be established unambiguously. With these two requirements in mind, we found the allylic alcohol **32**, readily available from the alcohol **5**, to be a useful intermediate (Scheme X). The geometry of the olefin of **32** was proved to be trans on the basis of the vicinal coupling constant (J = 15.5 Hz) for the vinyl protons. Deuteroboration of **32** yielded a mixture of all four possible products, **33**-d_R, **34**-d_S, **35**-d_S, and **36**-d_R, in nearly equal amounts. The gross structure of the isolated 1,2-diols **33**-d_R and **34**-d_S was confirmed by their susceptibility to periodate oxidation, while their stereochemistry was established by comparison with the authentic samples prepared by Sharpless asymmetric epoxidation of **32**.[28,29]

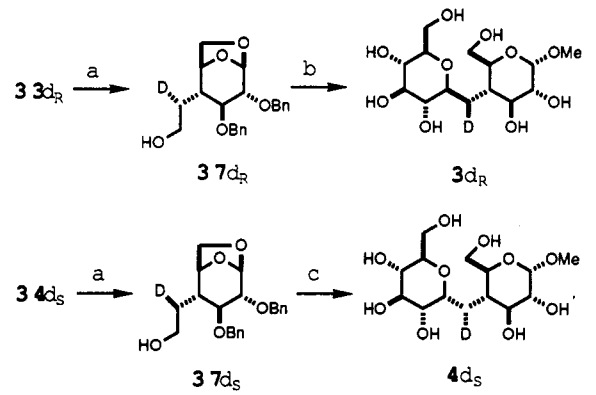
(28) For reviews on Sharpless asymmetric epoxidation, see: (a) Finn, M. G.; Sharpless, K. B. *Asymmetric Synth.* **1985**, *5*, 247. (b) Rossiter, B. E. *Asymmetric Synth.* **1985**, *5*, 193.

Scheme X[a]



[a] Reagents and conditions: (a) (i–v) same as (a) (i–v) in Scheme III; (vi) *o*-$NO_2PhSeCN$,[31] *n*-Bu_3P, PhH, followed by MCPBA oxidation (CH_2Cl_2) then Et_3N treatment; (vii) O_3, MeOH, −78 °C, followed by Me_2S then $NaBH_4$ workup, 0 °C; (viii) Swern oxidation; (ix) $Ph_3P{=}CHCO_2Me$, CH_2Cl_2; (x) DIBAL, CH_2Cl_2; (b) (i) BD_3, THF, followed by H_2O_2 workup; (ii) separation of regio- and stereoisomers.

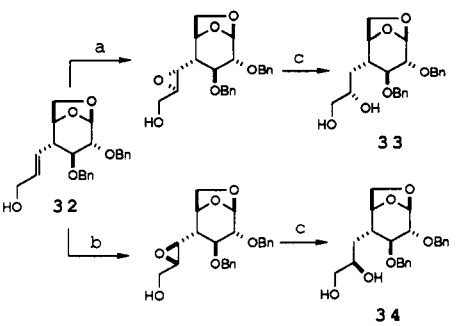
Scheme XI[a]



[a] Reagents and conditions: (a) (i) $NaIO_4$, $MeOH/H_2O$ (1:1); (ii) $NaBH_4$, $MeOH/Et_2O$; (b) see Schemes III–V; (c) see Schemes III, VI, and VII.

The 1,2-diols **33**-d_R and **34**-d_S were converted into the primary alcohols **37**-d_R and **37**-d_S, respectively (Scheme

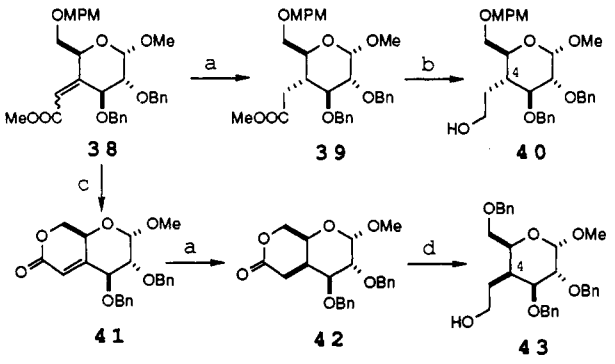
(29) Epoxidation of the allylic alcohol **32** in the presence of diethyl (−)-tartrate, followed by diisobutylaluminum hydride reduction,[30] gave **33**. The same sequence of reactions with diethyl (+)-tartrate gave the diol **34**. Comparison with **33** and **34** thus obtained established the stereochemistry of the secondary alcohol of the 1,2-diols isolated from deuteroboration as well as hydroboration of **32**. Coupled with the trans geometry of the olefinic bond of **32**, the stereochemistry of the deuterium labels was concluded as indicated.



Reagents and conditions: (a) *t*-BuOOH, diethyl (−)-tartrate, Ti(*i*-OPr)$_4$, CH_2Cl_2; (b) *t*-BuOOH, diethyl (+)-tartrate, Ti(*i*-OPr)$_4$, CH_2Cl_2; (c) DIBAL, PhH.

(30) Finan, J. M.; Kishi, Y. *Tetrahedron Lett.* **1982**, *23*, 2719.

Scheme XII[a]



[a] Reagents and conditions: (a) H_2, Pd/C, EtOH; (b) LAH, Et_2O; (c) CAN, CH_3CN/H_2O (10:1); (d) (i) LiOH, THF/H_2O (2:1); (ii) BnBr, NaH, n-$Bu_4N^+I^-$ (cat.), THF/DMF (10:3); (iii) LAH, Et_2O.

XI). Following the routes described for the unlabeled compounds, **37**-d_R and **37**-d_S were then converted into **3**-d_R and **4**-d_S.

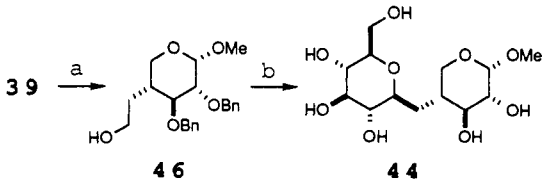
C.3 and C.5 Structural Modifications. The synthesis reported provides a stereocontrolled route to either α- or β-1,4-linked carbon disaccharides, as well as to the C.2′ epimers and the stereospecifically C.α-labeled analogues. However, it is clear that the choice of 1,6-anhydroglucose derivative **5** as the starting material limits the ability to modify the structure of the right-hand ring. In addition, while the 1,6-anhydro-*C*-maltose and 1,6-anhydro-*C*-cellobiose played an important role for the conformational analysis of this class of compounds,[2] the methanolysis of the 1,6-anhydro bridge and the purification of the methyl glycosides was laborious. To overcome these difficulties, the synthesis of the C.4-substituted methyl glycosides **40** and **43** was studied. In principle, both stereoisomers at C.4 can be derived from a single precursor by stereoselective reduction of an exocyclic olefin. Thus, the α,β-unsaturated ester **38**, a ca. 1:1 *E*/*Z* mixture readily available from 4,6-anisylidene α-methyl glucoside, might give access to either the equatorial or the axial product selectively.

Direct hydrogenation of **38** in the presence of 10% palladium on charcoal in ethanol gave exclusively the equatorial ester **39** in 98% yield (Scheme XII). The stereochemistry of **39** was assigned on the basis of the vicinal coupling constants ($J_{3,4}$ = 10.1 and $J_{4,5}$ = 10.7 Hz) and further confirmed by chemical correlation with an authentic sample.[32] Compound **39** was transformed into the alcohol **40** by lithium aluminum hydride reduction.

The opposite stereochemistry at C.4 was obtained by reduction of the bicyclic lactone **41**. Treatment of **38** with ceric ammonium nitrate (CAN) gave directly the α,β-unsaturated lactone **41** in 85% yield. Hydrogenation of the α,β-unsaturated lactone **41** gave the lactone **42** ($J_{3,4}$ = 5.0 and $J_{4,5}$ = 2.0 Hz) in almost quantitative yield (stereoselectivity: at least 18:1). The lactone **42** was then converted to the primary alcohol **43** in 70% overall yield in three steps.

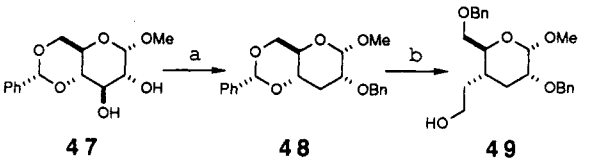
The observed stereoselectivity of hydrogenations may be attributed to steric constraints. Examination of molecular models shows that the bottom face of **38** is sterically more hindered, resulting in the equatorial product **39**. On the other hand, the catalyst approaches preferentially from the convex (bottom) face of **41**, yielding the axial product **42**.

Scheme XIII[a]



[a] Reagents and conditions: (a) (i) DDQ, pH 7 buffer, CH_2Cl_2; (ii) Swern oxidation; (iii) $RhCl(PPh_3)_3$, $PhCH_3$, 110 °C; (iv) LAH, Et_2O; (b) see Schemes III–V.

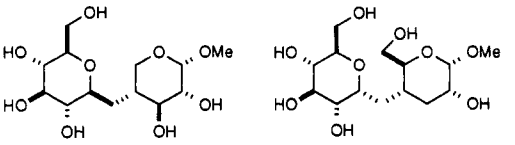
Scheme XIV[a]



[a] Reagents and conditions: (a) (i) BnBr, NaOH, THF/H_2O (15:1); (ii) MePhOCSCl, Py, CH_2Cl_2; (iii) n-Bu_3SnH, AIBN, 110 °C; (b) (i) $NaBH_3CN$, HCl, molecular sieves (3 Å), THF; (ii) Swern oxidation; (iii) $(MeO)_2(O)PCH_2CO_2Me$, t-BuOK, THF/DMF (5:2); (iv) H_2, Pd/C, EtOH; (v) LAH, Et_2O.

The primary alcohol **40** was successfully converted to the 1,4-linked *C*-disaccharides **3** and **4** by the same routes as the 1,6-anhydro precursors. Compound **43** could be used for the preparation of the carbon analogues of 4-*O*-α-D-glucopyranosyl-α-D-galactoside and 4-*O*-β-D-glucopyranosyl-α-D-galactoside.

One of the obvious advantages of this approach is that it allows for structural modifications of the right-hand pyranose ring. The flexibility and efficiency are illustrated by the synthesis of methyl C.5-(deshydroxymethyl)-*C*-cellobioside (**44**) and methyl C.3-deoxy-*C*-maltoside (**45**), both of which provided critical experimental support for the prediction of their preferred solution conformations primarily based on steric constraints.



The synthesis of **44** started with the deprotection of the MPM group of **39** (Scheme XIII). The oxidation of the resultant primary alcohol gave an aldehyde, which was subsequently decarbonylated in the presence of Wilkinson's catalyst[33] to give an ester in 75% overall yield. The ester was reduced to the primary alcohol **46** by lithium aluminum hydride. Compound **46** was converted to the C.5-(deshydroxymethyl)-*C*-cellobioside **44** via route A.

The synthesis of **45** started with the selective monobenzylation of α-methyl glucoside 4,6-benzylidene (**47**) to the desired C.2 benzylated product (Scheme XIV). An example of selective monoprotection similar to this case was given in an earlier section. After deoxygenation[34] of the C.3 alcohol followed by reductive opening of the ben-

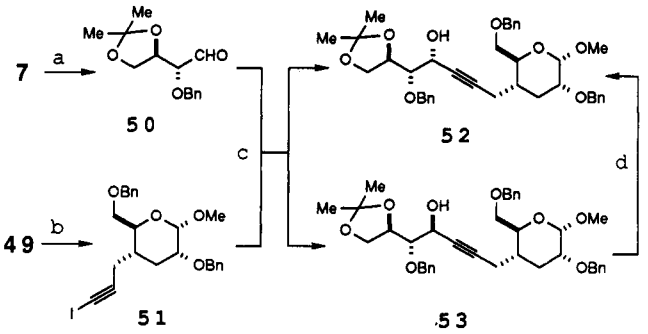
(31) Grieco, P. A.; Gilman, S.; Nishizawa, M. *J. Org. Chem.* **1976**, *41*, 1485.

(32) The primary alcohol derived from **5** was hydrogenated with $Pd(OH)_2$ on C in methanol, followed by methanolysis (HCl/MeOH) to give a triol, which was found to be identical with the hydrogenation ($Pd(OH)_2$ on C) product of **40**.

(33) (a) Tsuji, J.; Ohno, K. *Tetrahedron Lett.* **1965**, 3969. (b) Walborsky, H. M.; Allen, L. E. *J. Am. Chem. Soc.* **1971**, *93*, 5465.

(34) Robins, M. J.; Wilson, J. S.; Hansske, F. *J. Am. Chem. Soc.* **1983**, *105*, 4059.

Scheme XV[a]



[a] Reagents and conditions: (a) (i) MCPBA, CH_2Cl_2; (ii) LAH, Et_2O; (iii) Swern oxidation; (b) (i) Swern oxidation; (ii) CBr_4, PPh_3, CH_2Cl_2; (iii) *n*-BuLi, THF, −78 °C; (iv) I_2, morpholine, PhH; (c) $NiCl_2/CrCl_2$, THF; (d) (i) Swern oxidation; (ii) L-Selectride, THF.

zylidene group, the compound **48** was subjected to the similar sequence of reactions as the one summarized in Scheme XII, to furnish the primary alcohol **49** in good overall yield. However, the preparation of the phosphonium salt from **49** proved to be problematic.[35]

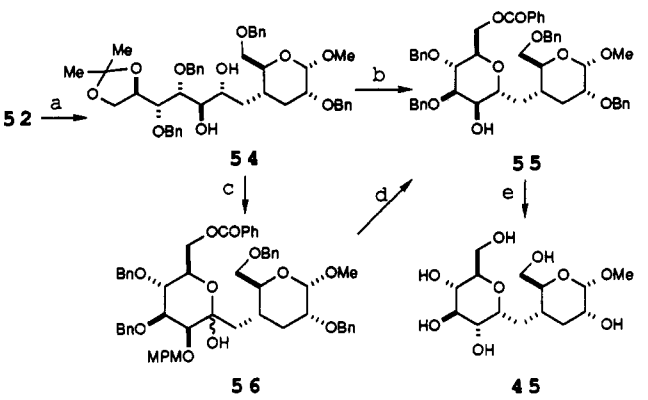
An alternative route using the nickel(II)/chromium(II)-mediated coupling reaction[36] was examined (Scheme XV). Alcohol **49** was converted to the iodoacetylene **51** in 4 steps. The four-carbon aldehyde **50** was prepared in three steps from the aldehyde **7**. Nickel(II)/chromium(II)-mediated coupling of **50** and **51** gave a separable 2:1 mixture of products **52** and **53** in 74% yield. The stereochemistry of **52** was established by chemical degradation.[37] The undesired diastereomer **53** was recycled into the desired alcohol **52** by Swern oxidation and subsequent L-Selectride reduction (the stereoselectivity = 6:1) in 80% yield.

Hydrogenation of **52** over Lindlar catalyst gave the *cis*-olefin. After benzylation, the *cis*-olefin was subjected to asymmetric osmylation to yield the diol **54** in 80% yield. Then, **54** was transformed into the protected form **55** of *C*-disaccharide via route C (Scheme XVI). Alternatively, **55** was also obtained from **54** by using route A; silane reduction of the hemiketal **56**, prepared from **54**, with phenyldimethylsilane in the presence of trimethylsilyl triflate in dichloromethane gave, exclusively and unexpectedly, the axial product **55** in 80% yield. The compound **55** was successfully transformed to methyl C.3-deoxy-*C*-maltoside (**45**).

Conclusion

We have developed three complementary routes to the $\alpha(1,4)$- and $\beta(1,4)$-linked carbon disaccharides. The flexibility of the synthesis has been demonstrated by the preparation of the compounds required for the conformational analysis of (1,4)-disaccharides, including the deuterated analogues $3d_R$ and $4d_S$, the C.2′ epimers **16** and **22**, the 1,6-anhydro compounds **15**, **17**, **21**, and **23**, methyl C.5-(deshydroxymethyl)-*C*-cellobioside (**44**), and methyl C.3-deoxy-*C*-maltoside (**45**). Although the synthetic studies have focused on the 1,4-linked carbon disaccharides, they are applicable to other linkages and configurations as well.[38]

Scheme XVI[a]



[a] Reagents and conditions: (a) (i) H_2, Lindlar cat., MeOH; (ii) BnBr, THF/DMF (3:1); (iii) OsO_4, *N,N′*-bis(mesitylmethyl)-(*R,R′*)-1,2-diphenyl-1,2-diaminoethane, CH_2Cl_2, −80 °C; (b) (i–iv) same as (b) (ii–v) in Scheme VIII; (v) TBS–Cl, imidazole, CH_2Cl_2; (vi) MsCl, NEt_3, Et_2O; (vii) TBAF, THF; (viii–ix) same as (c) (i–ii) in Scheme VIII; (x–xi) same as (d) (i–ii) in Scheme VIII; (c) see Schemes III and IV; (d) Me_2PhSiH, TMSOTf, CH_2Cl_2, −20 °C; (e) see Scheme VII.

Experimental Section

General Experimental Procedures. Only selected spectral data are presented in the Experimental Section. For general procedures, see ref 1b.

Experiments Outlined in Scheme III. Synthesis of 6. To the tosylate **5** (9.50 g, 28 mmol) in MeOH (100 mL) was added freshly prepared Na–Hg (43 g, 4%) with vigorous stirring at 0 °C. After 12 h at rt, the organic phase was decanted and the remaining mercury layer was washed with MeOH (3 × 20 mL). The combined organic layers were concentrated in vacuo to give the crude diol. To a stirred solution of the crude diol in a mixture of THF (200 mL) and DMF (100 mL) was added oil-free NaH (0.8 g, 33 mmol) and imidazole (cat.) at 0 °C. After 30 min, benzyl bromide (7.4 mL, 75 mmol) was added dropwise at 0 °C, followed by *n*-$Bu_4N^+I^-$ (cat.). After 24 h at rt, the reaction was cooled to 0 °C and the excess NaH was decomposed by addition of MeOH (5 mL). After 1 h, aqueous workup (CH_2Cl_2) and silica gel chromatography (4:1 hexanes:EtOAc) gave the desired allyl dibenzyl ether[39] (8.38 g, 81% overall yield) as a colorless oil.

To a solution of the allyl dibenzyl ether (8.34 g, 22.8 mmol) in 20% aqueous acetone (320 mL) was added NMMO (4.61 g, 34.2 mmol) and OsO_4 (237.7 mg, 0.91 mmol) at 0 °C. After 6 h at rt, the reaction was quenched by bubbling H_2S at 0 °C for 2 min and stirring for 30 min. The resulting black precipitate was filtered off through a pad of Celite, and the pad was washed with methanol (3 × 50 mL). The combined filtrates were concentrated in vacuo and filtered through a short column of silica gel (EtOAc) to give the crude diol.

The crude diol was dissolved in 50% aqueous MeOH (400 mL) and treated with $NaIO_4$ (9.0 g) at rt. After 2 h, the reaction was filtered through a cotton plug. Aqueous workup (EtOAc) gave the crude aldehyde as an oil. To a solution of the crude aldehyde in a mixture of MeOH and Et_2O (100 and 200 mL) was added $NaBH_4$ (3.40 g, excess) portionwise at 0 °C. After being stirred at 0 °C for 1 h, the reaction was quenched with saturated NH_4Cl. Aqueous workup (EtOAc) and silica gel chromatography (1:1 hexanes/EtOAc) afforded the primary alcohol[39] (8.05 g, 97% overall yield) as a colorless oil.

(35) During the attempted phosphonium salt preparations, formation of a tetrahydropyran ring involving the C.6 oxygen was observed.

(36) (a) Jin, H.; Uenishi, J.; Christ, W. J.; Kishi, Y. *J. Am. Chem. Soc.* **1986**, *108*, 5644. (b) Takai, K.; Tagashira, M.; Kuroda, T.; Oshima, K.; Utimoto, K.; Nozaki, H. *J. Am. Chem. Soc.* **1986**, *108*, 6048.

(37) Acetylene **51** was hydrogenated to the corresponding cis olefin in the presence of Lindlar catalyst then benzylated. The resultant olefin was treated with ozone to yield an aldehyde, which was found identical with **7**.

(38) The carbon analogues of several disaccharides have been prepared in these laboratories using the synthetic approaches described in this paper: these include the carbon analogues of $\alpha(1,3)$Gal-Gal, $\alpha(1,3)$Gal-Glu, and trehaloses.

(39) For complete spectroscopic data of this substance, see: Wang, Y. Ph.D. Dissertation, Harvard University, 1990.

To a solution of the primary alcohol (4.34 g, 11.7 mmol) in a mixture of Et_2O (100 mL) and Et_3N (2.0 mL, 13.5 mmol) was added a solution of MsCl (1.40 mL, 18.0 mmol) in Et_2O (10 mL) over 15 min at 0 °C. After 3 h, the reaction was poured into saturated $NaHCO_3$. Aqueous workup (Et_2O) and silica gel chromatography (1:1 hexanes/EtOAc) gave the desired mesylate[39] (5.29 g, 98% yield) as an oil.

To a solution of the mesylate (5.29 g, 11.5 mmol) in acetone (30.0 mL) containing $NaHCO_3$ (1.00 g, 12 mmol) was added a solution of NaI (40.0 g, 268 mmol) in acetone (20 mL). After 12 h, aqueous workup (Et_2O) and silica gel chromatography (1:1 hexanes:EtOAc) gave the iodide[39] (4.90 g, 83% yield) as an oil.

To a solution of the iodide (4.90 g, 9.5 mmol) in DMF (25 mL) was added PPh_3 (40 g, 152 mmol). The reaction was stirred at 110 °C for 4 h and concentrated in vacuo. Silica gel chromatography (2–20% MeOH/benzene) furnished **6** (5.43 g, 72% yield) as a foam. IR (neat): 3087 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.89 (1 H, m), 2.01 (1 H, m), 2.54 (1 H, dd, J = 7.0, 7.0 Hz), 3.37 (1 H, s), 3.38 (1 H, s), 3.51 (1 H, m), 3.76 (1 H, dd, J = 6.0, 6.6 Hz), 4.08 (1 H, m), 4.27 (1 H, d, J = 7.0 Hz), 4.61 (1 H, d, J = 5.4 Hz), 5.40 (1 H, s). HRMS: calcd for $C_{40}H_{40}O_4P$ (M − I) 615.2664, found 615.2656. $[\alpha]_D$: −22.5° (*c* 2.4, $CHCl_3$). Data for **6**-d_R. ^1H NMR ($CDCl_3$): The resonance at 1.89 ppm disappeared, and the coupling pattern of signals at 2.01, 2.53, 3.50 and 4.12 ppm was simplified. MS (FAB, NaI): 616 (M^+). Data for **6**-d_S. ^1H NMR ($CDCl_3$): The resonance at 2.01 ppm disappeared, and the coupling pattern of signals at 1.85, 2.46, 3.35 and 3.90 ppm was simplified. MS (FAB, NaI): 616 (M^+).

Preparation of Aldehyde 7. The primary alcohol corresponding to **7** (670 mg, 1.8 mmol) was subjected to Swern oxidation under standard conditions.[18] The crude aldehyde thus obtained was azeotroped with toluene and used without further purification.

Wittig Reaction of 6 and 7. To a solution of **6** (1.60 g, 2.16 mmol) in THF (24 mL) was added *n*-BuLi (2.23 M, 0.96 mL, 2.16 mmol) at 0 °C under Ar. The yellow ylide solution was stirred at 0 °C for 15 min and then cooled to −78 °C. The crude aldehyde **7** in THF (5 mL) was added dropwise to this solution. The reaction was then warmed to 0 °C and stirred for 30 min. Aqueous workup (CH_2Cl_2) and silica gel chromatography (4:1 hexanes/EtOAc) gave **8** (1.05 g, 82% yield) as an oil. IR (neat): 1585 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.35 (3 H, s), 1.40 (3 H, s), 1.70 (1 H, dd, J = 7.7, 7.7 Hz), 2.36 (2 H, m), 3.31 (1 H, dd, J = 1.4, 1.5 Hz), 3.37 (1 H, d, J = 1.5 Hz), 3.65 (1 H, dd, J = 5.3, 6.1 Hz), 3.78 (1 H, dd, J = 3.8, 3.8 Hz), 4.08 (1 H, d, J = 6.8 Hz), 4.21 (1 H, d, J = 6.1 Hz), 4.25 (1 H, ddd, J = 3.8, 6.8, 6.8 Hz), 4.29 (1 H, dd, J = 3.8, 7.6 Hz), 5.43 (1 H, s), 5.57 (2 H, m). ^1H NMR (C_6D_6): δ 5.47 (1 H, ddd, J = 11.1, 7.5, 7.5 Hz), 5.69 (1 H, dd, J = 11.0, 9.3 Hz). MS (DCI, NH_3): 724 (M + NH_4). HRMS: calcd for $C_{44}H_{50}O_8$ 706.350 54, found 706.350 46. $[\alpha]_D$: −38.5° (*c* 0.86, $CHCl_3$). Data for **8**-d_R. ^1H NMR ($CDCl_3$): The resonance at 2.36 ppm disappeared, and the coupling pattern of signals at 1.70 and 2.36 ppm was simplified. MS (FAB, NaI): 730 (M + Na). Data for **8**-d_S. ^1H NMR ($CDCl_3$): The resonance at 2.36 ppm disappeared, and the coupling pattern of signals at 1.70 and 2.27 ppm was simplified. MS (FAB, NaI): 730 (M + Na).

Osmylation of 8. Achiral Stoichiometric Procedure. To a solution of **8** (380.1 mg, 0.53 mmol) in a mixture of pyridine (7 mL) and THF (3 mL) was added OsO_4 (180.0 mg, 0.71 mmol) at −40 °C. After 30 h at −40 °C, the reaction was diluted with MeOH (50 mL) and stirred at 0 °C for 30 min. The reaction was worked up by the same procedure as given before. The product was purified by Chromatotron (2-mm plate, 1:1 hexanes/EtOAc) to give **9** (246.5 mg, 63.0% yield) and its diastereomeric diol (40.1 mg, 10.3% yield). An analytical sample of **9** was obtained by crystallization from hexanes (plates, mp 93–94 °C). IR (neat): 3479 cm^{-1} (br). ^1H NMR ($CDCl_3$): δ 1.32 (3 H, s), 1.40 (3 H, s), 1.60 (1 H, m), 1.96 (1 H, dd, J = 8.8, 2.9 Hz), 2.15 (1 H, m), 2.80 (1 H, d, J = 3.6 Hz), 3.03 (1 H, d, J = 3.0 Hz), 3.37 (1 H, s), 3.39 (1 H, s), 3.40 (1 H, dd, J = 8.3, 8.3 Hz), 3.43 (1 H, dd, J = 6.7, 10.6 Hz), 4.27 (1 H, ddd, J = 4.4, 6.8, 6.8 Hz), 4.36 (1 H, d, J = 5.4 Hz), 5.40 (1 H, s). MS (FAB): 741 (M + 1). $[\alpha]_D$: −16.0° (*c* 0.98, $CHCl_3$). Anal. Calcd for $C_{44}H_{52}O_{10}\cdot{}^1/_2H_2O$: C, 70.47; H, 7.12. Found: C, 70.42; H, 7.01. Data for **9**-d_R: ^1H NMR ($CDCl_3$): The resonance at 2.15 ppm disappeared, and the coupling pattern of signals at 1.60 and 1.96 ppm was simplified. MS (FAB, NaI): 764 (M + Na). Data for **9**-d_S. ^1H NMR ($CDCl_3$): The resonance at 1.56 ppm disappeared, and the coupling pattern of signals at 2.02 and 2.10 ppm was simplified. MS (FAB, NaI): 764 (M + Na).

Achiral Catalytic Procedure. To a solution of **8** (940.0 mg, 1.31 mmol) in 10:1 aqueous acetone (22 mL) was added NMMO (721.9 mg, 5.3 mmol) followed by addition of DABCO (300.0 mg, 2.7 mmol). The resulting mixture was cooled to 0 °C, and OsO_4 (17 mg, 0.067 mmol) was then added. After being stirred for 5 days at 5 °C, the reaction was worked up as described above to give **9** (590.3 mg, 61% yield), its diastereomeric diol (103.3 mg, 10.7% yield), and recovered olefin (150.1 mg, 16% yield).

Chiral Diamine Procedure. To **8** (300.0 mg, 0.41 mmol) in CH_2Cl_2 (3 mL) was added *N,N'*-bis(mesitylmethyl)-(*R,R'*)-1,2-diphenyl-1,2-diaminoethane (183.4 mg, 0.41 mmol), followed by addition of OsO_4 (120.0 mg, 0.45 mmol) at −80 °C. After being stirred at that temperature for 24 h, the reaction was worked up as described before to give **9** (252.4 mg, 80% yield) and its diastereomeric diol (4.3 mg, 4.0% yield).

Achiral Diamine Procedure. Following the chiral diamine osmylation procedure, **8** (140.3 mg, 0.20 mmol) was oxidized for 2 days at −80 °C in the presence of *N,N'*-bis(mesitylmethyl)-1,2-diaminoethane (89.4 mg, 0.2 mmol) to give **9** (98.0 mg, 66% yield) and its diastereomeric diol (5.4 mg, 3.6% yield).

Synthesis of 10. To a solution of **9** (500 mg, 0.68 mmol) in THF (20 mL) was added oil-free NaH (79.7 mg, 3.32 mmol) at 0 °C. After 30 min at 0 °C, MPM–Br (331 μL, 2.26 mmol) was added. After an additional 1.5 h at rt, the excess NaH was decomposed by addition of MeOH (3.0 mL, 7.40 mmol) at 0 °C. Aqueous workup and purification by Chromatotron (4-mm plate, 1:1 hexanes:EtOAc) gave **10** (385.3 mg, 66% yield), the di-MPM ether (108.9 mg, 19% yield), and the undesired mono-MPM ether (45.86 mg, 8% yield). IR (neat): 3488 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.30 (3 H, s), 1.45 (3 H, s), 1.65 (1 H, m), 2.03 (1 H, dd, J = 2.8, 9.6 Hz), 2.24 (1 H, ddd, J = 1.4, 9.6, 13.8 Hz), 2.98 (1 H, d, J = 4.2 Hz), 3.35 (1 H, s), 3.38 (1 H, s), 3.55 (1 H, dd, J = 3.7, 6.8 Hz), 3.69 (1 H, dd, J = 6.6, 6.7 Hz), 3.73 (3 H, s), 3.80 (1 H, m), 3.86 (1 H, dd, J = 3.8, 4.0 Hz), 3.90–3.97 (2 H, m), 4.12 (1 H, d, J = 6.6 Hz), 4.28 (1 H, dd, J = 6.6, 11.8 Hz), 4.37 (1 H, d, J = 6.7 Hz), 5.45 (1 H, s). MS (FAB): 861 (M + 1). $[\alpha]_D$: −11.0° (*c* 1.13, $CHCl_3$). HRMS calcd for $C_{52}H_{60}O_{11}Na$ (M + Na) 883.4033, found 883.4082. Data for **10**-d_R: ^1H NMR ($CDCl_3$): The resonance at 2.24 ppm disappeared, and the coupling pattern of signals at 1.78 and 2.16 ppm was simplified. MS (FAB, NaI): 884 (M + Na). Data for **10**-d_S: ^1H NMR ($CDCl_3$): The resonance at 1.65 ppm disappeared, and the coupling pattern of signals at 2.02 and 2.18 ppm was simplified. MS (FAB, NaI): 884 (M + Na).

Experiments Outlined in Scheme IV. Synthesis of Hemiketal 11. Swern oxidation of **10** (372.4 mg) gave the expected ketone[39] (350.7 mg, 94% yield; oil). To a solution of the ketone (155.0 mg) in THF (15.0 mL) was added 4 N HCl (6.0 mL). After 5 h, the reaction was cooled to 0 °C, neutralized to pH 7 with saturated $NaHCO_3$, and extracted with CH_2Cl_2 (2 × 150 mL). Purification by Chromatotron (2-mm plate, 1:1 hexanes/EtOAc) afforded the hemiketal (130.3 mg, 88% yield) as an oil.

To a solution of the hemiketal (41.7 mg, 0.51 mmol) in a mixture of CH_2Cl_2 (350 μL) and pyridine (21 μL) was added benzoyl chloride (17.7 μL, 0.15 μmol) at 0 °C. After 30 min, the reaction was quenched with saturated NH_4Cl. Aqueous workup (CH_2Cl_2) and preparative TLC (3:2 hexanes/EtOAc) gave **11** (39.1 mg, 83% yield) as an oil.

Silane Reduction of 11. To a solution of **11** (17.3 mg, 0.019 mmol) in CH_3CN (865 μL) was added $(n\text{-}Pr)_3SiH$ (39.0 μL, 0.19 mmol) and $BF_3\cdot Et_2O$ (23.0 μL, 0.19 mmol) at −20 °C. After 10 min at −20 °C, the reaction was diluted with CH_2Cl_2 (15 mL) and quenched with saturated $NaHCO_3$. Aqueous workup and preparative TLC (1:1:1 hexanes/EtOAc/pentane) gave **12** (10.9 mg, 74% yield, solid) and its axial stereoisomer (2.1 mg, 14% yield, oil). An analytical sample of **12** was prepared by recrystallization from MeOH to give colorless plates (mp 144–145 °C). IR (neat): 3480, 1956, 1719 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.95–2.09 (3 H, m), 2.40 (1 H, s), 3.31 (1 H, s), 3.32 (1 H, s), 3.48 (1 H, dd, J = 6.1, 6.2 Hz), 3.52–3.61 (2 H, m), 3.64 (1 H, dd, J = 2.3, 9.0 Hz), 3.75 (1 H, dd, J = 9.3, 9.4 Hz), 3.89 (1 H, d, J = 6.5 Hz), 3.91 (1 H, d, J = 2.8 Hz), 4.32 (1 H, d, J = 6.1 Hz), 5.40 (1 H, s). MS (DCI, NH_3): 804 (M + NH_4). Anal. Calcd for $C_{48}H_{50}O_{10}\cdot{}^1/_2H_2O$: C, 72.43; H, 6.46. Found: C, 72.42; H, 6.36. $[\alpha]_D$: −13.9° (*c* 1.1,

$CHCl_3$). Data for **12**-d_R: ^1H NMR ($CDCl_3$): The resonance at 2.00 ppm disappeared, and the coupling pattern of signals at 1.95 and 2.04 ppm was simplified. MS (FAB, NaI): 810 (M + Na).

Synthesis of 13. To a solution of **11** (46.5 mg, 0.051 mmol) in CH_2Cl_2 (5 mL) was added a solution of MeSH (~100 μL) in CH_2Cl_2 (1 mL), followed by the addition of $BF_3{\cdot}Et_2O$ (10 μL, 0.082 mmol) at 0 °C. After 10 min, the reaction was quenched with saturated $NaHCO_3$. Aqueous workup (CH_2Cl_2) and preparative TLC (1:2 EtOAc:hexanes) gave **13** (33.3 mg, 80% yield, an oil). IR (neat): 3845, 1720 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.82 (3 H, s), 2.05 (2 H, m), 2.49 (1 H, m), 2.77 (1 H, s), 3.33 (1 H, s), 3.53 (1 H, s), 3.59 (1 H, dd, J = 6.0, 6.0 Hz), 3.81 (1 H, d, J = 3.3 Hz), 3.85 (1 H, dd, J = 9.5, 9.6 Hz), 4.00 (1 H, d, J = 6.7 Hz), 4.11 (2 H, m), 4.22 (1 H, dd, J = 3.3, 11.2 Hz), 4.47 (1 H, dd, J = 6.8, 11.9 Hz), 4.59 (1 H, dd, J = 1.6, 10.5 Hz), 5.38 (1 H, s). MS (FAB, NaI): 855.6 (M + Na). $[\alpha]_D$: +47.8° (c 1.3, $CHCl_3$). Data for **13**-d_R. ^1H NMR ($CDCl_3$): The resonance at 2.05 ppm disappeared, and the coupling pattern of signals at 2.09 and 2.47 ppm was simplified. MS (FAB, NaI): 856 (M + Na).

Synthesis of 12 from 13. To a solution of **13** (30.3 mg, 0.036 mmol) in toluene (4 mL) was added n-Bu_3SnH (200 μL) and AIBN (2 mg). The reaction was heated at 110 °C for 30 min, cooled to rt, then concentrated in vacuo to give a residue. Purification by silica gel chromatography (3:1 hexanes/EtOAc) furnished **12** (26.3 mg, 91% yield) as a single product.

Experiments Outlined in Scheme V. Inversion of C.2' Stereocenter. Swern oxidation of **12** (13.0 mg) gave the expected ketone. To a solution of the crude ketone in THF was added $BH_3{\cdot}Et_3N$ (50 μL). After being stirred for 30 min, it was quenched with saturated NH_4Cl. Aqueous workup (CH_2Cl_2) and silica gel chromatography (2:1 hexanes/EtOAc) gave **14** (10.4 mg, 80% overall yield) as an oil. IR (neat): 3474, 1721 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.61 (1 H, ddd, J = 5.6, 9.8, 14.4 Hz), 1.99 (1 H, dd, J = 5.6, 7.9 Hz), 2.10 (1 H, s), 2.31 (1 H, ddd, J = 2.3, 8.9, 14.4 Hz), 3.30 (1 H, s), 3.33 (1 H, d, J = 8.6 Hz), 3.37 (1 H, ddd, J = 2.5, 9.1, 9.3 Hz), 3.43 (1 H, s), 3.92 (1 H, d, J = 6.5 Hz), 4.34 (1 H, d, J = 4.3 Hz), 4.43 (1 H, dd, J = 5.2, 11.8 Hz), 4.50 (1 H, dd, J = 1.6, 11.8 Hz), 5.40 (1 H, s). MS (DCI, NH_3): 804 (M + NH_4). HRMS: calcd for $C_{48}H_{50}O_{10}$ 786.340 37, found 786.339 12. $[\alpha]_D$: +2.6° (c 1.0, $CHCl_3$). Data for **14**-d_R. ^1H NMR ($CDCl_3$): The resonance at 1.61 ppm disappeared, and the coupling pattern of signals at 1.92 and 2.23 ppm was simplified. MS (FAB, NaI): 810 (M + Na).

Synthesis of 15. To a solution of **12** (12.6 mg, 0.16 μmol) in MeOH (1.5 mL) was added NaOMe (cat.). After 4 h, the reaction was quenched by the addition of water. Aqueous workup (CH_2Cl_2) and preparative TLC (1:1 hexanes/EtOAc) gave the expected diol (9.1 mg, 83% yield). To this diol (9.1 mg, 0.13 μmol) in MeOH (1 mL) was added 10% $Pd(OH)_2$ on C (cat.). The suspension was degassed under vacuum and refilled with H_2 several times, then the mixture was stirred for 3 h at rt. The catalyst was removed by filtration through Celite and the filtrate concentrated in vacuo to give **15** (4.2 mg, 98% yield, an oil). IR (neat): 3334 cm^{-1}. ^1H NMR (CD_3OD): δ 1.83 (1 H, dd, J = 1.4, 9.3 Hz), 1.85 (1 H, ddd, J = 3.2, 9.3, ca. 14–15 Hz), 2.05 (1 H, ddd, J = 1.4, 10.0, ca. 14–15 Hz), 3.20 (1 H, ddd, J = 2.1, 6.3, 9.1 Hz), 3.43 (1 H, s), 3.51 (1 H, dd, J = 2.7, 9.4 Hz), 3.54 (1 H, dd, J = 9.2, 9.4 Hz), 3.56 (1 H, s), 3.60 (1 H, ddd, J = <1, 3.3, 11.0 Hz), 3.65 (1 H, dd, J = 6.2, 11.9 Hz), 3.66 (1 H, dd, J = 5.3, 6.7 Hz), 3.73 (1 H, d, J = 2.7 Hz), 3.84 (1 H, dd, J = 2.1, 11.9 Hz), 4.10 (1 H, d, J = 6.7 Hz), 4.46 (1 H, d, J = 5.2 Hz), 5.29 (1 H, s). MS (DCI, NH_3): 341 (M + NH_4). HRMS: calcd for $C_{13}H_{22}O_9$ 322.126 37, found 322.126 72. $[\alpha]_D$: −53.1° (c 0.42, H_2O). Data for **15**-d_R. ^1H NMR (CD_3OD–D_2O): The resonance at 2.05 ppm disappeared, and the coupling pattern of two signals at 1.82 ppm was simplified.

Synthesis of 16. A solution of **15** (6.66 mg, 0.021 mmol) in methanol (1.0 mL) saturated with HCl was heated for 10 h at 90 °C in a sealed tube. The reaction was cooled and concentrated to dryness to furnish a 5:1 mixture of methyl α- and β-glycosides. This mixture in pyridine (1 mL) was treated with acetic anhydride (0.1 mL) and stirred at rt for 24 h. Aqueous workup (CH_2Cl_2) and purification by HPTLC (1:2:4 t-BuOMe:CCl_4:Et_2O) gave the pure heptaacetate methyl α-glycoside. To a solution of the heptaacetate in MeOH (2 mL) was added NaOH (1 mg). After 12 h, the solution was concentrated. The residue was subjected to polystyrene[1a] column with 1:4 aqueous MeOH to furnish the pure methyl glycoside **16** (5.4 mg, 81% yield). IR (neat): 3369 cm^{-1}. ^1H NMR (CD_3OD–D_2O): δ 1.65 (1 H, dddd, J = 3.8, 4.9, 10.1, 10.2 Hz), 1.75 (1 H, ddd, J = 3.8, 3.8, 15.1 Hz), 1.86 (1 H, ddd, J = 4.9, 8.9, 15.1 Hz), 3.17 (1 H, ddd, J = 2.2, 6.6, 8.9 Hz), 3.35 (3 H, s), 3.38 (1 H, dd, J = 3.7, 9.3 Hz), 3.43 (1 H, dd, J = 8.9, 9.2 Hz), 3.45 (1 H, dd, J = 3.2, 9.2 Hz), 3.60 (1 H, dd, J = 6.7, 11.6 Hz), 3.61 (1 H, dd, J = 5.4, 11.6 Hz), 3.63 (1 H, dd, J = 3.8, 8.9 Hz), 3.63 (1 H, dd, J = 9.3, 10.3 Hz), 3.72 (1 H, d, J = 2.2 Hz), 3.73 (1 H, ddd, J = 1.7, 5.2, 10.5 Hz), 3.83 (1 H, dd, J = 2.3, 11.6 Hz), 3.85 (1 H, dd, J = 1.9, 11.9 Hz), 4.68 (1 H, d, J = 3.7 Hz). MS (FAB, NaCl): 377 (M + Na). HRMS: calcd for $C_{14}H_{26}O_{10}$ 354.152 58, found 354.152 18. $[\alpha]_D$: +38.9° (c 0.4, MeOH). Data for **16**-d_R. ^1H NMR (CD_3OD–D_2O): The resonance at 1.86 ppm disappeared, and the coupling pattern of signals at 1.67 and 1.76 ppm was simplified. MS (FAB): 355.1 (M^+).

Synthesis of 17. Using the same procedure as given for **15**, **14** (10.0 mg, 0.013 mmol) was converted to **17** (4.5 mg, 90% yield, an oil). IR (neat): 3330 cm^{-1}. ^1H NMR (CD_3OD): δ 1.66 (1 H, ddd, J = 4.5, 9.9, 14.4 Hz), 1.89 (1 H, dd, J = 4.5, 9.9 Hz), 2.26 (1 H, ddd, J = 2.3, 8.9, 14.4 Hz), 3.09 (1 H, dd, J = 9.6, 9.8 Hz), 3.23 (1 H, ddd, J = 1.7, 5.9, 9.0 Hz), 3.25 (1 H, dd, J = 8.7, 9.6 Hz), 3.30 (1 H, ddd, J = 2.4, 8.7, 9.9 Hz), 3.35 (1 H, dd, J = 8.7, 8.7 Hz), 3.42 (1 H, s), 3.53 (1 H, s), 3.59 (1 H, dd, J = 5.9, 12.1 Hz), 3.66 (1 H, dd, J = 5.0, 6.7 Hz), 3.83 (1 H, d, J = 2.2 Hz), 3.84 (1 H, dd, J = 1.7, 11.1 Hz), 4.05 (1 H, d, J = 6.8 Hz), 4.47 (1 H, d, J = 5.0 Hz), 5.28 (1 H, s). MS (DCI, NH_3): 341 (M + NH_4). HRMS: calcd for $C_{13}H_{22}O_9$ 322.126 37, found 322.126 28. $[\alpha]_D$: −41.7° (c 0.48, H_2O). Data for **17**-d_R. ^1H NMR (CD_3OD): The resonance at 1.66 ppm disappeared, and the coupling pattern of signals at 1.89, 2.26, and 3.30 ppm was simplified.

Synthesis of 3. Using the same procedure as given for **16**, **17** (4.5 mg) was converted to **3** (3.8 mg, 80% yield, an oil). IR (neat): 3354 cm^{-1}. ^1H NMR (CD_3OD): δ 1.59 (1 H, ddd, J = 3.4, 9.4, 15.3 Hz), 1.72 (1 H, dddd, J = 3.4, 4.7, 10.3, 10.9 Hz), 2.08 (1 H, ddd, J = 1.7, 4.7, 15.3 Hz), 3.05 (1 H, dd, J = 9.1, 9.2 Hz), 3.19 (1 H, dd, J = 8.7, 9.7 Hz), 3.20 (1 H, ddd, J = 1.9, 6.8, 9.7 Hz), 3.28 (1 H, ddd, J = 1.7, 9.2, 9.2 Hz), 3.32 (1 H, dd, J = 8.8, 9.1 Hz), 3.35 (3 H, s), 3.38 (1 H, dd, J = 3.7, 9.3 Hz), 3.51 (1 H, dd, J = 6.8, 11.9 Hz), 3.58 (1 H, dd, J = 9.3, 10.3 Hz), 3.60 (1 H, dd, J = 5.4, 11.8 Hz), 3.70 (1 H, ddd, J = 1.7, 5.4, 10.9 Hz), 3.82 (1 H, dd, J = 1.7, 11.8 Hz), 3.82 (1 H, dd, J = 1.9, 11.9 Hz), 4.69 (1 H, d, J = 3.7 Hz). MS (FAB, NaCl): 377 (M + Na). HRMS: calcd for $C_{14}H_{26}O_{10}$ 354.152 58, found 354.152 50. $[\alpha]_D$: + 63.2° (c 0.50, CH_3OH). Data for **3**-d_R. ^1H NMR (CD_3OD): The resonance at 1.59 ppm disappeared, and the coupling pattern of signals at 1.72, 2.08, and 3.28 ppm was simplified. MS (FAB, NaCl): 378 (M + Na).

Experiments Outlined in Scheme VI. Synthesis of 18A and 18B. The mono-MPM ether **10** (201.4 mg, 0.23 mmol) in 60% aqueous acetic acid (10 mL) was heated to 40 °C for 20 h. The solution was cooled to rt and the solvent was removed in vacuo. The residue was purified by preparative TLC (3:1 EtOAc/hexanes) to give the expected triol[39] (151 mg, 80% yield, an oil).

To a stirred solution of the triol (200 mg, 0.23 mmol) in benzene (20 mL), was added $Pb(OAc)_4$ (400 mg, 0.90 mmol) at 0 °C. After 10 min, the reaction mixture was passed through a short silica gel column with EtOAc (50 mL). The combined filtrates were concentrated in vacuo to give the hemiacetal (186 mg, 98% yield, a colorless oil).

To a solution of the hemiacetal (80 mg, 0.12 mmol) in CH_2Cl_2 (4 mL) and pyridine (1 mL) was added p-nitrobenzoyl chloride (120 mg, 0.65 mmol) at 0 °C. After 2 h, the reaction was quenched with saturated $NaHCO_3$. Aqueous workup (CH_2Cl_2; cold 1 N HCl) and purification by silica gel chromatography (2:1 benzene/ether) gave **18A** (60 mg, 70% yield, an oil) and **18B** (20 mg, 22% yield, an oil). Data for **18A**. IR (neat): 1736 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.72 (1 H, ddd, J = 3.3, 10.8, 14.4 Hz), 2.08 (1 H, d, J = 9.6 Hz), 2.48 (1 H, ddd, J = 1.8, 12.3, 14.4 Hz), 3.37 (1 H, s), 3.45 (1 H, s), 3.61 (2 H, m), 3.70–3.75 (2 H, m), 3.78 (3 H, s), 4.06 (1 H, ddd, J = 2.0, 9.0, 11.0 Hz), 4.11 (1 H, d, J = 6.5 Hz), 4.29 (1 H, d, J = 5.1 Hz), 5.40 (1 H, s), 6.25 (1 H, s), 8.10–8.25 (4 H, AB, J = 9.8 Hz). MS (DCI, NH_3): 954 (M + NH_4). $[\alpha]_D$: −18.3° (c 1.01, $CHCl_3$). Data for **18B**. ^1H NMR ($CDCl_3$): δ 1.73 (1 H, ddd, J = 3.7, 10.4, 14.4 Hz), 1.95 (1 H, d, J = 8.9 Hz), 2.51 (1 H, ddd, J = 1.8, 9.7, 14.3 Hz), 3.29 (1 H, s), 3.32 (1 H, s), 3.65 (1 H, dd,

J = 5.9, 6.3 Hz), 3.71 (1 H, dd, J = 2.9, 9.3 Hz), 3.76 (3 H, s), 3.82 (1 H, dd, J = 1.2, 3.5 Hz), 3.89 (2 H, m), 4.01 (2 H, s), 4.05 (1 H, d, J = 3.9 Hz), 4.33 (1 H, ddd, J = 1.7, 10.3, 10.3 Hz), 4.39 (1 H, d, J = 5.3 Hz), 5.40 (1 H, s), 6.29 (1 H, s), 7.85 (4 H, AB, J = 8.8 Hz). MS (FAB, NaI): 960 (M + Na). $[\alpha]_D$: +31.0° (c 0.7, $CHCl_3$).

Synthesis of 19. To a solution of **18A** (46.5 mg, 0.52 μmol) in acetonitrile (5 mL) was added propargyl-TMS (150 μL) at −20 °C, and TMSOTf (25 μL, 0.20 mmol) was then added. After 30 min, the reaction was quenched with saturated $NaHCO_3$. Aqueous workup (CH_2Cl_2) and preparative TLC (1:1 hexanes/EtOAc) gave **19** (23.9 mg, 69% yield) as an oil. IR (neat): 2926, 1950 (w), 1734 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.85 (1 H, ddd, J = 3.5, 10.9, 14.6 Hz), 1.98 (1 H, dd, J = 3.5, 10.1 Hz), 2.17 (1 H, ddd, J = 2.4, 10.0, 14.4 Hz), 2.40 (1 H, d, J = 5.1 Hz), 3.37 (1 H, s), 3.47 (1 H, s), 3.71 (1 H, dd, J = 6.1, 9.2 Hz), 3.73 (1 H, dd, J = 4.8, 8.7 Hz), 3.77 (1 H, dd, J = 3.2, 6.0 Hz), 3.89 (1 H, ddd, J = 3.2, 4.2, 11.3 Hz), 4.18 (1 H, d, J = 6.2 Hz), 4.22 (1 H, dd, J = 6.0, 7.1 Hz), 4.37 (1 H, d, J = 5.4 Hz), 4.78 (2 H, m), 5.40 (1 H, s), 5.48 (1 H, dd, J = 7.3, 14.1 Hz). MS (DCI, NH_3): 708 (M + NH_4). HRMS: calcd for $C_{43}H_{46}O_8Na$ (M + Na) 713.3090, found 713.3092. $[\alpha]_D$: −1.8° (c 1.0, $CHCl_3$).

Experiments Outlined in Scheme VII. Synthesis of 21. Ozone was bubbled into a solution of **19** (9.85 mg, 0.14 μmol) in MeOH (1.5 mL) at −78 °C (ca. 30 s). After excess O_3 was purged by N_2, Me_2S (ca. 50 μL) was added at −78 °C and the reaction was warmed to 0 °C. $NaBH_4$ was added to the reaction until no aldehyde was observed by TLC (1:1 hexanes/EtOAc). The excess $NaBH_4$ was quenched by addition of saturated NH_4Cl. Aqueous workup (CH_2Cl_2) and preparative TLC (1:4 hexanes/EtOAc) afforded the expected diol (8.3 mg, 84% yield, a film), which was subjected to hydrogenolysis under the same conditions as given in Scheme V, to give **21** (4.5 mg, 97% yield, a film). IR (neat): 3336, 2931 cm^{-1}. ^1H NMR (CD_3OD): δ 1.79 (1 H, dd, J = 4.5, 9.0 Hz), 1.83 (1 H, ddd, J = 3.0, 9.2, 14.0 Hz), 2.06 (1 H, ddd, J = 4.5, 11.2, 14.0 Hz), 3.45 (1 H, s), 3.51 (1 H, ddd, J = 2.5, 6.4, 8.9 Hz), 3.61 (1 H, dd, J = 8.7, 9.0 Hz), 3.63 (1 H, s), 3.66 (1 H, dd, J = 5.0, 6.8 Hz), 3.71 (1 H, dd, J = 2.4, 8.7 Hz), 3.72 (1 H, dd, J = 6.4, 11.8 Hz), 3.75 (1 H, dd, J = 2.4, 3.0 Hz), 3.81 (1 H, dd, J = 2.3, 11.8 Hz), 4.03 (1 H, ddd, J = 2.4, 3.0, 11.2 Hz), 4.16 (1 H, d, J = 6.8 Hz), 4.50 (1 H, d, J = 5.0 Hz), 5.28 (1 H, s). MS (DCI, NH_3): 341 (M + NH_4). HRMS: calcd for $C_{13}H_{22}O_9$ 322.126 37, found 322.126 10. $[\alpha]_D$: −10.2° (c 0.6, H_2O).

Synthesis of 22. Using the same procedure as given for **15**, **21** (3.0 mg) was transformed to **22** (2.6 mg, 90% yield) as a 5:1 mixture of α- and β-anomers. An analytical sample of **22** was prepared via its heptaacetate derivative as described for **16**. IR (neat): 3338, 2928 cm^{-1}. ^1H NMR (CD_3OD): δ 1.67 (1 H, ddd, J = 4.6, 5.3, 14.4 Hz), 1.73 (1 H, dddd, J = 3.1, 5.3, 10.8, 11.3 Hz), 1.82 (1 H, ddd, J = 3.3, 9.0, 14.4 Hz), 3.35 (1 H, dd, J = 3.7, 9.4 Hz), 3.37 (3 H, s), 3.51 (1 H, dd, J = 3.7, 11.3 Hz), 3.56 (1 H, ddd, J = 2.4, 6.4, 11.3 Hz), 3.58 (1 H, dd, J = 7.6, 9.8 Hz), 3.62 (1 H, dd, J = 3.8, 11.3 Hz), 3.69 (1 H, dd, J = 9.4, 10.8 Hz), 3.71 (1 H, dd, J = 2.5, 3.7 Hz), 3.72 (1 H, ddd, J = 3.8, 7.0, 7.6 Hz), 3.73 (1 H, dd, J = 2.4, 11.6 Hz), 3.77 (1 H, dd, J = 2.5, 9.8 Hz), 3.79 (1 H, dd, J = 6.4, 11.6 Hz), 4.11 (1 H, ddd, J = 3.7, 4.6, 9.0 Hz), 4.69 (1 H, d, J = 3.7 Hz). MS (FAB, NaCl): 377 (M + Na). HRMS: calcd for $C_{14}H_{26}O_{10}$ 354.152 58, found 354.152 40. $[\alpha]_D$: +83.4° (c 0.2, $CHCl_3$). Data for **22**-d_8. ^1H NMR (CD_3OD): The resonance at 1.82 ppm disappeared, and the coupling pattern of signals at 1.65, 1.73, and 3.73 ppm was simplified. MS (FAB, NaI): 346 (M + Na).

Synthesis of 20. Using the same procedures as given in Scheme IV, the diol (prepared from **19** as described above; 17.0 mg) was converted to the expected monobenzoate[39] (15.0 mg, 85% yield). The monobenzoate (15.0 mg) was then subjected to Swern oxidation. The ketone thus obtained was dissolved in THF (1 mL) and reduced with 1.0 M BH_3·THF in THF (100 μL). The reaction was complete within 5 min and was quenched with saturated NH_4Cl. Aqueous workup (CH_2Cl_2) and preparative TLC (3:1 hexanes/EtOAc) gave **20** (11.6 mg, 80% yield, a film). IR (neat): 3450, 1718 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.88 (1 H, ddd, J = 2.5, 7.8, 14.4 Hz), 1.94 (1 H, dd, J = 6.3, 6.8 Hz), 2.14 (1 H, ddd, J = 5.4, 10.7, 14.4 Hz), 2.79 (1 H, d, J = 8.1 Hz), 3.35 (2 H, s), 3.54 (1 H, dd, J = 5.5, 6.6 Hz), 3.65 (1 H, m), 3.79 (1 H, dd, J = 5.7, 7.0 Hz), 4.04 (1 H, ddd, J = 2.5, 3.0, 10.6 Hz), 4.04 (1 H, d, J = 6.6 Hz), 4.25 (1 H, dd, J = 3.9, 7.8 Hz), 4.50 (2 H, m), 4.65 (1 H, dd, J = 11.7, 7.6 Hz), 5.40 (1 H, s). MS (DCI, NH_3): 804 (M + NH_4). HRMS: calcd for $C_{48}H_{50}O_{10}$ 786.340 37, found 786.340 01. $[\alpha]_D$: +8.1° (c 1.0, $CHCl_3$). Data for **20**-d_8. ^1H NMR ($CDCl_3$): The resonance at 2.14 ppm disappeared, and the coupling pattern of signals at 1.88, 1.94, and 4.25 ppm was simplified. MS (FAB, NaI): 810 (M + Na).

Synthesis of 23. Following the same procedure as given for **12**, **20** (10.6 mg) was transformed into **23** (3.8 mg, 90% overall yield, a film). IR (neat): 3352, 3338 cm^{-1}. ^1H NMR (CD_3OD): δ 1.78 (1 H, dd, J = 6.0, 8.4 Hz), 1.99 (1 H, ddd, J = 6.0, 10.1, ca. 14–15 Hz), 2.01 (1 H, ddd, J = 4.2, 8.4, ca. 14–15 Hz), 3.22 (1 H, dd, J = 8.5, 9.2 Hz), 3.44 (1 H, s), 3.52 (1 H, ddd, J = 2.3, 6.4, 9.2 Hz), 3.55 (1 H, dd, J = 8.5, 9.6 Hz), 3.61 (1 H, dd, J = 5.6, 9.6 Hz), 3.62 (1 H, s), 3.63 (1 H, dd, J = 6.4, 11.8 Hz), 3.66 (1 H, dd, J = 5.1, 6.7 Hz), 3.81 (1 H, dd, J = 2.3, 11.8 Hz), 4.09 (1 H, ddd, J = 4.2, 5.6, 10.1 Hz), 4.14 (1 H, d, J = 6.7 Hz), 4.53 (1 H, d, J = 5.1 Hz), 5.28 (1 H, s). MS (DCI, NH_3): 341 (M + NH_4). HRMS: calcd for $C_{13}H_{22}O_9$ 322.126 37, found 322.126 01. $[\alpha]_D$: +14.9° (c 0.5, CH_3OH). Data for **23**-d_8. ^1H NMR (CD_3OD): The resonance at 1.99 ppm disappeared, and the coupling pattern of signals at 1.75, 2.01 and 4.09 ppm was simplified. MS (FAB NaI): 346 (M + Na).

Synthesis of 4. Using the same procedure as given for **15**, **23** (4.9 mg) was transformed into **4** (4.3 mg, 90% overall yield, a film). An analytical sample of **4** was prepared via its heptaacetate derivative as described for **16**. IR (neat): 3352, 2926 cm^{-1}. ^1H NMR (CD_3OD): δ 1.75 (1 H, ddd, J = 5.3, 3.1, 15.0 Hz), 1.82 (1 H, dddd, J = 2.9, 5.3, 8.8, 10.6 Hz), 1.92 (1 H, ddd, J = 2.9, 10.3, 15.0 Hz), 3.16 (1 H, dd, J = 8.2, 9.0 Hz), 3.34 (1 H, dd, J = 3.7, 9.5 Hz), 3.35 (3 H, s), 3.49 (1 H, dd, J = 8.2, 9.2 Hz), 3.53 (1 H, dd, J = 5.6, 9.2 Hz), 3.60 (1 H, ddd, J = 2.7, 6.8, 9.0 Hz), 3.60 (1 H, dd, J = 6.8, 14.3 Hz), 3.62 (1 H, ddd, J = 2.3, 4.9, 8.8 Hz), 3.68 (1 H, dd, J = 4.9, 12.0 Hz), 3.75 (1 H, dd, J = 2.3, 12.0 Hz), 3.81 (1 H, dd, J = 9.5, 10.6 Hz), 3.81 (1 H, dd, J = 2.7, 14.3 Hz), 4.23 (1 H, ddd, J = 3.1, 5.6, 10.3 Hz), 4.69 (1 H, d, J = 3.7 Hz). MS (FAB, NaCl): 377 (M + Na). HRMS: calcd for $C_{14}H_{26}O_{10}$ 354.152 58, found 354.152 76. $[\alpha]_D$: +53.0° (c 0.4, CH_3OH). Data for **4**-d_8. ^1H NMR (CD_3OD): The resonance at 1.92 ppm disappeared, and the coupling pattern of signals at 1.75, 1.82 and 4.23 ppm was simplified. MS (FAB, NaI): 378 (M + Na).

Experiments Outlined in Scheme VIII. Synthesis of 25. Under the same conditions of Wittig reaction as given for **7**, **24** was converted to **25** (oil) in 67% yield. IR (neat): 3063 cm^{-1}. ^1H NMR (CD_3Cl): δ 1.33 (3 H, s), 1.38 (3 H, s), 1.78 (1 H, dd, J = 6.7, 8.8 Hz), 2.18 (1 H, ddd, J = 5.8, 6.2, 14.8 Hz), 2.69 (1 H, ddd, J = 9.3, 9.4, 14.8 Hz), 3.31 (1 H, s), 3.40 (1 H, s), 3.47 (1 H, dd, J = 5.5, 5.6 Hz), 3.70 (1 H, dd, J = 8.1, 8.4 Hz), 3.72 (1 H, dd, J = 6.1, 7.0 Hz), 3.84 (1 H, dd, J = 6.4, 8.1 Hz), 4.12 (1 H, d, J = 6.6 Hz), 4.30 (1 H, dd, J = 6.4, 14.1 Hz), 5.46 (1 H, s), 5.60 (1 H, dd, J = 9.6, 10.8 Hz), 5.69 (1 H, ddd, J = 5.9, 8.9, 11.0 Hz). MS (FAB, NaI): 729 (M + Na). HRMS: calcd for $C_{44}H_{50}O_8Na$ (M + Na) 729.3403, found 729.3451. $[\alpha]_D$: −24.3° (c 1.0, CH_3Cl). Data for **25**-d_8. ^1H NMR ($CDCl_3$): The resonance at 2.69 ppm disappeared, and the coupling pattern of signals at 1.78 and 2.18 ppm was simplified. MS (FAB, NaI): 730 (M + Na).

Synthesis of 26B. Using the same procedure of asymmetric osmylation as given for olefin **8**, **25** (180.0 mg) was transformed into the erythro diol[39] (125.0 mg, 70% yield, an oil) along with its diastereomer (8.3 mg, 4.6% yield, an oil).

To a solution of the erythro diol (156.3 mg) in benzene (5 mL) was added $MeOPhCH(OMe)_2$ and PPTS (5.0 mg). After refluxing for 30 min, the reaction was cooled and concentrated in vacuo. Silica gel chromatography (1:2 EtOAc/hexanes) afforded the expected anisylidene. This product was dissolved in DMF (7 mL), to which activated 3-Å molecular seives (350 mg) then $NaCNBH_3$ (250 mg) were added. After being cooled to 0 °C, a solution of CF_3CO_2H (0.7 mL) in DMF (3 mL) was added to this mixture over 10 min. After 16 h, the reaction was quenched with saturated $NaHCO_3$. Aqueous workup (CH_2Cl_2) and silica gel chromatography (1:2 EtOAc/hexanes) gave the desired mono-MPM ether alcohol[39] (125.0 mg, 78% yield, an oil) along with its regioisomer (regioselectivity ca. 5.3:1).

To a solution of the major mono-MPM ether alcohol (125.0 mg) in 5 mL of pyridine was added Ac_2O (200 μL) at rt. After 12 h, it was concentrated in vacuo to give a slightly colored oil. Silica gel chromatography (1:3 EtOAc/hexanes) gave the desired acetate

quantitatively. To a solution of the acetate in THF (10 mL) was added 3 N HCl (5 mL). After 10 h, the reaction was quenched with saturated $NaHCO_3$. Aqueous workup (CH_2Cl_2) and silica gel chromatography (1:1 EtOAc/hexanes) afforded the expected diol[39] (130.1 mg, 100% yield) as an oil.

To a solution of the diol (87.0 mg, 0.1 mmol) in pyridine (5 mL) was added *p*-TsCl (50 mg). After 12 h, the reaction was quenched with saturated $NaHCO_3$. Aqueous workup (CH_2Cl_2) and silica gel chromatography (1:2 EtOAc/hexanes) gave the expected monotosylate. To a stirred solution of the monotosylate in THF (4 mL) was added oil-free NaH (5 mg, 0.41 mmol) at 0 °C. After 3 h, the reaction was quenched with saturated NH_4Cl. Aqueous workup (CH_2Cl_2) and silica gel chromatography (1:1 EtOAc/hexanes) furnished **26B** (45.0 mg, 60% yield) as an oil. IR (neat): 3062, 1740 cm^{-1}. ^1H NMR (CD_3Cl): δ 1.86 (3 H, s), 1.89 (1 H, ddd, J = 4.2, 9.5, 14.1 Hz), 1.96 (1 H, dd, J = 2.9, 8.9 Hz), 2.10 (1 H, ddd, J = 3.2, 8.9, 14.1 Hz), 2.38 (1 H, dd, J = 2.7, 4.7 Hz), 2.53 (1 H, dd, J = 4.4, 4.5 Hz), 3.08 (1 H, dd, J = 3.1, 7.2 Hz), 3.13 (1 H, ddd, J = 2.8, 4.0, 7.0 Hz), 3.27 (1 H, s), 3.33 (1 H, s), 3.64 (1 H, dd, J = 6.1, 6.1 Hz), 3.69 (3 H, s), 3.71 (1 H, dd, J = 3.1, 11.1 Hz), 3.83 (1 H, ddd, J = 2.6, 2.9, 9.3 Hz), 4.09 (1 H, d, J = 6.9 Hz), 4.33 (1 H, d, J = 5.3 Hz), 5.43 (1 H, s), 5.61 (1 H, dd, J = 2.5, 8.4 Hz). MS (FAB, NaI): 867 (M + Na). $[\alpha]_D$: -8.4° (c 1.0, CH_3Cl). Data for **26B**-d_5. ^1H NMR ($CDCl_3$): The resonance at 1.89 ppm disappeared, and the coupling pattern of signals at 1.96, 2.10, and 3.83 ppm was simplified. MS (FAB, NaI): 868 (M + Na).

Synthesis of 27. To a stirred solution of **26B** (37.5 mg) in 10:1 aqueous CH_3CN (4.4 mL) was added CAN (100 mg) at 0 °C. After being stirred at 0 °C for 20 min, the reaction was quenched with saturated $NaHCO_3$. Aqueous workup (CH_2Cl_2) and silica gel chromatography (2:1 EtOAc/hexanes) gave **27** (31.0 mg, 96% yield, an oil) as single product. IR (neat): 3477, 1737 cm^{-1}. ^1H NMR (CD_3Cl): δ 1.78 (1 H, ddd, J = 3.0, 9.2, 14.2 Hz), 1.87 (1 H, dd, J = 4.8, 8.9 Hz), 2.06 (1 H, ddd, J = 5.0, 10.4, 14.6 Hz), 2.15 (3 H, s), 3.31 (1 H, s), 3.38 (1 H, s), 3.61 (1 H, ddd, J = 3.0, 4.5, 8.3 Hz), 3.70 (1 H, dd, J = 6.2, 6.2 Hz), 3.74 (1 H, dd, J = 4.9, 7.2 Hz), 3.77 (1 H, s), 3.80 (1 H, dd, J = 2.9, 8.2 Hz), 3.83 (1 H, dd, J = 3.2, 8.9 Hz), 3.96 (1 H, ddd, J = 2.1, 2.1, 11.1 Hz), 4.19 (1 H, d, J = 6.6 Hz), 4.39 (1 H, d, J = 5.6 Hz), 5.21 (1 H, dd, J = 2.5, 2.7 Hz), 5.41 (1 H, s). MS (FAB, NaI): 747 (M + Na). HRMS: calcd for $C_{43}H_{48}O_{10}Na$ (M + Na) 747.3145, found 747.3121. $[\alpha]_D$: +21.4° (c 1.4, CH_3Cl). Data for **27**-d_5. ^1H NMR (CD_3Cl): The resonance at 2.06 ppm disappeared, and the coupling pattern of signals at 1.78, 1.87, and 3.96 ppm was simplified. MS (FAB, NaI): 748 (M + Na).

Synthesis of 20. Transformation of **27** to **20** was carried out as described in Scheme VIII, and the spectroscopic data were given before.

Experiments Outlined in Scheme IX. Synthesis of 28. To a solution of dibenzyl ether primary alcohol (an intermediate of transformation of **5** to **6** in Scheme III; 2.50 g, 6.8 mmol) in THF (20 mL) was added PhSSPh (1.75 g, 8.0 mmol) and Bu_3P (2.0 mL, 7.5 mmol). The reaction was heated to reflux for 2 days. Aqueous workup (CH_2Cl_2) and silica gel chromatography (1:10 EtOAc/hexanes) gave the desired thioether (1.90 g, 61% yield, an oil) along with recovered starting material (510.1 mg, 20%). To a solution of the thioether (1.90 g, 4.1 mmol) in CH_2Cl_2 (100 mL) was added MCPBA (1.5 g, 75%) portionwise. After 1 h at rt, aqueous workup (CH_2Cl_2) and silica gel chromatography (1:2 EtOAc/hexanes) afforded **28** (1.53 g, 79% yield) as an oil. IR (neat): 3069 cm^{-1}. ^1H NMR (CD_3Cl): δ 1.90 (1 H, dd, J = 7.1, 7.2 Hz), 2.05 (2 H, m), 3.05 (2 H, m), 3.20 (1 H, s), 3.33 (1 H, s), 3.72 (1 H, dd, J = 6.1, 6.2 Hz), 4.12 (1 H, d, J = 6.8 Hz), 4.31 (1 H, d, J = 5.5 Hz), 5.41 (1 H, s). MS (FAB, NaI): 517 (M + Na). HRMS: calcd for $C_{28}H_{30}O_6SNa$ (M + Na) 517.1661, found 517.1645. $[\alpha]_D$: -98.8° (c 0.7, CH_3Cl).

Synthesis of 29. To a solution of **28** (237.4 mg, 0.48 mmol) in THF (4 mL) was added *n*-BuLi (0.25 mL, 0.58 mmol, 2.3 M) dropwise at -78 °C. After 10 min, $BF_3{\cdot}Et_2O$ (63 mL, 0.51 mmol) was added at -78 °C and stirred for 5 min. A solution of **24** (180 mg, 0.48 mmol) in THF (1 mL) was added at -78 °C. After 10 min, the reaction was warmed and kept at 0 °C for 20 min then quenched with saturated $NaHCO_3$. Aqueous workup (CH_2Cl_2) gave an oil. This oil was dissolved in MeOH (10 mL). Freshly prepared Na-Hg (2.5 g, 3%) was then added, and the reaction was stirred overnight at 0 °C. The solution was decanted, and the mercury layer was washed with MeOH. The combined organic solution was concentrated to one-third its volume. Aqueous workup (CH_2Cl_2) and silica gel chromatography (1:5 EtOAc/hexanes) gave **29** (158.9 mg, 47% yield, an oil) along with **25** (31.6 mg, 9.4% yield, an oil). IR (neat): 3063 cm^{-1}. ^1H NMR (CD_3Cl): δ 1.30 (3 H, s), 1.40 (3 H, s), 1.76 (1 H, dd, J = 7.2, 7.5 Hz), 2.37 (1 H, ddd, J = 6.2, 6.8, 13.8 Hz), 2.48 (1 H, ddd, J = 7.4, 7.6, 14.4 Hz), 3.37 (1 H, s), 3.39 (1 H, s), 3.68 (1 H, dd, J = 6.0, 6.1 Hz), 3.72 (1 H, dd, J = 4.1, 4.1 Hz), 3.87 (1 H, dd, J = 4.3, 7.2 Hz), 3.95 (2 H, s), 4.10 (1 H, d, J = 6.5 Hz), 4.23 (1 H, m), 5.43 (1 H, s), 5.58 (1 H, m), 5.65 (1 H, m). MS (FAB, NaI): 729 (M + Na). HRMS: calcd for $C_{44}H_{50}O_8Na$ (M + Na) 729.3403, found 729.3390. $[\alpha]_D$: -56.0° (c 1.4, CH_3Cl).

Synthesis of 30D. Following the same procedure of asymmetric osmylation as given for olefin **8**, **29** (423.1 mg, 0.60 mmol) was transformed into the expected threo diol[39] (267.7 mg, 60% yield, an oil) along with its diastereomer (7.8 mg, stereoselectivity ca. 18:1). Using the same procedure as given for **9**, this threo diol (201.3 mg, 0.27 mmol) was transformed into the desired mono-MPM ether[39] (148.5 mg, 65% yield, an oil) along with the undesired mono-MPM ether[39] (48.5 mg, selectivity ca. 3:1).

To a solution of the mono-MPM ether (18.3 mg, 0.021 mmol) in 1 mL of pyridine was added 3,4,5-trimethoxybenzoyl chloride (40 mg) and DMAP (0.5 mg). After being stirred at rt for 2 days, the reaction was concentrated in vacuo to give a solid. Silica gel chromatography (1:2 EtOAc/hexanes) afforded the desired 3,4,5-trimethoxybenzoate[39] (16.0 mg, 71% yield). To a solution of the 3,4,5-trimethoxybenzoate in THF (2 mL) was added 3 N HCl (1 mL). The reaction was stirred for 1 day. Aqueous workup (CH_2Cl_2) and silica gel chromatography (1:1 EtOAc/hexanes) afforded the desired diol[39] (15.7 mg, 91% yield) as an oil. Using the same procedure given previously (see Scheme VIII), this diol (15.7 mg, 0.016 mmol) was transformed into **30D** (14.3 mg, 91% yield, an oil). IR (neat): 2927, 1714 cm^{-1}. ^1H NMR (CD_3Cl): δ 1.85 (2 H, m), 1.94 (1 H, m), 2.54 (1 H, dd, J = 2.6, 4.7 Hz), 2.58 (1 H, dd, J = 4.2, 4.6 Hz), 3.25 (1 H, dd, J = 3.1, 6.4 Hz), 3.28 (1 H, m), 3.32 (1 H, s), 3.33 (1 H, s), 3.50 (1 H, dd, J = 6.1, 6.2 Hz), 3.76 (3 H, s), 3.75 (1 H, m), 3.81 (6 H, s), 3.81 (1 H, m), 3.90 (3 H, s), 3.95 (2 H, m), 3.98 (1 H, dd, J = 3.1, 6.7 Hz), 4.01 (1 H, m), 5.38 (1 H, s), 5.68 (1 H, dd, J = 4.3, 6.7 Hz). MS (FAB, NaI): 1019 (M + Na). HRMS: calcd for $C_{59}H_{64}O_{14}Na$ (M + Na) 1019.4190, found 1019.4210. $[\alpha]_D$: -12.9° (c 0.7, CH_3Cl).

Synthesis of 31. To a stirred solution of **30D** (10.4 mg, 0.011 mmol) in a 10:1 mixture of CH_2Cl_2 and phosphate buffer pH 7 solution (2:0.2 mL) was added DDQ (20 mg) at 0 °C. After 3 h, the reaction was quenched with saturated $NaHCO_3$. Aqueous workup (CH_2Cl_2) gave an oil. The oil was dissolved in CH_2Cl_2 (2 mL), and *p*-TsOH (1 mg) was added into the reaction. After 3 h, the reaction was quenched with saturated $NaHCO_3$. Aqueous workup (CH_2Cl_2) and silica gel chromatography (1:1 EtOAc/hexanes) yielded **31** (8.0 mg, 89% yield, an oil) as a single product. IR (neat): 3494, 1715 cm^{-1}. ^1H NMR (CD_3Cl): δ 1.90 (3 H, m), 3.28 (1 H, ddd, J = 3.1, 3.6, 11.4 Hz), 3.31 (1 H, s), 3.40 (1 H, s), 3.60 (1 H, m), 3.65 (1 H, m), 3.68 (1 H, dd, J = 2.9, 9.2 Hz), 3.72 (1 H, dd, J = 6.1, 6.2 Hz), 3.79 (1 H, ddd, J = 2.7, 4.1, 11.3 Hz), 3.85 (1 H, dd, J = 9.4, 9.4 Hz), 3.86 (1 H, m), 3.90 (6 H, s), 3.93 (3 H, s), 4.12 (1 H, d, J = 6.7 Hz), 4.33 (1 H, d, J = 5.4 Hz), 5.41 (1 H, s), 5.60 (1 H, d, J = 2.8 Hz). MS (FAB, NaI): 899 (M + Na). HRMS: calcd for $C_{51}H_{56}O_{13}Na$ (M + Na) 899.3619, found 899.3646. $[\alpha]_D$: -15.0° (c 0.8, CH_3Cl).

Experiments Outlined in Scheme X. Synthesis of 32. To the dibenzyl ether primary alcohol (an intermediate of the transformation of **5** to **6** in Scheme III; 2.03 g, 5.4 mmol) in benzene (30 mL) was added *o*-$O_2NPhSeCN$ (1.7 g, 5.4 mmol), followed by addition of *n*-Bu_3P (1.7 mL, 5.4 mmol). After 10 min, the reaction was diluted with CH_2Cl_2 (200 mL) and MCPBA (3.3 g, 60%, 5.94 mmol) was added to the solution at rt. After 15 min, Et_3N (4.7 mL, 33.7 mmol) was added to the solution and stirred for 30 min. Aqueous workup (CH_2Cl_2) and silica gel chromatography (1:1 hexanes/EtOAc) gave the expected olefin[39] (1.85 g, 91% yield) as an oil.

The olefin (1.85 g, 5.2 mmol) was ozonized under the same conditions as given in Scheme VII, followed by Me_2S and $NaBH_4$ treatments. Silica gel chromatography (2:1 hexanes/EtOAc) afforded the expected primary alcohol[39] (1.55 g, 84% yield) as

an oil. The primary alcohol was subjected to Swern oxidation, then Horner–Emmons reaction with $Ph_3P{=}CHCO_2Me$ (3.07 g) at 0 °C, to yield the expected trans unsaturated ester[39] (1.13 g, 90% yield, a colorless oil).

To the trans unsaturated ester (950 mg, 2.31 mmol) in CH_2Cl_2 (30 mL) at 0 °C was added dropwise a 1.0 M hexane solution of DIBAL (3.4 mL, 3.47 mmol) over 5 min. After 1 h, the reaction was quenched with MeOH (2.3 mL) and water (3.2 mL) and stirred for 30 min. The precipitate was filtered off through a pad of Celite, and the pad was thoroughly washed with Et_2O (200 mL). The combined filtrates were concentrated in vacuo. Silica gel chromatography (2:1 EtOAc/hexanes) gave **32** (869.8 mg, 98% yield) as an oil. IR (neat): 3470 (br) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.45 (1 H, d, J = 8.9 Hz), 3.40 (1 H, s), 3.42 (1 H, s), 3.72 (1 H, dd, J = 6.8, 5.3 Hz), 4.11 (1 H, d, J = 5.6 Hz), 4.17 (1 H, d, J = 6.8 Hz), 4.38 (1 H, d, J = 5.3 Hz), 5.45 (1 H, s), 5.69–5.80 (1 H, ddd, J = 5.8, 9.0, 15.5 Hz), 5.97–6.08 (1 H, dd, J = 9.0, 15.5 Hz). MS (DCI, NH_3): 400 (M + NH_4). HRMS: calcd for $C_{23}H_{26}O_5Na$ (M + Na) 405.1678, found 405.1689. $[\alpha]_D$: −63.7° (c 1.0, $CHCl_3$).

Synthesis of 33-d_R and 34-d_S. To a solution of **32** (1.22 g, 3.2 mmol) in THF (40 mL) was added dropwise a 1.0 M THF solution of BD_3 (10.0 mL, 10.0 mmol) over 10 min at 0 °C. After 4 h at rt, the reaction was cooled to 0 °C and 1 M NaOH (100 drops) was slowly added, followed by 30% H_2O_2 (95 drops). The mixture was stirred for 1 h. Aqueous workup (CH_2Cl_2) and silica gel chromatography (2:1 EtOAc/hexanes) afforded a mixture of **33**-d_R and **34**-d_S (540 mg, 44% yield) along with a mixture of **35**-d_S and **36**-d_R (380 mg, 31% yield).

Separation of **33**-d_R and **34**-d_S was best achieved via the corresponding acetonides. Thus, the mixture of **33**-d_R and **34**-d_S (540 mg in 15 mL) was treated with 2,2-dimethoxypropane (2.4 mL, 1.90 mmol) and camphorsulfonic acid (cat.) at 0 °C. After 12 h, the reaction was quenched with saturated $NaHCO_3$. Aqueous workup (CH_2Cl_2) and preparative TLC (1:2 hexanes/EtOAc) gave the R-deuterated acetonide[39] (295 mg, 48% yield) and the S-deuterated acetonide[39] (266 mg, 44% yield) for a combined yield of 92%.

To a solution of R-deuterated acetonide (295 mg, 0.74 mmol) in THF (20 mL) was added 3 N HCl (4 mL). After 12 h, the reaction was neutralized with saturated $NaHCO_3$. Aqueous workup (CH_2Cl_2) and silica gel chromatography (2:1 EtOAc/hexanes) furnished **33**-d_R (270.0 mg, ~100% yield, an oil). Using the same procedure, the S-deuterated acetonide (266 mg, 0.64 mmol) was transformed into **34**-d_S (245 mg, ~100% yield, an oil). Data for **33**-d_R. IR (neat): 3442 cm^{-1}. ^1H NMR (CD_3Cl): δ 1.90 (1 H, m), 2.10 (1 H, d, J = 9.6 Hz), 2.96 (1 H, s), 3.41 (1 H, dd, J = 7.4, 11.1 Hz), 3.42 (2 H, s), 3.63 (1 H, dd, J = 2.9, 11.1 Hz), 3.79 (2 H, m), 3.87 (1 H, m), 4.23 (1 H, d, J = 6.6 Hz), 5.50 (1 H, s). MS (FAB, NaI): 424 (M + Na). HRMS: calcd for $C_{23}H_{27}O_6DNa$ (M + Na): 424.1846, found 424.1862. $[\alpha]_D$: −57.2° (c 2.3, CH_3Cl). Data for S-deuterated **34**-d_S. IR (neat): 3439 cm^{-1}. ^1H NMR (CD_3Cl): δ 1.82 (1 H, dd, J = 2.6, 9.6 Hz), 2.07 (1 H, d, J = 9.4 Hz), 2.88 (1 H, s), 3.38 (1 H, dd, J = 7.6, 11.0 Hz), 3.43 (2 H, s), 3.55 (1 H, dd, J = 3.1, 11.1 Hz), 3.68 (1 H, ddd, J = 2.9, 3.6, 7.5 Hz), 3.76 (1 H, dd, J = 6.1, 6.1 Hz), 3.78 (2 H, m), 4.21 (1 H, d, J = 6.7 Hz), 4.43 (1 H, d, J = 5.3 Hz), 5.48 (1 H, s). MS (FAB, NaI): 424 (M + Na). HRMS: calcd for $C_{23}H_{27}O_6DNa$ (M + Na) 424.1845, found 424.1853. $[\alpha]_D$: −34.5° (c 2.6, CH_3Cl).

Experiments Outlined in Scheme XI. Using the same sequences of reactions as given in Schemes III–V, VII, and VIII, specifically mono-deuterated C-disaccharides **3**-d_R and **4**-d_S were synthesized from **33**-d_R and **34**-d_S, respectively. The spectroscopic data of intermediates are given under the corresponding non-deuterated substances.

Experiments Outlined in Scheme XII. Synthesis of 39. To a solution of **38** (903 mg, 1.64 mmol) in EtOH (150 mL) was added Pd on C (1.0 g, 10%) under Ar. The suspension was degassed under vacuum and refilled with H_2 several times. After being stirred under H_2 for 3 h, the suspension was filtered through a pad of Celite and the pad was washed with EtOH (3 × 20 mL). The combined filtrates were concentrated in vacuo to give **39** (889 mg, 98% yield, an oil) as a single product. IR (neat): 1734 cm^{-1}. ^1H NMR (CD_3Cl): δ 2.26 (2 H, m), 2.50 (1 H, m), 3.37 (3 H, s), 3.49 (3 H, s), 3.55 (2 H, m), 3.58 (1 H, dd, J = 2.5, 9.3 Hz), 3.78 (1 H, m), 3.80 (3 H, s), 4.67 (1 H, d, J = 3.6 Hz). MS (FAB, NaI): 573 (M + Na). HRMS: calcd for $C_{32}H_{38}O_8Na$ (M + Na) 573.2465, found 573.2455. $[\alpha]_D$: +6.7° (c 2.0, CH_3Cl).

Synthesis of 40. To a solution of **39** (889.3 mg) in Et_2O (50 mL) was added LAH (0.4 g) portionwise at 0 °C. After being stirred at 0 °C for 1 h, the reaction was quenched with water (0.4 mL), 15% NaOH (1.2 mL), and water (1.2 mL). The precipitate was filtered off through a pad of Celite and the pad was washed with ether (3 × 30 mL). The combined filtrates were dried over $MgSO_4$, filtered, and concentrated in vacuo to give an oil. Silica gel chromatography (1:1 EtOAc/hexanes) gave **40** (715.2 mg, 85% yield) as an oil. IR (neat): 3450 cm^{-1}. ^1H NMR (CD_3Cl): δ 1.52 (1 H, m), 1.60 (1 H, m), 1.85 (1 H, m), 3.38 (3 H, s), 3.51 (1 H, m), 3.66 (1 H, ddd, J = 3.3, 6.4, 10.7 Hz), 3.68 (1 H, dd, J = 9.4, 10.3 Hz), 3.80 (3 H, s), 4.67 (1 H, d, J = 3.4 Hz). HRMS: Calcd for $C_{31}H_{38}O_7Na$ (M + Na) 545.2515, found 545.2521. $[\alpha]_D$: +11.9° (c 1.2, CH_3Cl).

Synthesis of 41. To a solution of **38** (8.90 g) in 10:1 aqueous CH_3CN (550 mL) was added CAN (25 g, excess) at 0 °C. After 3 h at 0 °C, the reaction was quenched with saturated $NaHCO_3$ (200 mL) and solid $NaHSO_3$. Aqueous workup (CH_2Cl_2) and silica gel chromatography (1:1 EtOAc/hexanes) gave **41** (5.41 g, 85% yield, colorless needles, mp 138–139.5 °C). IR (neat): 1743 cm^{-1}. ^1H NMR (CD_3Cl): δ 3.44 (3 H, s), 3.63 (1 H, dd, J = 3.2, 9.9 Hz), 4.12 (1 H, dd, J = 9.2, 11.0 Hz), 4.47 (1 H, dd, J = 6.1, 11.0 Hz), 4.52 (1 H, dd, J = 1.2, 7.4 Hz), 4.55 (1 H, dd, J = 1.4, 9.6 Hz), 4.67 (1 H, d, J = 2.9 Hz), 6.20 (1 H, dd, J = 1.4, 2.3 Hz). MS (FAB, NaI): 419 (M + Na). Anal. Calcd for $C_{22}H_{24}O_6$: C, 69.68; H, 6.10. Found: C, 69.58; H, 6.10. $[\alpha]_D$: +40.3° (c 1.6, CH_3Cl).

Synthesis of 42. Using the same procedure as given for **38**, **41** (8.00 g, 20.0 mmol) was hydrogenated to yield **42** (8.00 g, quantitative yield). IR (neat): 1735 cm^{-1}. ^1H NMR (CD_3Cl): δ 2.44 (1 H, dd, J = 3.9, 16.2 Hz), 2.68 (1 H, dd, J = 4.1, 16.2 Hz), 2.91 (1 H, m), 3.38 (3 H, s), 3.43 (1 H, m), 4.01 (1 H, dd, J = 5.3, 10.1 Hz), 4.09 (1 H, ddd, J = 2.0, 6.6, 6.9 Hz), 4.61 (1 H, d, J = 3.8 Hz). MS (FAB, NaI): 421 (M + Na). $[\alpha]_D$: +23.4° (c 0.6, CH_3Cl).

Synthesis of 43. To a solution of **42** (8.00 g, 20.2 mmol) in 2:1 aqueous THF (150 mL) was added LiOH (0.87 g, 37.1 mmol). After 5 min, the suspension was concentrated to dryness. The residue was azeotroped with toluene. The residue was dissolved in a mixture of THF (100 mL) and DMF (30 mL). To this solution was added oil-free NaH (1.4 g, 58 mmol), followed by addition of BnBr (6.5 mL, 58.3 mmol). After addition of n-$Bu_4N^+I^-$ (20 mg), the reaction was stirred overnight. The reaction was quenched with MeOH. Aqueous workup (CH_2Cl_2) gave an oil, which was subjected to LAH reduction under the same conditions as before, to yield **43** (6.97 g, 70% yield overall, an oil). IR (neat): 3425 cm^{-1}. ^1H NMR (CD_3Cl): δ 1.61 (1 H, m), 1.81 (1 H, m), 2.22 (1 H, m), 3.39 (3 H, s), 3.48 (1 H, dd, J = 6.2, 9.8 Hz), 3.54 (1 H, dd, J = 6.8, 9.8 Hz), 3.54 (1 H, m), 3.64 (1 H, dd, J = 3.9, 10.1 Hz), 3.99 (1 H, dd, J = 5.0, 9.8 Hz), 4.10 (1 H, ddd, J = 1.8, 6.6, 7.1 Hz), 4.63 (1 H, d, J = 4.0 Hz). MS (FAB, NaI): 515 (M + Na). HRMS: calcd for $C_{30}H_{36}O_6Na$ (M + Na) 515.2410, found 515.2446. $[\alpha]_D$: +23.5° (c 1.0, CH_3Cl).

Experiments Outlined in Scheme XIII. Synthesis of 46. Under the same DDQ deprotection conditions as before (see Scheme IX), **39** (1.23 g) was converted to the expected hydroxy ester[39] (610 mg, 65% yield, an oil). The hydroxy ester (1.10 g) was subjected to Swern oxidation, and the product was purified by silica gel chromatography (1:2 EtOAc/hexanes) to give the aldehyde as an oil. The resultant aldehyde was azeotroped with toluene (3 × 20 mL) and then dissolved in toluene (20 mL). The solution was refluxed for 30 min with a Dean–Stark trap containing activated 3-Å molecular sieves. Then $RhCl(PPh_3)_3$ (2.29 g) was added to the reaction. After being refluxed for 6 h, the reaction was cooled and concentrated in vacuo to give a residue. Purification by silica gel chromatography (2:1 ether/hexanes) gave 5-deshydroxymethyl ester[39] (0.85 g, 83% overall yield from the hydroxy ester) as an oil. Using the same procedure given for **39**, this ester (810 mg, 2.1 mmol) was transformed into **46** (710 mg, 95% yield, an oil). IR (neat): 3600–3200 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.37 (1 H, ddd, J = 6.2, 12.7, 12.7 Hz), 1.77 (1 H, m), 1.86 (1 H, m), 3.38 (3 H, s), 3.44 (1 H, dd, J = 11.6, 11.6 Hz), 4.63 (1 H, d, J = 2.9 Hz). MS (FAB, NaI): 395 (M + Na). $[\alpha]_D$: +33.8° (c 1.0, $CHCl_3$).

Synthesis of 44. Following the same procedures as given in Scheme III, **46** (710 mg) was transformed into the mesylate[39] (95%

yield, an oil), iodide[39] (94% yield, an oil), then phosphonium salt[39] (95% yield, a foam). Using the same conditions of Wittig reaction as given for **6**, this phophonium salt (933.5 mg) was transformed into the *cis*-olefin[39] (670.0 mg, 76% yield, an oil).

Asymmetric osmylation of the *cis*-olefin (250.0 mg) was conducted under the same conditions as for **8** to yield the expected erythro diol[39] (195.3 mg, 75% yield, an oil) along with a small amount of its diastereomer (stereoselectivity = ca. 30:1). Employing the same monoprotection procedure as given for **9**, the major erythro diol (216.63 mg) was transformed into the desired mono-MPM ether[39] (203.8 mg, 81% yield).

The mono-MPM ether (203.8 mg) was subjected to Swern oxidation to yield the ketone (203.8 mg, ~100% yield, an oil), which was treated with 3 N HCl (8.5 mL) in THF (20 mL). After 12 h, aqueous workup (CH_2Cl_2) gave the hemiketal as an oil. The hemiketal (188.6 mg) was converted to the expected benzoate[39] (178.1 mg, 88% yield, an oil) as given before. Employing the same conditions for monothioketal preparation and reduction as given for **11**, this benzoate (35.0 mg, 0.037 mmol) was transformed into the protected form[39] of the *C*-disaccharide (20.1 mg, 80% overall yield, an oil).

Using the same procedure as given before, this substance (20.1 mg, 0.32 mmol) was subjected to inversion of the C.2′ stereochemistry to yield the protected form[39] of **44** (18.5 mg, 92% overall yield). As before (see Scheme V), the protected substance (12.3 mg) was converted to **44** (4.2 mg, 87% overall yield). IR (neat): 3318 cm^{-1}. ^1H NMR (CD_3OD): δ 1.61 (1 H, ddd, J = 2.0, 9.5, 14.6 Hz), 1.79 (1 H, ddd, J = 3.1, 10.0, 14.4 Hz), 1.93 (1 H, m), 3.01 (1 H, dd, J = 8.8, 8.9 Hz), 3.13 (1 H, ddd, J = 2.0, 9.8, 9.8 Hz), 3.19 (1 H, dd, J = 2.0, 5.6 Hz), 3.22 (1 H, dd, J = 9.5, 9.8 Hz), 3.36 (3 H, s), 3.36 (1 H, dd, J = 3.6, 9.1 Hz), 3.41 (2 H, m), 3.60 (1 H, ddd, J = 2.2, 5.8, 11.9 Hz), 3.83 (1 H, dd, J = 2.3, 11.9 Hz), 4.64 (1 H, d, J = 3.4 Hz). MS (FAB, NaI): 347 (M + Na). HRMS: calcd for $C_{13}H_{23}O_9$ (M − H) 323.1341, found 323.1335. $[\alpha]_D$: +64.5° (*c* 0.4, MeOH).

Experiments Outlined in Scheme XIV. Synthesis of 48. To a solution of **47** (20.0 g) in a mixture of THF (1.5 L) and water (100 mL) was added powdered NaOH (60 g) portionwise. After 30 min, benzyl bromide (50 mL) was added slowly via a dropping funnel over 1 h. After vigorously stirring for 12 h, the reaction was quenched with MeOH (50 mL) and stirred for 1 h. After concentrating in vacuo to one-third of its original volume, aqueous workup (CH_2Cl_2) and silica gel chromatography (1:1 EtOAc/hexanes) gave C.2-monobenzyl ether[39] (9.00 g, 40% yield, an oil) along with C.3-monobenzyl ether (10% yield) and C.2,C.3-dibenzyl ether (5% yield).

To a solution of C.2-monobenzyl ether (2.90 g, 7.8 mmol) in CH_2Cl_2 (8 mL) was added pyridine (2.73 mL, 35 mmol) and then *p*-tolyl chlorothionoformate (2.4 mL, 13 mmol). After 2 h, aqueous workup (CH_2Cl_2) and silica gel chromatography (1:2 EtOAc/hexanes) gave the expected thionocarbonate as an oil. To a solution of the thionocarbonate in toluene (50 mL) was added *n*-Bu_3SnH (4 mL, 14 mmol) and AIBN (10 mg). Then the reaction was placed in a preheated oil bath (110 °C) and refluxed for 1 h. The reaction was cooled and concentrated to give an oil. Silica gel chromatography (hexanes to 1:1 EtOAc/hexanes) gave **48** (2.0 g, 72% yield) as a solid. The solid was recrystallized from aqueous EtOH to give colorless needles (mp 95.5–96.5 °C). IR (neat): 3063 cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.06 (1 H, q, J = 11.6 Hz), 2.28 (1 H, ddd, J = 4.2, 4.4, 11.5 Hz), 3.46 (3 H, s), 3.50 (1 H, ddd, J = 4.2, 9.2, 11.8 Hz), 3.60 (1 H, ddd, J = 3.8, 4.2, 11.8 Hz), 3.66 (1 H, dd, J = 10.3, 10.3 Hz), 3.77 (1 H, ddd, J = 4.8, 9.6, 10.1 Hz), 4.70 (1 H, d, J = 3.0 Hz), 5.50 (1 H, s). MS (FAB, NaI): 379 (M + Na). Anal. Calcd for $C_{21}H_{24}O_5$: C, 70.76; H, 6.79. Found: C, 70.54; H, 6.78. $[\alpha]_D$: +19.2° (*c* 1.0, $CHCl_3$).

Synthesis of 49. To a solution of **48** (1.60 g, 4.5 mmol) in THF (100 mL) was added solid $NaBH_3CN$ (4.0 g, 64 mmol) and 3-Å molecular seives (2 g). Then 5 mL of ether saturated with HCl was added dropwise over 2 h. After being stirred overnight, the reaction was quenched with saturated $NaHCO_3$. The precipitate was filtered off through a pad of Celite, and the pad was washed with CH_2Cl_2 (3 × 50 mL). Aqueous workup and silica gel chromatography (1:2 EtOAc/hexanes) gave the expected C.4-alcohol[39] (1.20 g, 75% yield) as an oil.

The C.4-alcohol (725.7 mg) was subjected to Swern oxidation, then Horner–Emmons reaction ($(MeO)_2P(O)CH_2CO_2Me$, *t*-BuOK, THF/DMF (5:2), 0 °C) gave the expected α,β-unsaturated ester[39] (803.1 mg, 96% yield, an oil) as a single stereoisomer (NMR). Using the same procedure as given for **38**, the α,β-unsaturated ester (803.1 mg) was hydrogenated to yield the equatorial ester[39] (800.0 mg, quantitative) as an oil. Then, employing the same procedure as given for **39**, this ester (800.3 mg) was transformed into **49** (593.1 mg, 81% yield, an oil). IR (neat): 3480 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.32 (1 H, m), 1.55 (1 H, m), 1.58 (1 H, q, J = 12.1 Hz), 1.91 (2 H, m), 3.40 (3 H, s), 3.55 (2 H, m), 3.65 (1 H, m), 4.74 (1 H, d, J = 3.3 Hz). MS (FAB, NaI): 409 (M + Na). $[\alpha]_D$: +43.3° (*c* 1.0, $CHCl_3$).

Experiments Outlined in Scheme XV. Synthesis of 51. The alcohol **49** (650.0 mg, 1.7 mmol) was subjected to Swern oxidation to yield the aldehyde (650.0 mg, quantitative) as an oil.

To a solution of CBr_4 (1.13 g, 3.4 mmol) in CH_2Cl_2 (15 mL) was added PPh_3 (1.79 g, 6.8 mmol). After 30 min, a solution of the aldehyde (650.0 mg, 1.7 mmol) in CH_2Cl_2 (5 mL) was added at 0 °C. After 2 h at 0 °C, the reaction was concentrated to a half of its original volume. Silica gel chromatography (hexanes to 1:3 EtOAc:hexanes) gave the expected dibromoolefin[39] (853.3 mg, 93% overall yield) as an oil.

To a solution of the dibromoolefin (853.3 mg, 1.5 mmol) in THF (5 mL) was added *n*-BuLi (1.63 mL, 3.75 mmol, 2.3 M) via syringe at −78 °C. After 1 h at that temperature, the reaction was quenched with saturated NH_4Cl. Aqueous workup (CH_2Cl_2) and silica gel chromatography (1:3 EtOAc/hexanes) afforded the acetylene[39] (475.0 mg, 83% yield) as an oil.

To a solution of I_2 (1.20 g, 4.7 mmol) in benzene (6 mL) was added morpholine (0.70 mL, 6.4 mmol). After 10 min, a solution of the acetylene (475 mg, 1.2 mmol) in benzene (4 mL) was added and the reaction was placed in a preheated oil bath (50 °C) for 3 h. The reaction was cooled and quenched with saturated $NaHCO_3$. Aqueous workup (CH_2Cl_2) and silica gel chromatography (1:3 EtOAc/hexanes) gave **51** (456.7 mg, 75% yield) as an oil. IR (neat): 3090 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.80 (1 H, q, J = 11.9 Hz), 1.93 (1 H, m), 1.99 (1 H, ddd, J = 4.0, 4.0, 11.6 Hz), 2.23 (1 H, dd, J = 7.1, 17.1 Hz), 2.37 (1 H, dd, J = 4.1, 17.0 Hz), 3.41 (3 H, s), 3.64 (1 H, ddd, J = 3.4, 3.4, 10.1 Hz), 4.74 (1 H, d, J = 3.3 Hz). MS (FAB, NaI): 529 (M + Na). HRMS: calcd for $C_{24}H_{27}O_4INa$ (M + Na) 529.0852, found 529.0868. $[\alpha]_D$: +28.4° (*c* 2.0, $CHCl_3$).

Synthesis of 50. The aldehyde **7** was prepared under the standard conditions of Swern oxidation of the primary alcohol. To a solution of **7** (1.60 g, 4.3 mmol) in a mixture of CH_2Cl_2 and phosphate pH 7 buffer (100:50 mL) was added MCPBA (2.5 g) portionwise. After 3 h, the reaction was quenched with saturated $NaHCO_3$ and $Na_2S_2O_3$. Aqueous workup (CH_2Cl_2) gave the expected formate ester.

To a solution of this ester in Et_2O (100 mL) was added $LiAlH_4$ (0.3 g) at 0 °C. After 1 h at 0 °C, the reaction was quenched with water (0.3 mL), 15% NaOH (1.2 mL) and water (1.2 mL). The white precipitate was filtered off through a pad of Celite, and the pad was washed with Et_2O (3 × 20 mL). The combined filtrates were dried over $MgSO_4$, filtered, and concentrated in vacuo to give the crude product as an oil. Silica gel chromatography (1:2 EtOAc/hexanes) afforded the desired noralcohol (856.1 mg, 80% overall yield from the primary alcohol) as an oil. The noralcohol was subjected to Swern oxidation to yield **50**. Data for the noralcohol: IR (neat): 3584 cm^{-1}. ^1H NMR (CD_3Cl): δ 1.35 (3 H, s), 1.43 (3 H, s), 3.52 (1 H, ddd, J = 2.5, 4.2, 6.7 Hz), 3.70 (1 H, dd, J = 1.8, 11.3 Hz), 3.83 (1 H, dd, J = 4.0, 11.9 Hz), 3.87 (1 H, dd, J = 6.0, 8.5 Hz), 4.09 (1 H, dd, J = 4.4, 8.4 Hz), 4.18 (1 H, q, J = 6.3 Hz). MS (FAB): 253 (M + 1). HRMS (FAB, NaI): calcd for $C_{14}H_{20}O_4Na$ (M + Na) 275.1258, found 275.1276. $[\alpha]_D$: +33.4° (*c* 0.7, CH_3Cl).

Coupling of 50 and 51. A mixture of **50** (198.0 mg, 0.79 mmol) and **49** (420.3 mg, 0.78 mmol) was azeotroped with toluene. After being dried on high vacuum for 30 min, the mixture was placed in a glove box and THF (5 mL) was added. Then $CrCl_2$ (~300 mg) and subsequently $CrCl_2$ containing 0.2% $NiCl_2$ (~50 mg) was added. After 12 h, aqueous workup (EtOAc) and silica gel chromatography (1:2 EtOAc/hexanes) gave **52** (226.1 mg, 43% yield, an oil) and **53** (110.0 mg, 21.5% yield, an oil). Spectroscopic data of **52**. IR (neat): 3520 cm^{-1}. ^1H NMR (CD_3Cl): δ 1.33 (3 H, s), 1.40 (3 H, s), 1.82 (1 H, q, J = 12.1 Hz), 1.95 (1 H, m), 2.0 (1 H, ddd, J = 4.0, 4.3, 11.8 Hz), 2.12 (1 H, ddd, J = 1.9, 7.6, 16.9

Hz), 2.27 (1 H, ddd, J = 2.0, 2.1, 16.8 Hz), 3.38 (3 H, s), 3.64 (1 H, ddd, J = 2.6, 2.8, 10.2 Hz), 3.83 (1 H, m), 4.05 (1 H, m), 4.32 (1 H, m), 4.50 (1 H, m), 4.73 (1 H, d, J = 3.2 Hz). MS (FAB, NaI): 653 (M + Na). HRMS: calcd for $C_{38}H_{46}O_8Na$ (M + Na) 653.3090, found 653.3098. $[\alpha]_D$: +35.7° (c 0.7, CH_3Cl). Spectroscopic data of **53**. IR (neat): 3450 cm^{-1}. ^1H NMR (CD_3Cl): δ 1.35 (3 H, s), 1.42 (3 H, s), 1.78 (1 H, q, J = 12.0 Hz), 1.93 (1 H, m), 2.02 (1 H, ddd, J = 4.1, 4.3, 11.9 Hz), 2.10 (1 H, ddd, J = 1.7, 7.4, 16.9 Hz), 2.24 (1 H, ddd, J = 1.9, 3.9, 16.9 Hz), 2.41 (1 H, d, J = 5.3 Hz), 3.38 (3 H, s), 3.63 (1 H, ddd, J = 3.1, 3.1, 10.3 Hz), 3.70 (1 H, dd, J = 3.8, 5.4 Hz), 3.95 (1 H, dd, J = 6.7, 8.4 Hz), 4.05 (1 H, dd, J = 6.4, 8.4 Hz), 4.27 (1 H, m), 4.72 (1 H, d, J = 3.3 Hz). MS (FAB, NaI): 653 (M + Na). HRMS: calcd for $C_{38}H_{46}O_8Na$ (M + Na) 653.3090, found 653.3083. $[\alpha]_D$: +35.7° (c 0.9, CH_3Cl).

Conversion of 53 to 52. The alcohol **53** (280.2 mg, 0.44 mmol) was subjected to Swern oxidation to yield the ketone (280.2 mg, ~100% yield). To a solution of the ketone (280.2 mg, 0.44 mmol) in THF (5 mL) was added L-Selectride (1.0 M, 1.0 mL) at 0 °C. After 1 h, the reaction was quenched with saturated NH_4Cl. Aqueous workup (CH_2Cl_2) and silica gel chromatography (1:2 EtOAc/hexanes) gave **52** (226.9 mg, 80% yield).

Experiments Outlined in Scheme XVI. Synthesis of 54. To a solution of **52** (112.0 mg, 0.18 mmol) in MeOH (50 mL) was added Lindlar catalyst (20 mg). The suspension was evacuated under vacuum and refilled with H_2 several times. After being stirred under H_2 for 3 h, the suspension was filtered through a pad of Celite and the pad was washed with MeOH (3 × 15 mL). The combined filtrates were concentrated in vacuo to give the expected *cis*-allylic alcohol.[39] To a solution of the *cis*-allylic alcohol in a mixture of THF and DMF (2 and 0.7 mL) was added NaH (30 mg), followed by BnBr (0.05 mL) at 0 °C. After 5 h, the reaction was quenched with MeOH. Aqueous workup (CH_2Cl_2) and silica gel chromatography (1:3 EtOAc/hexanes) afforded the desired monobenzylated product[39] (102.5 mg, 80% overall yield) as an oil.

Following the same asymmetric osmylation procedure as given for **8**, this product (91.0 mg) was transformed into **54** (50.2 mg, 56% yield, an oil) along with its diastereomeric erythro diol (3.0 mg, 3.3% yield) and recovered olefin (25.0 mg, 27% yield). IR (neat): 3450 cm^{-1}. ^1H NMR (CD_3Cl): δ 1.33 (3 H, s), 1.40 (1 H, m), 1.43 (3 H, s), 1.50 (1 H, q, J = 11.9 Hz), 1.96 (1 H, m), 2.02 (1 H, ddd, J = 3.1, 4.4, 11.9 Hz), 2.41 (1 H, d, J = 4.8 Hz), 3.03 (1 H, d, J = 4.9 Hz), 3.41 (3 H, s), 3.55 (2 H, m), 3.60 (2 H, m), 3.68 (1 H, dd, J = 3.2, 6.2 Hz), 4.00 (1 H, dd, J = 7.1, 8.3 Hz), 4.08 (1 H, m), 4.30 (1 H, m), 4.75 (1 H, d, J = 3.2 Hz). MS (FAB, NaI): 779 (M + Na), 176 (100). HRMS: calcd for $C_{45}H_{56}O_{10}Na$ (M + Na) 779.3771, found 779.3796. $[\alpha]_D$: +26.8° (c 1.6, CH_3Cl).

Synthesis of 55. Following the same procedure as given for **9**, **54** (35.3 mg) was transformed into the desired mono-MPM ether[39] (25.3 mg, 62% yield) along with some undesired mono-protected compound (6.1 mg; regioselectivity ca. 4:1). Then, using the same sequence of reaction as given in Scheme VIII, this substance (24.0 mg, 0.03 mmol) was transformed into the diol (16.0 mg, 70% yield).

To a solution of this diol (10.3 mg, 0.012 mmol) in CH_2Cl_2 (2 mL) was added imidazole (5 mg) and TBS-Cl (10 mg). After 1 h, the reaction was quenched with saturated NH_4Cl. Aqueous workup (CH_2Cl_2) and preparative TLC (1:2 EtOAc/hexanes) gave the expected mono-TBS product[39] (11.3 mg), which was then converted to the desired mesylate (10.7 mg) as before. To a solution of the mesylate (10.7 mg) in THF (2 mL) was added a solution of TBAF (100 μL, 0.1 M). After 20 min, the reaction was quenched with saturated NH_4Cl. Aqueous workup (CH_2Cl_2) and preparative TLC afforded the desired epoxide[39] (7.9 mg, 77% yield) as an oil.

Using the same procedure as given for **26B**, this epoxide (7.0 mg) was cyclized into the expected tetrahydropyran (5.0 mg, 81% yield, an oil). Upon hydrolysis of the acetate then benzoylation, this substance yielded **55**, which was identical with the product derived via silane reduction of **56**. IR (neat): 3488, 1719 cm^{-1}. ^1H NMR (CD_3Cl): δ 1.10 (1 H, ddd, J = 3.1, 11.0, 14.1 Hz), 1.42 (1 H, q, J = 11.9 Hz), 1.75 (1 H, ddd, J = 3.1, 11.7, 14.8 Hz), 2.00 (1 H, m), 2.11 (1 H, ddd, J = 4.1, 4.3, 11.6 Hz), 3.33 (1 H, ddd, J = 4.6, 4.6, 11.9 Hz), 3.38 (3 H, s), 3.52 (1 H, m), 3.53 (3 H, s), 3.91 (1 H, ddd, J = 2.6, 6.3, 6.5 Hz), 4.03 (1 H, ddd, J = 3.2, 3.3, 12.1 Hz), 4.41 (1 H, dd, J = 3.1, 11.6 Hz), 4.48 (1 H, dd, J = 6.7, 11.6 Hz). MS (FAB, NaI): 825 (M + Na). $[\alpha]_D$: +51.0° (c 1.0, CH_3Cl).

Synthesis of 55 via 56. Using the same procedure as given for selective monoprotection of **9**, **54** (50.1 mg, 0.067 mmol) was transformed into the expected mono-MPM ether[39] (41.0 mg, 71% yield, an oil) along with di-MPM-ether (9.0 mg, 14% yield, an oil). Following the same procedure as given for **10**, this mono-MPM ether (32.1 mg, 0.036 mmol) was transformed to the corresponding ketone (quantitative, an oil), then to **56** (27.7 mg, 80% yield, an oil). IR (neat): 3583 cm^{-1}, 3379, 1720. ^1H NMR (CD_3Cl): δ 1.28 (1 H, dd, J = 2.2, 14.6 Hz), 1.55 (1 H, dd, J = 13.2, 13.2 Hz), 1.96 (1 H, dd, J = 4.6, 14.7 Hz), 2.10 (2 H, m), 3.35 (1 H, ddd, J = 4.5, 4.6, 11.2 Hz), 3.37 (3 H, s), 3.45 (1 H, m), 3.56 (1 H, d, J = 11.6 Hz), 3.67 (1 H, d, J = 2.6 Hz), 3.81 (1 H, dd, J = 2.9, 11.8 Hz), 3.83 (3 H, s), 4.02 (1 H, ddd, J = 2.1, 4.3, 12.4 Hz), 4.07 (1 H, dd, J = 9.1, 9.8 Hz), 4.23 (1 H, dd, J = 2.7, 9.0 Hz), 4.48 (1 H, dd, J = 4.5, 11.5 Hz). MS (FAB, NaI): 961 (M + Na). $[\alpha]_D$: +15.8° (c 0.8, CH_3Cl).

To a solution of **56** (21.5 mg, 0.023 mmol) in CH_2Cl_2 was added $PhMe_2SiH$ (50 μL) and TMSOTf (5 μL) at −20 °C. After 3 min, the reaction was quenched with saturated $NaHCO_3$. Aqueous workup (CH_2Cl_2) and preparative TLC (1:1 EtOAc/hexanes) gave **55** (16.1 mg, 87% yield) as an oil.

Synthesis of 45. Using the same procedure as given Scheme V, **55** (10.3 mg) was converted into the corresponding gluco alcohol[39] (91% yield, an oil), then to **45** (4.7 mg, ~100% yield, an oil). IR (neat): 3583, 3472 cm^{-1}. ^1H NMR (CD_3OD): δ 1.30 (1 H, ddd, J = 3.1, 11.4, 14.5 Hz), 1.41 (1 H, q, J = 12.0 Hz), 1.85 (1 H, ddd, J = 2.9, 12.1, 14.4 Hz), 1.96 (1 H, dddd, J = 2.9, 4.3, 11.4, 11.9 Hz), 3.22 (1 H, dd, J = 8.9, 9.5 Hz), 3.40 (3 H, s), 3.40 (2 H, m), 3.51 (1 H, dd, J = 8.7, 9.5 Hz), 3.72 (1 H, dd, J = 2.3, 11.9 Hz), 3.78 (1 H, dd, J = 2.4, 11.8 Hz), 4.03 (1 H, ddd, J = 3.1, 5.9, 12.2 Hz), 4.61 (1 H, d, J = 3.4 Hz). MS (FAB, NaI): 361 (M + Na). HRMS: calcd for $C_{14}H_{26}O_9$ 337.1497, found 337.1489. $[\alpha]_D$: +136.5° (c 0.5, CH_3Cl).

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Supplementary Material Available: Complete spectroscopic data and ^1H NMR spectra (74 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.