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Chelation-Assisted Regioselective C−O Bond Cleavage Reactions of Acetals by Grignard Reagents. A General Procedure for the Regioselective Synthesis of Protected Polyols Having One Free Hydroxy Group

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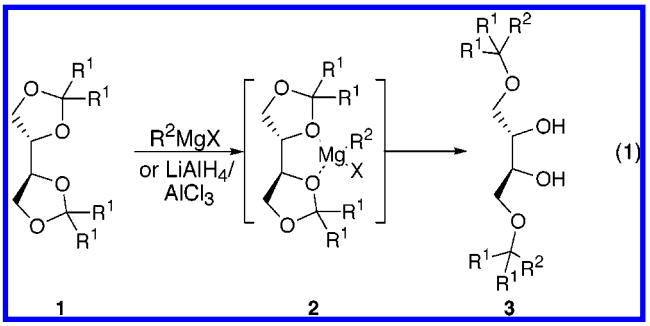
Acetals containing a neighboring heteroatom react with the Grignard reagent in aromatic hydrocarbon solvents regioselectively. The auxiliary moiety can be hydroxy, alkoxy, or amino but not sulfur. Chelation plays a key role in directing the regioselectivity of this ring opening reaction. The reactions of acetonide derivatives of monosaccharides under these conditions afford the corresponding products having only one free hydroxy group at the specific position. Fully protected mannosamine derivative is prepared in good yield. The stereochemistry of the carbon center where auxiliary group is attached can be either syn or anti to the acetal oxygen moiety where cleavage of the C−O bond occurs. However, difference in reactivity has been found in the reaction of tris-acetonide of sorbitol with MeMgI. Regioselective ring opening of the acetal group at the anomeric carbon generates a hemiacetal which underwent further nucleophilic addition to furnish the corresponding alcohol stereoselectively.

Differentiation of a contiguous polyol by the regioselective protection leading to the product having only one or two free hydroxy group(s) at the selected position(s) is valuable in synthesis.[1] Acetal and ortho ester functionalities are widely used protective groups for such polyols. Direct transformation of a polyol into the corresponding acetal or ortho ester leaving certain hydroxy groups intact would be the ideal situation but successful only in limited cases.[2] Multistep protection and deprotection are occasionally required. Selective conversion of an acetal moiety with a nucleophile into a hydroxyalkyl ether serves as a practical arsenal for this purpose.[3−11] The reaction has been demonstrated to be particularly important for the diastereoselective ring opening of cyclic chiral acetals.[3] Lewis acids are occasionally used to assist such reactions. Reductive cleavage of benzylidene acetals or the like has been used for the regioselective synthesis of certain monosaccharide derivatives.[8] Trimethylaluminum has been employed to facilitate the alkylative ring opening reaction.[5] However, a mixture of regioisomers is occasionally obtained. Although reactions of the Grignard reagent with acetals have been known for more than three decades[5] and the mechanism for this transformation has been extensively investigated,[6] not much synthetic use has been reported.[5,7] We recently uncovered a convenient synthesis of tunable C_2-chiral diols **3** by the regioselective ring opening of bisketals of threitol **1** with a variety of Grignard reagents in benzene (eq 1).[9]



(1)

Applications of this strategy to the synthesis of myo-inositol derivatives having one or two free hydroxy group-

(1) Greene, T. A.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley: New York, 1991. (b) Kocienski, P. J. *Protective Groups*; Thieme: New York, 1994.

(2) For a recent review, see: Hanessian, S., Ed.; *Preparative Carbohydrate Chemistry*; Marcel Dekker: New York, 1997. See also: Lee, H. W.; Kish, Y. *J. Org. Chem.* **1985**, *50*, 4402.

(3) (a) Bartlett, P. A.; Johnson, W. S.; Elliott, J. D. *J. Am. Chem. Soc.* **1983**, *105*, 2088. (b) Mori, A.; Fujiwara, J.; Maruoka, K.; Yamamoto, H. *Tetrahedron Lett.* **1983**, *24*, 4581.

(4) (a) Takano, S.; Kurotaki, A.; Sekiguchi, Y.; Satoh, S.; Hirama, M.; Ogasawara, K. *Synthesis* **1986**, 811. (b) Takano, S.; Akiyama, M.; Ogasawara, K. *Chem. Pharm. Bull.* **1984**, *32*, 791. (c) Takano, S.; Akiyama, M.; Sato, S.; Ogasawara, K. *Chem. Lett.* **1983**, 1593. (d) Takano, S.; Ohkawa, T.; Ogasawara, K. *Tetrahedron Lett.* **1988**, *29*, 1823. (e) Gilbert, I. H.; Holmes, A. B.; Young, R. C. *Tetrahedron Lett.* **1990**, *31*, 2633. (f) Gilbert, I. H.; Holmes, A. B.; Pestchanker, N. J.; Young, R. C. *Carbohydr. Res.* **1992**, *234*, 117.

(5) (a) Mori, I.; Ishihara, L. A.; Flippin, L. A.; Nozaki, K.; Yamamoto, H.; Bartlett, P. A.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 6107. (b) Denmark, S. E.; Almstead, N. G. *J. Am. Chem. Soc.* **1991**, *113*, 8089; *J. Org. Chem.* **1991**, *56*, 6458, 6485. (c) Sammakia, T.; Smith, R. S. *J. Org. Chem.* **1992**, *57*, 2997; *J. Am. Chem. Soc.* **1992**, *114*, 10998.

(6) (a) Blomberg, C.; Vreugdenhil, A. D.; Homsma, T. *Recl. Trav. Chim.* **1963**, *82*, 355. (b) Mallory, R. A.; Rovinski, S.; Scheer, I. *Proc. Chem. Soc. London* **1964**, 416.

(7) For reviews, see: (a) Trofimov, B. A.; Korostova, S. E. *Russ. Chem. Rev.* **1975**, *44*, 41. (b) Mukaiyama, T.; Murakami, M. *Synthesis* **1987**, 1043. (c) Alexakis A.; Mangeney, P. *Tetrahedron: Asymmetry* **1990**, *1*, 477. (d) Luh, T.-Y. *Pure Appl. Chem.* **1996**, *68*, 635. (e) Luh, T.-Y. *Synlett* **1996**, 201.

(8) Garegg, P. J. *Pure Appl. Chem.*, **1984**, *56*, 845. Garegg, P. J. *Acc. Chem. Res.* **1992**, *25*, 575. For chelative reductive cleavage of acetals, see: Evans, D. A.; Kaldor, S. W.; Jones, T. K.; Clardy, J.; Stout, T. J. *J. Am. Chem. Soc.* **1990**, *112*, 7001. Takano, S.; Kurotaki, A.; Sekiguchi, Y.; Satoh, S.; Hirama, M.; Ogazawara, K. *Synthesis* **1986**, 811.

(9) Yuan, T.-M.; Hsieh, Y.-T.; Yeh, S.-M.; Shyue, J.-J.; Luh, T.-Y. *Synlett* **1996**, 53.

(10) Yeh, S.-M.; Lee, G.-H.; Wang, Y.; Luh, T.-Y. *J. Org. Chem.* **1997**, *62*, 8315.

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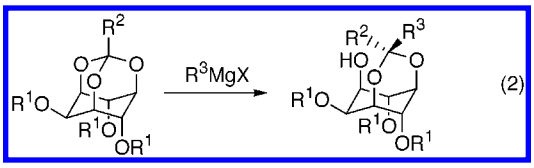
(s) have been executed (eq 2).[10] The Grignard reagent can vary among primary, secondary, and arylmagnesium halides. It is believed that chelation has played a key role in directing the regioselectivity of this ring opening reaction. Accordingly, a possible chelation intermediate

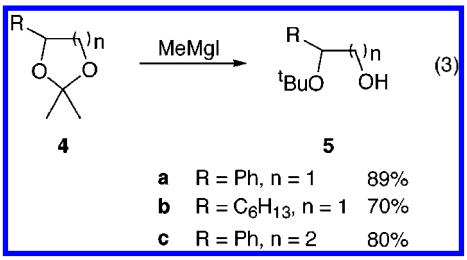


2 has been postulated to rationalize the selectivity of this reaction. We felt that this reaction could be extended to the selective protection/deprotection of various polyhydroxy-compounds having only *one or two* free hydroxyl group. Described herein is a full account which demonstrates a useful regioselective ring-opening reaction of acetals with Grignard reagents.[11]

Results and Discussion

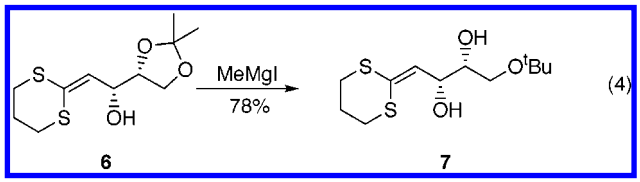
Prototype. On the basis of the chelation strategy depicted above (eq 1), acetonides can be cleaved regioselectively with Grignard reagents when a neighboring heteroatom is present.[11] Accordingly, selective cleavage of one of the two C−O bonds in the acetal-protected monosaccharides will offer a powerful arsenal for the selective synthesis of various monosaccharide derivatives having only one free hydroxy group at the specific position.

In the beginning of this investigation, we compared the selectivity of the ring opening reactions of unchelated acetonides to those of chelated ones. Thus, acetals **4** were treated with 4 equiv of MeMgI in refluxing benzene-ether (5:1) for 20 h. After the usual workup procedure, the corresponding hydroxyalkyl ethers **5** were obtained in good yields (eq 3).[4] Both five- and six-membered aceto-

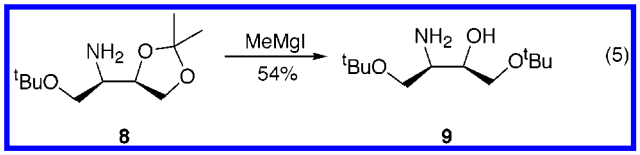


nides behaved similarly and the C−O bond of the less-hindered site in **4** was cleaved regioselectively. Presumably, the oxygen atom on this site would coordinate to magnesium preferentially, resulting in the regioselective protection of the more-hindered hydroxy group of the diol.

The presence of a neighboring oxygen or nitrogen moiety changed the selectivity of the ring-opening reaction. For example, the reaction of **6** with MeMgI afforded the corresponding diol **7** in 78% yield (eq 4). The neighboring amino group behaved similarly (eq 5). As

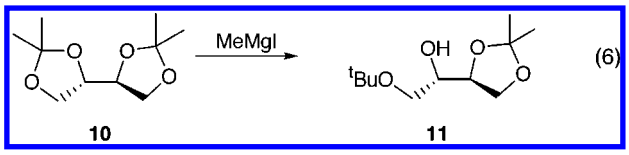


depicted in eq 1, the hydroxy group in **6** or the amino group in **8** apparently plays a pivotal role in determining

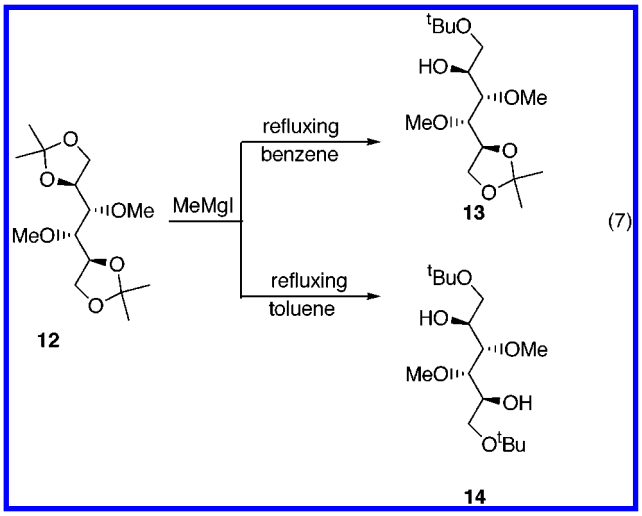


the regioselectivity of the ring opening reaction. The stereochemistry in **9** was unambiguously proved by X-ray diffraction (Figure 1, Supporting Information).

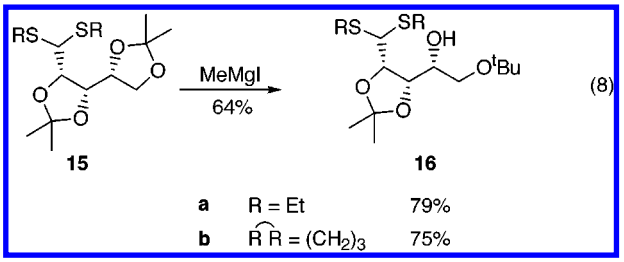
When bis-acetonide **10** was treated with MeMgI in benzene at 60 °C, mono-hydroxy compound **11** was obtained in 48% yield (eq 6). Mannitol derivative **12** was



transformed into the corresponding mono-hydroxy product **13** in refluxing benzene (eq 7). When more drastic conditions were employed, diol **14** was isolated in good yield (eq 7). When an unsymmetrical bis-acetonide **15**



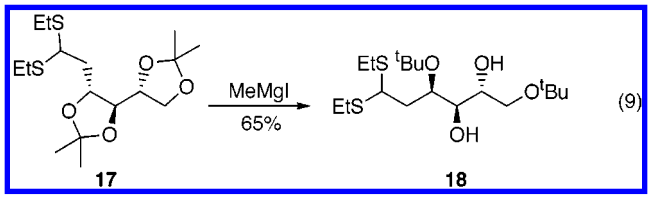
was employed, the less hindered heterocycle underwent alkylative ring opening (eq 8). This protocol serves as a powerful arsenal for the synthesis of various carbohydrate derivatives having selectively one free hydroxy group at the specific position.

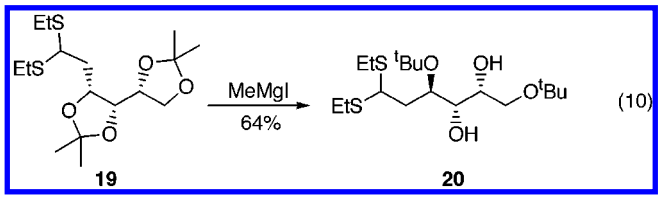


Stereochemistry of the Auxiliary. As can be seen from eqs 4−7, the stereochemistry of the carbon center where auxiliary group is attached can be either syn or anti to the acetal oxygen moiety where cleavage of the C−O bond occurs. In a similar manner, stereoisomers **17**

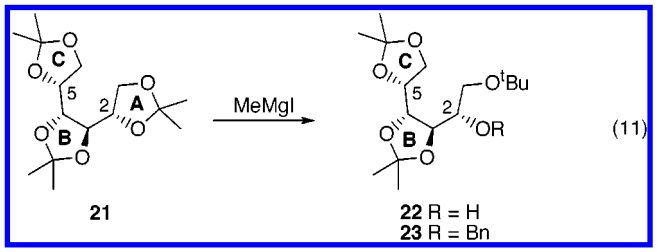
(11) For preliminary communications, see: Cheng, W.-L.; Yeh, S.-M.; Luh, T.-Y. *J. Org. Chem.* **1993**, *58*, 5576. Chen, Y.-H.; Luh, T.-Y.; Lee, G.-H.; Peng, S.-M. *J. Chem. Soc., Chem. Commun.* **1994**, 2369.

and **19** were transformed into respective diols **18** and **20** smoothly upon treatment with MeMgI (eqs 9 and 10).

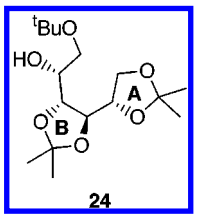




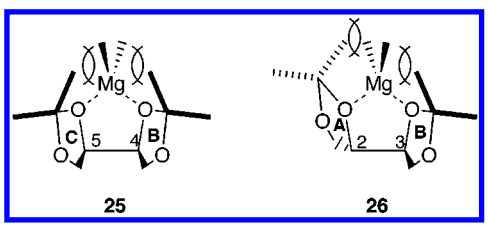
However, difference in the reactivity has been found in the reaction of tris-acetonide of sorbitol **21** with MeMgI (eq 11). The structure of product **22** was determined by X-ray crystallography of the corresponding benzyl ether **23** (Figure 2, Supporting Information). 5-Hydroxy derivative **24** was not detected.



The regioselectivity of the reaction of **21** can be rationalized by considering the relative stability of the chelation intermediates **25** and **26**.[12] In **25**, the magnesium chelates with the oxygen atoms at C_4 and C_5 which will lead to the formation of **24**. The relative configuration

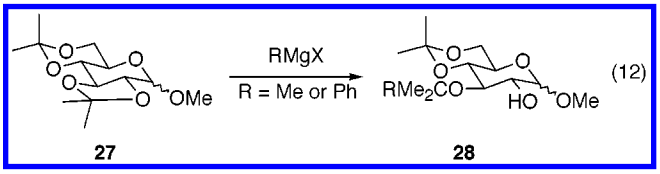


at C_4 and C_5 can be considered as meso form of a threitol derivative. As can be seen from **25**, severe steric interaction might be expected between the two endo-methyl groups and the endo-ligand on magnesium. Intermediate **26** on alkylative ring opening will furnish **22**. Since only



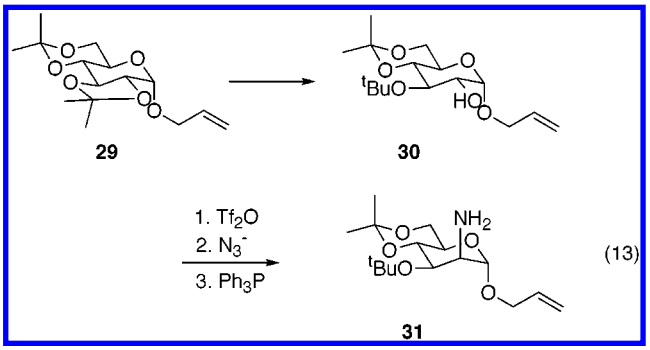
one of the endo-methyl groups will interact with one of the ligands on magnesium in **26**, the steric repulsion might be expected to be less than that in **25**. Accordingly, chelation intermediate **26** may be formed preferentially and determine the selectivity.

Monosaccharide Derivatives Having One Free Hydroxy Group. In our preliminary communication, we disclosed the usefulness of the chelation-controlled selective alkylative ring-opening of acetonides of methyl glucosides **27** (eq 12).[11] The reaction provides a useful entry toward a glucoside derivative **28** having a free hydroxy group at C_2. The chelation of the anomeric

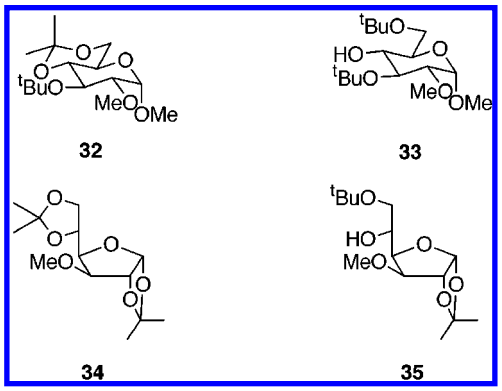


methoxy group and the neighboring oxygen function at C_2 in **27** with magnesium may explain the results. It is noteworthy that the anomeric methoxy group can be either α or *β*. Furthermore, the trans-fused five-membered acetonide moiety in **27** apparently is more reactive because the steric strain will be released upon alkylative ring-opening reaction.

The extension of this reaction to allyl glucoside **29** also afforded the corresponding mono-hydroxy derivative **30**. Further transformations[13] led to a convenient synthesis of fully protected mannosamine **31** (eq 13).



Upon treatment with with MeMgI, glucosides **32** and **34** afforded **33** and **35** in 58% and 55% yield, respectively.

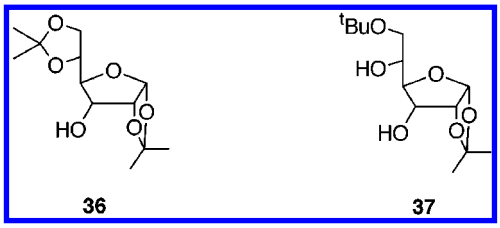


The presence of a *β*-methoxy group at C_3 in **34** seems to be irrelevant for the selectivity of this ring-opening process because the reaction of allose derivative **36**, a C_3 epimer of **34**, also afforded 54% yield of the corresponding 5-OH product **37**. These results suggested that chelation

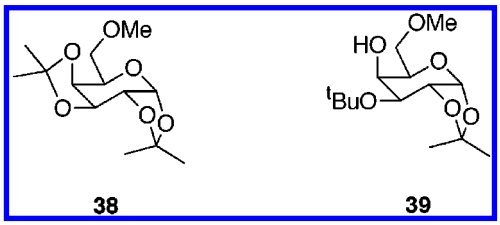
(12) Alternatively, the formation of complexes **25** and **26** may be fast and reversible and the Curtin-Hammett principle may apply for the rationalization of the selectivity.

(13) Knouzi, N.; Vaultier, M.; Carrié, R. *Bull. Soc. Chim. Fr.* **1985**, *5*, 815.

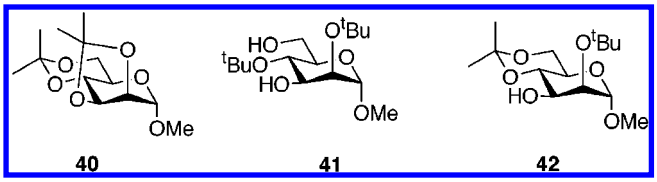
with the oxygen atom on the five-membered furanose heterocycle may play a pivotal role in these reactions.



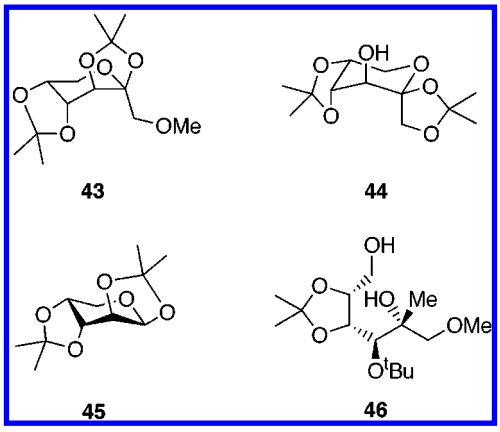
Galactose derivative **38** was converted into the 4-hydroxy derivative **39** in 52% yield. Presumably, chelation with the methoxy group at C_6 controls the regioselectivity. The conformational rigidity may prohibit chelate formation with oxygen atoms attached at C_2 and C_3 in **38**.



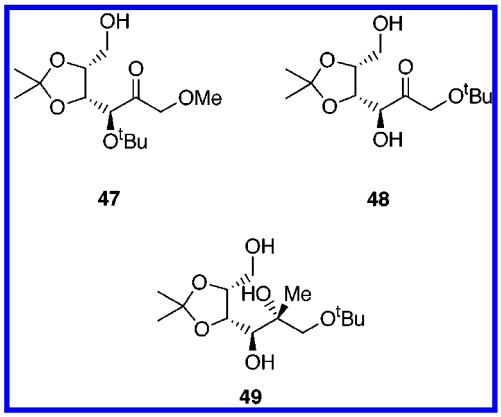
Treatment of mannose derivative **40** with MeMgI in refluxing benzene for 24 h afforded **41** in 51% yield. Intermediate **42** was isolated when the same reaction was carried out for 3 h.



Reactions at the Anomeric Center. Stereoselective displacement of one of the carbon−oxygen bonds by a carbon−carbon bond at the anomeric center paves the way for the synthesis of C-glycosides. The use of acetal protective group for the anomeric hydroxy group abounds. Accordingly, regioselective ring opening of the acetal group at the anomeric carbon will generate a hemiacetal which can further react with the nucleophile leading to an alcohol stereoselectively. This idea was executed with fructopyranose and arabinopyranose derivatives **43**−**45**.

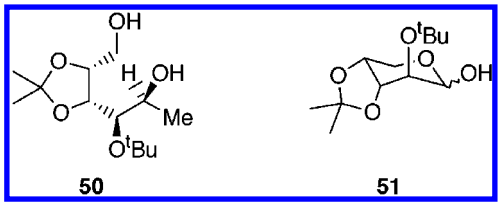


By considering the structure of fructopyranose **43** the methoxy group at C_1 would assist the cleavage to occur at C_2. Thus, treatment of **43** with MeMgI under usual conditions gave **46** selectively in 75% yield. Presumably, the reaction produces intermediate **47** which will further react with MeMgI stereoselectively to yield **46**. In a



similar manner, the hydroxy group at C_3 in **44** can also aid the regioselective ring opening of the acetonide at C_2. Accordingly, the reaction of **44** with MeMgI in refluxing benzene afforded alcohol **49** in 55% yield. Intermediate **48** may be involved and further transformed into **49** by excess MeMgI. The stereoselectivities in both reactions can readily be rationalized by means of chelation with the neighboring oxygen function.

Arabinose derivative **45** does not have a neighboring oxygen atom for chelate formation with magnesium. In addition, both acetonide rings are cis fused with the perhydropyran ring. In a manner similar to that described in eq 4, the least-hindered C−O bond in **45** was cleaved selectively and the hemiacetal **51** thus generated reacted with an additional mole of the Grignard reagent to yield **50** stereoselectively.



Conclusions

In summary, we have demonstrated a useful simple procedure using the Grignard reagent to partially deprotect acetonides of vicinal diols leading to the corresponding *tert*-butyl hydroxyalkyl ethers regioselectively. Chelation has played a pivotal role to direct the regioselectivity of this ring opening process. The reaction offers a powerful arsenal in selective protection−deprotection of hydroxy groups in carbohydrates leading to various monosaccharide derivatives having only one free hydroxy group at the specific position.

Experimental Section

General Procedure for Reactions of Acetonides with Grignard Reagent. To a solution of acetonide in benzene under N_2 was added, in one portion, the Grignard reagent (4 equiv). The mixture was stirred at 60 °C or heated under reflux, and the reaction was monitored by TLC. The cooled mixture was poured into water, and the organic layer was separated. The aqueous solution was extracted with Et_2O, and the organic layers were washed with 10% aqueous NaOH, water, and brine and dried ($MgSO_4$). The solvent was evapo-

rated in vacuo, and the residue was chromatographed on silica gel to afford the product.

2-*tert*-Butoxy-2-phenylethanol (5a). In a manner similar to that described in the general procedure, a benzene solution of **4a** (310 mg, 1.2 mmol) with MeMgI (2.4 mL, 2.0 M in Et_2O, 4.8 mmol) was refluxed for 20 h to give **5a**[14] (300 mg, 89%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.14 (s, 9 H), 2.26 (dd, J = 3.8, 9.4 Hz, 1 H), 3.45−3.52 (m, 2H), 4.60 (dd, J = 4.5, 8.2 Hz, 1 H), 7.21−7.45 (m, 5 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 28.8, 67.8, 74.9, 75.4, 126.3, 127.3, 128.2, 142.2.

2-*tert*-Butoxyoctan-1-ol (5b). In a manner similar to that described in the general procedure, the reaction of **4b** (438 mg, 2.4 mmol) with MeMgI (4.8 mL, 2.0 M in Et_2O, 9.6 mmol) in refluxing benzene for 20 h afforded **5b**[15] (343 mg, 70%): bp 80 °C (1 mmHg); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.84 (t, J = 6.8 Hz, 3 H), 1.18 (s, 9 H), 1.31−1.46 (m, 10 H), 2.07 (br s, 1 H), 3.36−3.40 (m, 1 H), 3.48−3.56 (m, 2 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.0, 22.6, 25.5, 28.7, 29.5, 31.8, 33.6, 65.2, 71.6, 73.9; HRMS calcd for $C_{12}H_{27}O_2$ (M + 1) 203.2011, found 203.2021.

3-*tert*-Butoxy-3-phenylpropan-1-ol (5c). In a manner similar to that described in the general procedure, a mixture of **4c** (93 mg, 0.5 mmol) and MeMgI (1.0 mL, 2.0 M in Et_2O, 2.0 mmol) was converted to **5c** (84 mg, 80%): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.14 (s, 9H), 1.90 (br q, J = 6.0 Hz, 2 H), 3.05 (br t, J = 6.0 Hz, 1 H), 3.70 (br q, J = 6.0 Hz, 2 H), 4.77 (br t, J = 6.0 Hz, 1 H), 7.21−7.34 (m, 5H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 28.6, 41.5, 60.9, 74.4, 75.1, 125.9, 126.8, 128.2, 145.4; HRMS calcd for $C_{13}H_{20}O_2$ 208.1463, found 208.1468.

2-Deoxy-*O*^{5}-*tert*-butyl-D-*threo*-pent-1-enose Trimethylene Dithioacetal (7). In a manner similar to that described in the general procedure, **6** (134 mg, 0.51 mmol) in benzene (20 mL) was allowed to react with MeMgI (2.0 mL, 2.0 mmol) under refluxing conditions for 28 h to afford **7** (112 mg, 78%): $[\alpha]_D^{32}$ +7.7° (*c* 0.03, $CHCl_3$); IR (neat) ν 3443 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.17 (s, 9 H), 2.09−2.16 (m, 2 H), 2.77−2.95 (m, 5 H), 3.04 (d, J = 3.2 Hz, 1 H), 3.36 (dd, J = 3.5, 9.2 Hz, 1 H), 3.44 (dd, J = 3.5, 9.2 Hz, 1 H), 3.52−3.54 (m, 1 H), 4.59−4.64 (m, 1 H), 5.91 (d, J = 8.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.5, 27.4, 29.1, 29.4, 63.4, 70.0, 72.9, 73.6, 129.7, 132.7; HRMS calcd for $C_{12}H_{22}O_3S_2$ 278.1010, found 278.1017.

***O*^{1}-*tert*-Butyl-*O*^{3},*O*^{4}-isopropylidene-L-threitol (11).** A solution of **10** (4.0 g, 19.8 mmol) and MeMgI (2 M solution in ether, 4 equiv) in dry benzene (80 mL) was stirred at room temperature for 5 days. Saturated NH_4Cl (50 mL) was introduced, and the mixture was extracted with ether (3 × 100 mL). The organic layer was washed with brine and dried ($MgSO_4$), and the solvent was removed in vacuo. The residue obtained was chromatographed on silica gel (hexane/EtOAc = 9/1) to afford **11** (2.1 g, 48%) as a colorless liquid: $[\alpha]_D^{26}$ +4.9° (*c* 2.9, $CHCl_3$); IR (neat) ν 3450 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.11 (s, 9 H), 1.29 (s, 3 H), 1.35 (s, 3 H), 2.53 (br s, 1 H), 3.32 (dd, J = 6.0, 8.9 Hz, 1 H), 3.38 (dd, J = 6.0, 8.9 Hz, 1 H), 3.63 (q, J = 6.0 Hz, 1 H), 3.78−3.83 (dd, J = 6.0, 8.1 Hz, 1 H), 3.97−4.01 (dd, J = 6.0, 8.1 Hz, 1 H), 4.11 (q, J = 6.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.2, 26.2, 27.3, 62.8, 65.8, 71.2, 73.1, 76.9, 108.9; HRMS calcd for $C_{10}H_{19}O_4$ (M − CH_3) 203.1283, found 203.1288.

2(*R*)-Amino-1-*tert*-butoxy-*O*^{3},*O*^{4}-isopropylidene-3(*S*),4-butanediol (8). To an ice-cooled solution of **11** (1.84 g, 8.43 mmol) and Et_3N (1.71 g, 16.9 mmol) in CH_2Cl_2 (30 mL) was added a solution of MsCl (1.45 g, 12.6 mmol) in CH_2Cl_2 (30 mL) dropwise over a period of 30 min. After the addition was over, the reaction mixture was warmed to room temperature and stirred for 24 h, and the reaction was then quenched with HCl (10%). CH_2Cl_2 (50 mL) was introduced, and the organic layer was washed with NaOH (10%), water, and brine and dried ($MgSO_4$), and the solvent was evaporated in vacuo. The residue was chromatographed on silica gel (hexane/EtOAc 9/1) to yield the corresponding mesylate as a colorless liquid (2.3 g, 92%): $[\alpha]_D^{26}$ −6.0° (*c* 2.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.16 (s, 9 H), 1.33 (s, 3 H), 1.41 (s, 3 H), 3.10 (s, 3 H), 3.53 (dd, J = 4.8, 10.5 Hz, 1 H), 3.61 (dd, J = 6.6, 10.5 Hz, 1 H), 3.89 (dd, J = 6.6, 9.0 Hz, 1 H), 4.05 (dd, J = 6.6, 9.0 Hz, 1 H), 4.25 (q, J = 6.6 Hz, 1 H), 4.61 (dt, J = 4.8, 6.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.3, 26.1, 27.3, 38.6, 61.5, 65.5, 73.8, 75.2, 82.0, 109.6; HRMS calcd for $C_{11}H_{21}O_6S$ (M − CH_3) 281.1058, found 281.1046.

A solution of the mesylate (2.3 g, 7.76 mmol) and sodium azide (1.0 g, 15.4 mmol) in dry DMF (60 mL) was stirred at 130 °C for 24 h, cooled to room temperature, diluted with water (300 mL), and extracted with ether (3 × 200 mL). The organic layer was washed with brine and dried ($MgSO_4$), and the solvent was evaporated in vacuo to give crude azide as a colorless liquid (1.23 g, 65%): IR (neat) ν 2097 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.13 (s, 9 H), 1.31 (s, 3 H), 1.40 (s, 3 H), 3.40−3.46 (m, 1 H), 3.53−3.63 (m, 2 H), 3.83−3.92 (m, 1 H), 3.97−4.06 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.2, 26.4, 27.3, 62.3, 63.2, 66.6, 73.6, 75.1, 109.5; HRMS calcd for $C_{10}H_{18}O_3N_3$ (M − CH_3) 228.1348, found 228.1340.

A suspension of the azide (2.0 g, 8.2 mmol) in absolute EtOH (70 mL) and Pd/C (10%, 200 mg) was stirred under an atmosphere of H_2 for 8 h. The reaction mixture was filtered over Celite and washed with EtOH. The solvent was removed in vacuo, and the residue was chromatographed on silica gel (2% MeOH in $CHCl_3$) to afford **8** as a colorless liquid (1.41 g, 79%): $[\alpha]_D^{26}$ −4.2° (*c* 5.0, $CHCl_3$); IR (neat) v 3376, 3310 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.14 (s, 9 H), 1.31 (s, 3 H), 1.37 (s, 3 H), 1.62 (s, 2 H), 2.96−3.02 (m, 1 H), 3.23 (dd, J = 6.6, 9.0 Hz, 1 H), 3.46 (dd, J = 6.6, 9.0 Hz, 1 H), 3.80−3.87 (m, 1 H), 3.95−4.02 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.3, 26.6, 27.5, 53.3, 63.4, 66.1, 72.8, 77.5, 108.6; HRMS calcd for $C_{11}H_{24}O_3N$ (M^+ + 1) 218.1756, found 218.1727.

1,4-Bis-*tert*-butoxy-3(*R*)-amino-2(*S*)-butanol (9). To a solution of MeMgI in ether (1.8 mL, 2.0 M solution in ether) was added **8** (100 mg, 0.46 mmol) under N_2 atmosphere. The ether was removed under reduced pressure. To this was added dry benzene (5.0 mL), the resulting reaction mixture was stirred at 60 °C for 48 h and cooled to room temperature, and MeOH was added to quench the excess Grignard reagent. The solvent was removed in vacuo, and the residue was chromatographed on silica gel (3% MeOH in $CHCl_3$) to afford **9** as a white solid (58 mg, 54%). Further crystallized from hexane to yield colorless needles: mp 81−82 °C; $[\alpha]_D^{25}$ +3.7° (*c* 1.5, $CHCl_3$); IR (KBr) ν 3357, 3284, 3158 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.13 (s, 18 H), 2.48 (s, 3 H), 2.93−2.99 (m, 1 H), 3.31−3.48 (m, 4 H), 3.59 (q, J = 6.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.4, 53.2, 63.2, 63.7, 72.6, 73.0; HRMS calcd for $C_{12}H_{28}O_3N$ (M^+ + 1) 234.2069, found 234.2055. Anal. Calcd for $C_{12}H_{27}O_3N$: C, 61.77; H, 11.66; N, 6.0. Found C, 61.28, H, 11.21, N, 5.38.

***O*^{1}-*tert*-Butyl-*O*^{3},*O*^{4}-dimethyl-*O*^{5},*O*^{6}-isopropylidene-D-mannitol (13).** Under N_2 atmosphere, to a benzene solution (40 mL) of **12**[16] (0.87 g, 3.0 mmol) was added MeMgI (6 mL, 2M in ether, 12 mmol). The mixture was refluxed for 22 h. Saturated NH_4Cl (40 mL) was added, and the mixture was extracted with ether (40 mL × 3). The organic layer was washed with NaOH (10%, 40 mL) and brine and then dried ($MgSO_4$). The solvent was evaporated in vacuo, and the residue was chromatographed on silica gel (hexane/EtOAc 4/1) to give **13** as a colorless liquid (0.75 g, 82%): $[\alpha]_D^{27}$ +12.5° (*c* 0.05, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18 (s, 9 H), 1.32 (s, 3 H), 1.38 (s, 3 H), 2.64 (d, J = 6.4 Hz, 1 H), 3.28 (dd, J = 1.8, 8.4 Hz, 1 H), 3.41 (s, 3H), 3.45 (dd, J = 5.2, 8.9 Hz, 1 H), 3.50 (s, 3 H), 3.55 (dd, J = 3.6, 8.9 Hz, 1 H), 3.61 (dd, J = 1.8, 6.3 Hz, 1 H), 3.73−3.82 (m, 1H), 3.94 (dd, J = 6.3, 8.0 Hz, 1 H), 4.06 (dd, J = 6.3, 8.0 Hz, 1 H), 4.15 (q, J = 6.3 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.5, 26.6, 27.5, 60.1, 60.9, 62.1, 66.7, 69.3, 73.2, 75.9, 80.7, 80.8, 108.4. Anal. Calcd for $C_{15}H_{30}O_6$: C, 58.80; H, 9.87. Found C, 58.65; H, 9.87.

***O*^{1},*O*^{6}-Bis-*tert*-butyl-*O*^{3},*O*^{4}-dimethyl-D-mannitol (14).** Under N_2 atmosphere, to a solution of MeMgI (30 mL, 1.7 M in

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toluene, 51 mmol) was added **12** (1.49 g in 10 mL toluene, 5.13 mmol). The mixture was refluxed for 72 h and worked up in a similar manner as described above to give **14** as a colorless liquid (1.25 g, 76%): $[\alpha]_D^{28}$ +10.1° (c 0.07, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.19 (s, 18 H), 2.67 (d, J = 6.4 Hz, 2 H), 3.46−3.53 (m, 10 H, embodied a singlet at δ 3.47 (6 H)), 3.58 (dd, J = 3.6, 8.8 Hz, 2 H), 3.76−3.84 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.5, 60.1, 62.2, 69.4, 73.1, 80.1; HRMS calcd for $C_{16}H_{35}O_6$ (M + 1) 323.2433, found 323.2437.

***O*²,*O*³-Isopropylidene-*O*⁵-*tert*-butyl-D-xylose Diethyl Dithioacetal (16a).** Following the general procedure, **15a** (171 mg, 0.51 mmol) in benzene (20 mL) was allowed to react with MeMgI (2.0 mL, 2.0 mmol) under 60 °C for 14 h to afford **16a** (142 mg, 79%) $[\alpha]_D^{32}$ −46.5° (*c* 0.05, $CHCl_3$); IR (neat) ν 3479 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.12 (s, 9 H), 1.16−1.21 (two overlapping triplets, 6 H), 1.35 (s, 3 H), 1.38 (s, 3 H), 2.38 (d, J = 6.2 Hz, 1 H), 2.59−2.71 (m, 4 H), 3.33−3.42 (m, 2 H), 3.76−3.79 (m, 1 H), 3.84 (d, J = 5.4 Hz, 1 H), 4.08 (dd, J = 2.7, 7.6 Hz, 1 H), 4.33 (dd, J = 5.4, 7.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.3, 14.4, 25.0, 25.4, 27.1, 27.2, 27.5, 53.0, 63.7, 70.0, 73.4, 79.6, 79.7, 109.8; HRMS calcd for $C_{16}H_{32}O_4S_2$ 352.1742, found 352.1750.

***O*²,*O*³-Isopropylidene-*O*⁵-*tert*-butyl-D-xylose Trimethylene Dithioacetal (16b).** In a manner similar to that described in the general procedure, **15b** (164 mg, 0.51 mmol) in benzene (20 mL) was allowed to react with MeMgI (2.0 mL, 2.0 mmol) under 60 °C for 18 h to afford **16b** (128 mg, 75%): $[\alpha]_D^{32}$ −13.9° (*c* 0.05, $CHCl_3$); IR (neat) ν 3479 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.18 (s, 9 H), 1.41 (s, 3 H), 1.43 (s, 3 H), 1.97−2.04 (m, 2 H), 2.35 (d, J = 6.0 Hz, 1 H), 2.72−2.80 (m, 2 H), 2.90−2.98 (m, 2 H), 3.38−3.47 (m, 2 H), 3.80−3.83 (m, 1 H), 4.04 (d, J = 5.4 Hz, 1 H), 4.09 (dd, J = 2.7, 7.5 Hz, 1 H), 4.41 (dd, J = 5.4, 7.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.7, 27.0, 27.1, 27.5, 28.7, 29.0, 47.7, 63.7, 70.0, 73.4, 78.8, 79.3, 110.0; HRMS calcd for $C_{15}H_{28}O_4S_2$ 336.1429, found 336.1417.

2-Deoxy-*O*³,*O*⁶-bis-*tert*-butyl-D-*arabino*-hexose Diethyl Dithioacetal (18). In a manner similar to that described in the general procedure, **17** (178 mg, 0.51 mmol) in benzene (20 mL) was allowed to react with MeMgI (2.0 mL, 2.0 mmol) under refluxing conditions for 34 h to give **18** (127 mg, 65%): $[\alpha]_D^{32}$ −17.1° (*c* 0.05, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.20 (s, 9 H), 1.25 (s, 9 H), 1.21−1.32 (two overlapping triplets, 6 H), 1.93 (dt, J = 7.2, 14.4 Hz, 1 H), 2.27 (ddd, J = 6.2, 7.2, 14.4 Hz, 1 H), 2.52−2.74 (m, 4 H), 3.34 (d, J = 5.0 Hz, 1 H), 3.48−3.58 (m, 3 H), 3.62−3.68 (m, 2 H), 3.88 (t, J = 7.2 Hz, 1 H), 4.17 (dt, J = 2.5, 6.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.3, 14.4, 23.4, 24.4, 27.4, 28.7, 38.2, 47.7, 65.2, 69.7, 69.9, 73.7, 73.8, 75.2; HRMS calcd for $C_{18}H_{38}O_4S_2$ 382.2212, found 382.2212.

2-Deoxy-*O*³,*O*⁶-di-*tert*-butyl-D-*lyxo*-hexose Diethyl Dithioacetal (20). In a manner similar to that described in the general procedure, **19** (179 mg, 0.51 mmol) in benzene (20 mL) was allowed to react with MeMgI (2.0 mL, 2.0 mmol) under refluxing conditions for 18 h to give **20** (124 mg, 64%): $[\alpha]_D^{32}$ −21.3° (*c* 0.02, $CHCl_3$); IR (neat) ν 3447 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.16 (s, 9 H), 1.18−1.22 (two overlapping triplets, 6 H), 1.23 (s, 9 H), 1.93−2.11 (m, 2 H), 2.51−2.73 (m, 4 H), 2.96 (d, J = 5.5 Hz, 1 H), 3.22 (d, J = 3.6 Hz, 1 H), 3.43 (dd, J = 4.8, 9.1 Hz, 1 H), 3.50 (dd, J = 4.8, 9.1 Hz, 1 H), 3.67−3.70 (m, 1 H), 3.83−3.91 (m, 2 H), 3.95−4.02 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.4, 24.0, 24.4, 27.4, 28.9, 39.8, 47.5, 63.7, 69.3, 72.2, 72.5, 73.4, 75.0; HRMS calcd for $C_{18}H_{38}O_4S_2$ 382.2212, found 382.2209.

***O*³,*O*⁴;*O*⁵,*O*⁶-Bis-isopropylidene-*O*¹-*tert*-butyl-D-sorbitol (22).** A benzene solution (25 mL) of **21**[17] (0.15 g, 0.48 mmol) was treated with MeMgI (2.0 mL, 2.0 mmol) under reflux for 5 h. After cooling, the mixture was diluted with ether and quenched with saturated NH_4Cl. The organic layer was washed with brine and dried ($MgSO_4$). The solvent was removed in vacuo and the residue was chromatographed on silica gel (hexane/EtOAc 4/1) to give **22** (0.13 g, 86%): $[\alpha]_D^{23}$ +7.0° (*c* 14.8, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.18 (s, 9 H), 1.31 (s, 3 H), 1.35 (s, 3 H), 1.39 (s, 6 H), 2.14 (s, 1 H), 3.43 (d, J = 6.1 Hz, 2 H), 3.80 (dt, J = 2.6, 6.1 Hz, 1 H), 3.91−3.97 (m, 2 H), 3.99−4.05 (m, 2 H), 4.08−4.11 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.3, 26.6, 26.9, 27.2, 27.5, 63.7, 67.7, 69.7, 73.3, 77.1, 77.2, 80.3, 109.4, 109.7; HRMS calcd for $C_{16}H_{31}O_6$ (M^+ + 1) 319.2120, found 319.2128.

***O*³,*O*⁴;*O*⁵,*O*⁶-Bis-isopropylidene-*O*²-benzyl-*O*¹-*tert*-butyl-D-sorbitol (23).** A THF solution (15 mL) of **22** (0.23 g, 0.72 mmol) was treated with NaH (0.07 g, 2.92 mmol) at room temperature for 15 min followed by benzyl bromide (0.11 mL, 0.86 mmol). The mixture was stirred for 16 h, and saturated $NaHCO_3$ (15 mL) was introduced. The organic layer was washed with brine and dried ($MgSO_4$). The solvent was removed in vacuo, and the residue was chromatographed on silica gel (hexane/EtOAc 20/1) to give **23** (0.24 g, 82%): $[\alpha]_D^{24}$ +26.9 (*c* 12, $CHCl_3$), mp 65−67 °C; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.18 (s, 9 H), 1.32 (s, 3 H), 1.35 (s, 6 H), 1.38 (s, 3 H), 3.55−3.69 (m, 3 H), 3.82−3.86 (m, 1 H), 4.02−4.10 (m, 4 H), 4.60, 4.83 (AB q, J = 11.7 Hz, 2 H), 7.21−7.36 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.3, 26.6, 26.8, 27.1, 27.5, 63.1, 67.6, 73.2, 73.4, 77.2, 80.5, 109.3, 109.5, 127.4, 127.6, 128.2, 128.4; HRMS calcd for $C_{23}H_{36}O_6$ 408.2512, found 408.2522.

Allyl *O*²,*O*³;*O*⁴,*O*⁶-Bis-isopropylidene-α-D-glucopyranoside (29). To a solution of allyl α-D-glucopyranoside[18] (3.02 g, 13.7 mmol) in dry acetone (100 mL) was added TsOH (0.03 g, 0.16 mmol) and 2-methoxypropene (8 mL, 55 mmol), and the reaction was stirred for 2 h at 20 °C and quenched with Et_3N (5 mL). The solvent was removed in vacuo, and the residue was chromatographed on silica gel (EtOAc/hexane 1/9) to afford **29** (3.15 g, 76.6%) as a colorless oil: $[\alpha]_D^{27}$ +86.6° (*c* 0.05, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz) δ 1.38 (s, 3 H), 1.39 (s, 3 H), 1.42 (s, 3 H), 1.49 (s, 3 H), 3.45−3.59 (m, 2 H), 3.71−3.88 (m, 3 H), 3.97−4.23 (m, 3 H), 5.11−5.18 (m, 2 H), 5.27 (d, J = 17.2 Hz, 1 H), 5.89 (ddt, J = 5.3, 10.9, 17.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 19.0, 26.3, 26.7, 28.9, 62.2, 65.0, 68.7, 73.7, 73.9, 76.7, 96.9, 99.5, 111.3, 117.4, 133.4. Anal. Calcd for $C_{15}H_{24}O_6$: C, 59.98; H, 8.05. Found C, 59.94; H, 8.12.

Allyl *O*³-*tert*-butyl-*O*⁴,*O*⁶-isopropylidene-α-D-glucopyranoside (30). The ethereal solution of MeMgI (2.4 mL, 2 M ether, 6.1 mmol) was evacuated to remove ether, and the residue was dissolved in benzene (175 mL). A solution of **29** (0.92 g, 3.06 mmol) in benzene (25 mL) was then added, the mixture was stirred at 50−60 °C for 1.5 h, and the reaction was quenched with NH_4Cl solution (50 mL). Organic layer was separated, and the aqueous solution was extracted with ether (200 mL). The combined organic layers were washed successively with water and brine and dried ($MgSO_4$). Solvent was removed in vacuo to yield the residue which was chromatographed on silica gel (EtOAc/hexane 1/4) to afford **30** (0.83 g, 86%) as a colorless oil: $[\alpha]_D^{27}$ +110.8° (*c* 0.05, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz) δ 1.21 (s, 9 H), 1.37 (s, 3 H), 1.44 (s, 3 H), 2.06 (d, J = 7.9 Hz, 1 H), 3.30−3.55 (m, 2 H), 3.55−3.88 (m, 4 H), 4.04 (dd, J = 6.4, 12.8 Hz, 1 H), 4.22 (dd, J = 5.4, 12.8 Hz, 1 H), 4.92 (d, J = 3.8 Hz, 1 H), 5.21 (dd, J = 1.5, 10.2 Hz, 1 H), 5.29 (dd, J = 1.5, 17.3 Hz, 1 H), 5.92 (ddt, J = 5.7, 10.2, 17.3 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 19.0, 29.0, 29.3, 62.5, 64.3, 68.5, 72.2, 72.4, 73.3, 74.5, 98.3, 99.1, 118.0, 133.6; HRMS calcd for $C_{16}H_{28}O_6$ 316.1886, found 316.1889.

Allyl 2-amino-2-deoxy-*O*⁴,*O*⁶-isopropylidene-*O*³-*tert*-butyl-α-D-mannopyranoside (31). Pyridine (1.5 mL, 19.0 mmol) was added at −10 °C to a solution of **30** (3.0 g, 9.5 mmol) in CH_2Cl_2 (60 mL). After brief stirring, Tf_2O (1.2 mL, 11.4 mmol) was slowly added over a period of 30 min, and the mixture was stirred for 2 h at 0 °C. Cold water (20 mL) was then introduced. The aqueous layer was extracted with ether (50 mL), and the combined organic layers were dried ($MgSO_4$). The solvent was removed in vacuo to yield the crude triflate (3.6 g, 8.8 mmol, 93%) which was dissolved in DMF (60 mL). NaN_3 (2.86 g, 44.0 mmol) was added, and the mixture was

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stirred at 80 °C for 18 h. Then water was introduced, and the mixture was extracted with ether (60 mL). The organic layer was successively washed with water and brine and dried ($MgSO_4$). The solvent was removed in vacuo to give the residue which was chromatographed on silica gel (EtOAc/hexane 1:4) to afford the corresponding azide (2.17 g, 72.3%) as a colorless oil: $[\alpha]_D$29 +72.4° (*c* 0.05, $CHCl_3$); IR (KBr) ν 2107 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.22 (s, 9 H), 1.36 (s, 3 H), 1.49 (s, 3 H), 3.50−4.05 (m, 7 H), 4.13 (ddt, J = 1.2, 5.3, 12.9 Hz, 1 H), 4.50 (d, J = 1.2 Hz, 1 H), 5.17−5.32 (m, 2 H), 5.88 (m, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 19.3, 28.4, 29.2, 62.2, 65.3, 65.4, 68.1, 69.3, 70.2, 75.0, 98.4, 99.7, 117.9, 133.4. Anal. Calcd for $C_{16}H_{27}N_3O_5$: C, 56.29; H, 7.97; N, 12.31. Found C, 56.34; H, 8.32; N, 12.14.

Triphenylphosphine[13] (2.52 g, 9.60 mmol) was added to a solution of the azide (3.27 g, 9.60 mmol) in THF (80 mL), and the mixture was stirred for 2 h. Water (0.25 mL) was then added, and the mixture was stirred at ambient temperature for an additional 12 h. Hexane (50 mL) was introduced, and the slurry was filtered. The filtrate was dried ($MgSO_4$), and the solvent was removed in vacuo to give the residue which was chromatographed on silica gel (EtOAc/hexane 1/2) to afford **31** (2.34 g, 78%) as a colorless oil: $[\alpha]_D^{29}$ +57.4° (*c* 0.05, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz) δ 1.17 (s, 9 H), 1.35 (s, 3 H), 1.46 (s, 3 H), 3.11 (br, 1 H), 3.60−3.85 (m, 7 H), 3.39 (ddt, J = 1.2, 6.1, 13.0 Hz, 1 H), 4.13 (ddt, J = 1.2, 5.2, 13.0 Hz, 1 H), 4.73 (br s, 1 H), 5.14−5.31 (m, 2 H), 5.89 (ddt, J = 5.5, 10.4, 17.3 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 19.2, 28.6, 29.2, 56.2, 62.5, 65.1, 67.9, 68.6, 69.8, 74.3, 99.5, 100.9, 117.3, 133.9. Anal. Calcd for $C_{16}H_{29}NO_5$: C, 60.93; H, 9.27; N, 4.44. Found C, 60.92; H, 8.99; N, 3.95.

Methyl *O*^{2}-Methyl-*cO*^{3},*O*^{6}-di-*tert*-butyl-α-D-glucopyranoside (33). In a manner similar to that described in the general procedure, a benzene solution of **32** (280 mg, 0.92 mmol) and MeMgI (4.0 mL, 2.0 M in Et_2O, 8.0 mmol) was refluxed for 48 h. After usual workup and chromatographic separation (SiO_2, hexane/EtOAc 3/1), **33** was obtained (170 mg, 58%): $[\alpha]_D^{29}$ +76.4° (*c* 0.01, $CHCl_3$); ^1H NMR ($CDCl_3$, 200 MHz) δ 1.24 (s, 18 H), 1.79 (br, 1 H), 3.02 (dd, J = 3.4, 9.4 Hz, 1 H), 3.26 (t, J = 9.0 Hz, 1 H), 3.37 (s, 3 H), 3.45 (s, 3 H), 3.57 (m, 1 H), 3.60−3.80 (m, 3 H), 4.80 (d, J = 3.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 29.2, 29.3, 54.8, 59.5, 62.4, 71.4, 72.6, 72.7, 75.3, 77.2, 82.1, 97.6; HRMS calcd for $C_{16}H_{32}O_6$ 320.2199, found 320.2192.

O^1,*O*^{2}-Isopropylidene-*O*^{3}-methyl-*O*^{6}-*tert*-butyl-α-D-glucofuranose (35). In a manner similar to that described in the general procedure, a benzene solution of **34** (274 mg, 1.0 mmol) was treated with MeMgI (3.0 mL, 2.0 M in Et_2O, 6.0 mmol) under reflux for 12 h followed by usual workup to give **35** (140 mg, 55%): $[\alpha]_D^{28}$ −29.9° (*c* 0.09, $CHCl_3$); IR (neat) ν 3507 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.16 (s, 9 H), 1.29 (s, 3 H), 1.45 (s, 3 H), 2.79 (d, J = 5.3 Hz, 1 H), 3.39 (m, 1 H), 3.43 (s, 3 H), 3.58 (dd, J = 3.2, 8.0 Hz, 1 H), 3.84 (d, J = 2.9 Hz, 1 H), 3.96 (m, 1 H), 4.05 (dd, J = 2.9, 8.0 Hz, 1 H), 4.53 (d, J = 3.7 Hz, 1 H), 5.85 (d, J = 3.7 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.1, 26.6, 27.4, 57.95, 63.3, 67.8, 73.2, 79.7, 81.6, 84.0, 104.9, 111.5. Anal. Calcd for $C_{14}H_{26}O_6$: C, 57.91; H, 9.03. Found: C, 57.79; H, 9.13.

***O*^{1},*O*^{2}-Isopropylidene-*O*^{6}-*tert*-butyl-α-D-allofuranose (37).** In a manner similar to that described in the general procedure, a benzene solution of **36**[19] (260 mg, 1.0 mmol) was treated with MeMgI (2.0 mL, 2.0 M in Et_2O, 4.0 mmol) under reflux for 20 h followed by usual workup to give **37**[20] (150 mg, 54%): $[\alpha]_D^{32}$ +23.1° (*c* 0.04, $CHCl_3$); mp 59−61 °C; IR (KBr) ν 3491, 3364 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.20 (s, 9 H), 1.34 (s, 3 H), 1.56 (s, 3 H), 2.40 (d, J = 4.2 Hz, 1 H), 3.48 (dd, J = 4.8, 9.0 Hz, 1 H), 3.64 (dd, J = 3.4, 6.0 Hz, 1 H), 3.73 (d, J = 4.7 Hz, 1 H), 3.89 (dd, J = 3.8, 9.0 Hz, 1 H), 3.98 (m, 1 H), 4.08 (m, 1 H), 4.64 (t, J = 4.2 Hz, 1 H), 5.75 (d, J = 3.7 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.4, 26.7, 27.3, 62.7, 70.1, 70.9, 74.3, 79.6, 80.9, 103.8, 112.9. Anal. Calcd for $C_{13}H_{24}O_6$: C, 56.49; H, 8.75. Found: C, 56.00; H, 8.80.

***O*^{3}-*tert*-Butyl-*O*^{6}-methyl-*O*^{1},*O*^{2}-isopropylidene-α-D-galactopyranose (39).** In a manner similar to that described in the general procedure, a toluene solution of **38**[21] (274 mg, 1.0 mmol) was treated with MeMgI (2.0 mL, 2.0 M in Et_2O, 4.0 mmol) at 60 °C for 40 h followed by usual workup to give **39** (150 mg, 52%): $[\alpha]_D^{28}$ +20.51° (*c* 0.4, $CHCl_3$); IR (neat) ν 3443 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.23 (s, 9 H), 1.32 (s, 3 H), 1.48 (s, 3 H), 2.84 (d, J = 2.9 Hz, 1 H), 3.37 (s, 3 H), 3.56 (dd, J = 6.3, 10.0 Hz, 1 H), 3.64 (dd, J = 5.8, 10.0 Hz, 1 H), 3.76 (t, J = 4.5 Hz, 1 H), 3.80−3.84 (m, 1 H), 3.90−4.03 (m, 2 H), 5.54 (d, J = 1.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.5, 27.6, 28.5, 59.3, 67.2, 70.3, 71.8, 75.4, 97.3, 108.0. Anal. Calcd for $C_{14}H_{26}O_6$: C, 57.91; H, 9.03. Found: C, 57.86; H, 9.01.

Methyl *O*^{2},*O*^{4}-Bis-*tert*-butyl-α-D-mannopyranoside (41). In a manner similar to that described in the general procedure, MeMgI (30 mmol, 30 mL in 1.0 M ether solution) was evacuated to remove ether. A benzene solution (30 mL) of **40**[22] (1.37 g, 5.0 mmol) was then introduced, and the reaction was refluxed for 24 h, quenched with NH_4Cl, and extracted with ether. The organic layer was washed with water and brine and dried ($MgSO_4$). The solvent was removed in vacuo, and the residue was chromatographed on silica gel (hexane/EtOAc 7/3) to yield **41** (0.78 g, 51%): mp 82−83 °C; $[\alpha]_D^{27}$ +4.4°(*c* 2.5, $CHCl_3$); IR (KBr) ν 3439, 3377 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.22 (s, 9 H), 1.23 (s, 9 H), 2.03 (t, J = 6.4 Hz, 1 H), 2.09 (d, J = 9.2 Hz, 1 H), 3.31 (s, 3 H), 3.48 (ddd, J = 3.2, 5.2, 8.8 Hz, 1 H), 3.57 (dd, J = 7.2, 8.8, Hz, 1 H), 3.65 (ddd, J = 4.0, 7.6, 9.2 Hz, 1 H), 3.71 (ddd, J = 5.6, 7.2, 11.6 Hz, 1 H), 3.77−3.83 (m, 2 H), 4.60 (d, J = 2.0 Hz, 1 H);^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.5, 29.1, 54.8, 62.3, 69.5, 71.5, 71.6, 71.8, 74.8, 75.3, 101.1; HRMS calcd for $C_{15}H_{30}O_6$ 306.2042, found 306.2047. Anal. Calcd: C, 58.78; H, 9.87. Found: C, 58.77; H, 9.76.

Methyl *O*^{2}-*tert*-Butyl-*O*^{4},*O*^{6}-isopropylidene-α-D-mannopyranoside (42). In a manner similar to that described in the general procedure, a benzene solution (50 mL) of MeMgI (32.8 mmol) and **40** (500 mg, 1.82 mmol) was stirred at 40 °C for 24 h. The mixture was cooled to room temperature, and the reaction was quenched with NH_4Cl and extracted with ether (3 × 50 mL). The organic layer was washed with brine and dried ($MgSO_4$). The residue obtained was chromatographed over silica gel (hexane/EtOAc 4/1) to give, in addition to **41** (120 mg, 23%), **42** (200 mg, 38%) as a colorless oil: $[\alpha]_D^{24}$ +2.3°(*c* 4.0, $CHCl_3$); IR (neat) ν 3483 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.20 (s, 9 H), 1.33 (s, 3 H), 1.51 (s, 3 H), 3.37 (s, 3 H), 3.42 (d, J = 1.7 Hz, 1 H), 3.52−3.61 (m, 2 H), 3.63−3.69 (m, 2 H), 4.07−4.12 (m, 2 H), 4.86 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.1, 27.3, 27.9, 55.0, 63.9, 67.3, 72.7, 74.1, 75.1, 78.0, 98.2, 109.5; HRMS calcd for $C_{14}H_{26}O_6$ 290.1729, found 290.1732.

Acetonide 46. In a manner similar to that described in the general procedure, a benzene solution (50 mL) of MeMgI (8.0 mmol) and **43** (520 mg, 2.0 mmol) was refluxed for 18 h followed by usual workup to give **46** (460 mg, 75%): $[\alpha]_D^{28}$ +47.07° (*c* 0.09, $CHCl_3$); mp 90−92 °C; IR (KBr) ν 3391 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.14 (s, 3 H), 1.21 (s, 9 H), 1.34 (s, 3 H), 1.39 (s, 3 H), 2.62 (t, J = 5.2 Hz, 1 H), 3.09 (d,J = 9.1 Hz, 2 H), 3.18 (s, 1 H), 3.36 (s, 3 H), 3.51 (d, J = 9.2 Hz, 1 H), 3.74 (m, 1 H), 4.00 (d, J = 9.3 Hz, 1 H), 4.26 (m, 2 H); ^{13}C NMR (75 MHz) δ 25.4, 28.1, 29.31, 58.9, 62.1, 69.8, 73.8, 75.7, 77.9, 78.3. Anal. Calcd for $C_{15}H_{30}O_6$: C, 58.79; H, 9.87. Found: C, 58.52; H, 9.79.

Acetonide 49. In a manner similar to that described in the general procedure, a benzene solution (50 mL) of MeMgI (4.0 mmol) and **44** (260 mg, 1.0 mmol) was refluxed for 18 h followed by usual workup to give **49** (160 mg, 55%): $[\alpha]_D^{28}$ +1.85° (*c* 0.01, $CHCl_3$); mp 125−126 °C; IR (KBr) ν 3353 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.15 (s, 3 H), 1.18 (s, 9 H), 1.37 (s, 3 H), 1.49 (s, 3 H), 2.97 (dd, J = 5.1, 7.7 Hz, 1 H), 3.07 (s,

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3 H), 3.22 (d, J = 8.6 Hz, 1 H), 3.39 (d, J = 8.6 Hz, 1 H), 3.57 (t, J = 8.5 Hz, 1 H), 3.70 (m, 3 H), 4.22 (dt, J = 4.9, 9.0 Hz, 1 H), 4.42 (dd, J = 1.5, 6.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.2, 25.2, 27.2, 27.4, 61.6, 67.3, 72.1, 73.1, 73.6, 74.5, 78.1, 108.2. Anal. Calcd for $C_{14}H_{28}O_6$: C, 57.50; H, 9.66. Found: C, 57.23; H, 9.63.

Acetonide 50. In a manner similar to that described in the general procedure, a benzene solution (20 mL) of MeMgI (20 mmol) and **45**[23] (1.15 g, 5.0 mmol) was refluxed for 24 h followed by usual workup to give **50** (0.83 g, 63%): mp 62−63 °C; $[\alpha]_D^{27}$ +35.5°(*c* 4.5, $CHCl_3$); IR (KBr) ν 3507 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.21 (d, J = 7.2 Hz, 3 H), 1.23 (s, 9 H), 1.33 (s, 3 H), 1.42 (s, 3 H), 2.63 (br s, 2 H), 3.64−3.67 (m, 2 H), 3.72−3.73 (m, 2 H), 4.25 (q, J = 6.0 Hz, 1 H), 4.31 (dd, J = 6.3, 7.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.3, 25.0, 27.6, 28.8, 61.4, 66.6, 72.2, 75.5, 76.6, 77.7, 107.9; HRMS calcd for $C_{13}H_{27}O_5$ (M + 1) 263.1858, found 263.1857.

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Supporting Information Available: NMR spectra for **5c**, **7**−**9**, **11**, **14**, **16a**,**b**, **18**, **20**, **22**, **23**, **29**−**31**, **33**, **42**, and **50** and the X-ray crystallographic data for **9** and **23** (36 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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