Stereoselective Glucal Epoxide Formation[1]

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Introduction

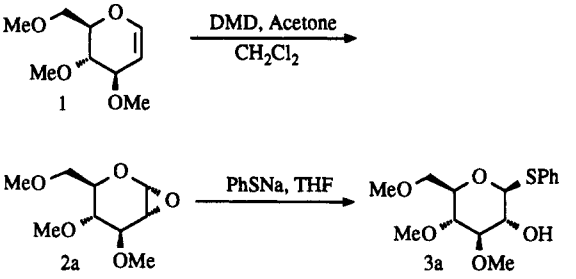
1,2-Anhydro sugars (glycal epoxides)[2-4] are important intermediates in the synthesis of oligosaccharides and other anomerically-substituted carbohydrate derivatives. Glycal epoxides were first prepared by Brigl,[2] but have recently become more accessible by dimethyldioxirane (DMD) oxidation of glycals.[4] In many cases the epoxides are formed stereoselectively by DMD oxidation. The nucleophilic opening of α-epoxides takes place via C-1 attack to give β-glycoside derivatives with a high degree of stereoselectivity.[4]

We required sulfide **3a** for an ongoing study in our lab, and the nucleophilic opening of a glucal epoxide offered an excellent method for its preparation. 3,4,6-Tri-*O*-methyl-D-glucal **1** was oxidized[4] with DMD (Scheme I) to give exclusively the α-anomer **2a**. Reaction of the epoxide **2a** with sodium phenylthiolate in THF proceeds in good yield to give predominantly the β-substituted phenyl thioglycoside **3a** (47%). Alternatively, addition of sodium azide to the epoxide **2a** yielded the β-azide **3b**. Despite the successes of DMD chemistry there are several drawbacks to this method. Solutions of DMD must be generated and rigorously dried because the intermediate epoxides readily react with water. The typical volume for a run is less than 100 mL, and concentrations seldom exceed 0.1 M, making reaction scales greater than a few millimoles difficult. Alternative dioxiranes[5] may be prepared at higher concentrations, but the precursor ketones are expensive or difficult to remove and the dioxiranes readily decompose.

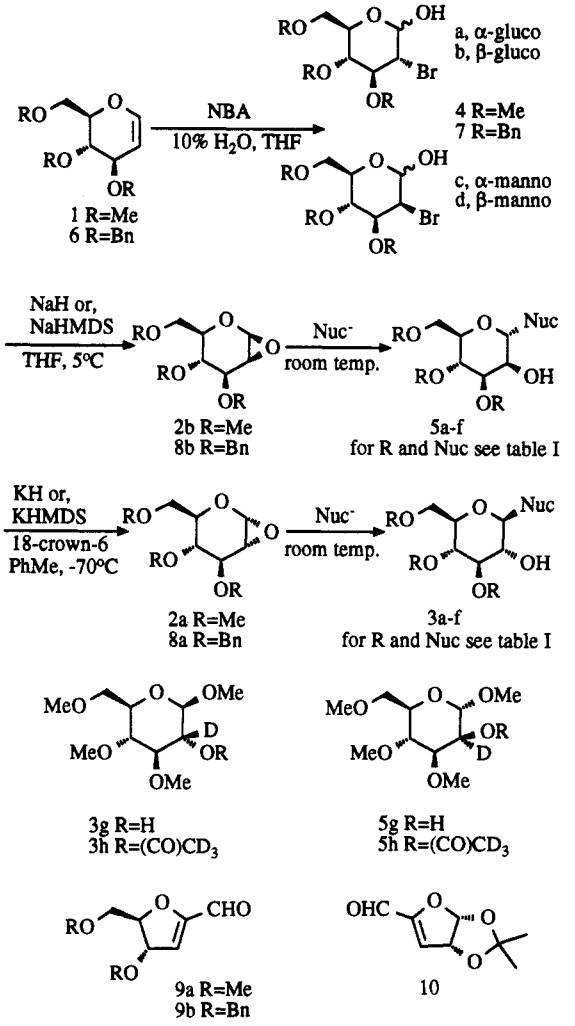
Results and Discussion

We wish to report an alternative approach to stereoselective glycal epoxidations involving the formation and cyclization of bromohydrins. A diastereoisomeric mixture of bromohydrins **4** was prepared from tri-*O*-methyl-D-glucal **1** and 1.1 equiv of *N*-bromoacetamide (NBA) in aqueous THF at 5 °C (Scheme II). Little selectivity was obtained in this step.[6] Typically, ratios of α-gluco- (**4a**), β-gluco- (**4b**), α-manno- (**4c**), and β-mannopyranoses (**4d**)

Scheme I



Scheme II



(1) This work was presented in part at the 203rd National Meeting of the American Chemical Society, San Francisco, CA, April 5-10, 1992.

(2) Brigl, P. Z. *Physiol. Chem.* **1922**, *122*, 257.

(3) Hickinbottom, W. J. *J. Chem. Soc.* **1928**, 3140. Lemieux, R. U. *Can. J. Chem.* **1953**, *31*, 949. Lemieux, R. U.; Huber, G. *J. Am. Chem. Soc.* **1956**, *78*, 4117. Lemieux, R. U.; Howard, J. *Methods Carbohydr. Chem.* **1963**, *2*, 400. Zachoval, J.; Schuerch, C. *J. Polymer Sci. Part C* **1969**, *28*, 187. Sondheimer, S.; Yamaguchi, H.; Schuerch, C. *Carbohydr. Res.* **1979**, *74*, 327. Sharkey, P. F.; Eby, R.; Schuerch, C. *Carbohydr. Res.* **1981**, *96*, 223. Trumbo, D. L.; Schuerch, C. *Carbohydr. Res.* **1985**, *135*, 195. Bergmann, M.; Schotte, H. *Ber. Dtsch. Chem. Ges.* **1921**, *54*, 440. Haworth, W. N.; Hirst, E. L. *J. Chem. Soc.* **1930**, 2615. Haworth, W. N.; Hirst, E. L.; Streight, H. R.; Thomas, H. A.; Webb, J. I. *J. Chem. Soc.* **1930**, 2636. Hirst, E. L.; Woolvin, L. S. *J. Chem. Soc.* **1931**, 1131. Levene, P. A.; Raymond, A. L. *J. Biol. Chem.* **1930**, *88*, 513. Levene, P. A.; Tipson, R. S. *J. Biol. Chem.* **1931**, *93*, 631. Wood, H. B., Jr.; Fletcher, H. G., Jr. *J. Am. Chem. Soc.* **1957**, *79*, 3234. Sweet, F.; Brown, R. K. *Can. J. Chem.* **1966**, *44*, 1571.

(4) (a) Halcomb, R. L.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6661. (b) Chow, K.; Danishefsky, S. *J. Org. Chem.* **1990**, *55*, 4211. (c) Gordon, D. M.; Danishefsky, S. J. *Carbohydr. Res.* **1990**, *206*, 361. (d) Dushin, R. G.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1992**, *114*, 3471.

(5) Mello, R.; Fiorentino, O.; Sciacovelli, O.; Curci, R. *J. Org. Chem.* **1988**, *53*, 3890. (b) Murray, R. W.; Singh, M.; Jeyaraman, R. *J. Am. Chem. Soc.* **1992**, *114*, 1346.

(6) We attempted some variation in hydroxybromination conditions: ether, THF, or CH_3CN as solvent with NBA, NBS. The rate and yield of the reaction were affected, and to a lesser extent the product distribution. For examples of alkoxyhalogenation see: Fischer, E.; Bergmann, M.; Schotte, H. *Chem. Ber.* **1920**, *53*, 509. Lemieux, R. U.; Fraser-Reid, B. *Can. J. Chem.* **1964**, *42*, 532. Lemieux, R. U.; Fraser-Reid, B. *Can. J. Chem.* **1965**, *43*, 1460. Tatsuta, K.; Fujimoto, K.; Kinoshita, M. *Carbohydr. Res.* **1977**, *54*, 85. Gnichtel, H.; Rebentisch, D.; Tompkins, T. C.; Gross, P. H. *J. Org. Chem.* **1982**, *47*, 2691. Bischofberger, K.; Eitelman, S. J.; Jordan, A. *Carbohydrate Res.* **1979**, *74*, 145. Lundt, I.; Thiem, J.; Prahst, A. *J. Org. Chem.* **1984**, *49*, 3063. Horton, D.; Waldemar, P.; Varela, O. *J. Org. Chem.* **1986**, *51*, 3479. Friesen, R. W.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1989**, *111*, 6656. Kottenhahn, M.; Kessler, H. *Liebigs Ann. Chem.* **1991**, 727.

0022-3263/93/1958-3761$04.00/0

of 2.2:1.0:3.0:3.1, respectively (manno/gluco 1.9:1), were observed. The ratios were determined by integration of the anomeric protons of **4a–d** in the ^{1}H NMR spectrum of the crude product.[7] The ^{1}H NMR spectrum recorded in $CDCl_3$ showed a resonance at δ 5.45 (brd s) which was assigned to the α-manno diastereomer **4c**. The equatorial/equatorial arrangement of C1-H and C2-H results in a small coupling constant. The α-gluco (**4a**) and β-manno (**4d**) diastereomers were assigned to resonances at δ 5.30 (d, J = 3.0 Hz) and 4.58 (d, J = 1.5 Hz), respectively. The observed coupling constants are consistent with an axial/equatorial arrangement of C1-H and C2-H.[8] The β-gluco diastereomer **4b** showed a resonance at 4.75 (d, J = 8.6 Hz), with a coupling constant typical of an anti-periplanar relationship for C1-H and C2-H.[8] The mixture of bromohydrins was reacted with sodium hydride in THF at 5 °C to yield predominantly the β-epoxide.[9,10] The epoxide was trapped with sodium phenylthiolate to give a 3:1 mixture of the α- and β-phenyl thioglycosides **5a** and **3a**, respectively.[11] Varying the conditions of the epoxide formation significantly altered the reaction diastereoselectivity.[12] Reaction of the mixture of bromohydrins **4** with potassium hydride and 18-crown-6 in toluene at –70 °C and trapping of the epoxide with sodium phenylthiolate gave a 1:10 mixture of α- and β-phenyl thioglycosides **5a** and **3a**. Sodium azide, methoxide, and benzyloxide were also effective nucleophiles (see Table I) for the trapping of the epoxides and showed similar diastereomer distributions. In some cases, improved yields were observed when either potassium or sodium hexamethyldisilazide was used as the base in place of the metal hydrides. The product distribution was unaltered by changing the ether protecting group from methyl to benzyl. Thus, reaction of tri-*O*-benzyl-D-glucal **6** with NBA in 10% aqueous THF gave four diastereoisomeric bromohydrins **7a–d** (100%). Reaction of **7** with NaH in THF followed by trapping with PhSNa gave the α- and β-phenyl thioglycosides **5e** and **3e** in 2.9:1 ratio. Alternatively, reaction of **7** with KHMDS/18-crown-6 in toluene at low temperature and trapping with PhSNa gave a 1:5.3 ratio of the α- and β-phenyl thioglycosides **5e** and **3e**. The epoxides **2a** and **2b** were also generated and trapped *in situ* by reaction of the bromohydrins **4** with both cesium carbonate and sodium methoxide in methanol solution. α-Methyl mannoside **5a** and β-methyl glucoside **3d** were formed in a ratio of 1:3. An additional product, tentatively identified as aldehyde **9a**, was also isolated. The structural assignment was based upon comparison of the spectral data of the related aldehyde **10**.[13] Similarly, cyclization and *in situ* trapping of tribenzyl bromohydrins **7** with cesium carbonate in methanol gave the α-methyl mannoside **5f**, the β-methyl glucoside **3f** (1:4 ratio), and aldehyde **9b**.

This switch in diastereoselectivity is noteworthy. Epoxide formation would be expected to proceed via neighboring group participation with inversion of the C-2 stereochemistry. Thus, a mixture of manno and gluco bromohydrins in a ratio of 1.9:1 would be expected to yield the α and β epoxides, respectively, in a ratio of 1.9:1 (via cyclization of the appropriate anomer). Trapping of the epoxides with a nucleophile would in turn yield the α-manno and β-gluco products in a ratio of 1:1.9. It is clear that some additional process is taking place.

The reaction of bromohydrins **4a–d** with NaH was repeated in THF-d_8, and the reaction progress was followed by ^{1}H NMR spectroscopy. After 4 h the signals due to the anomeric protons of the bromohydrin had disappeared and two new signals at δ 4.83 and 4.79 ppm assigned as the α and β epoxides, respectively (ratio 1:3), had developed. A similar experiment with a single isomer, bromohydrin **4a**, revealed a rapid equilibration to an α/β mixture (upon NaH addition) followed by the gradual appearance of a single epoxide peak at δ 4.79 ppm. After 22 h only signals due to the epoxide remained. Addition of PhSNa resulted

Table I. Epoxide Formation and Trapping

		base	nucleophile (Nuc$^-$)	yield (% isolated)	ratio: α-manno (**5**): β-gluco (**3**) after purification	ratio: α-manno (**5**): β-gluco (**3**) (crude product)
a	R = Me	NaH	PhSNa	51	2.6:1	(3:1)
		NaHMDS		35	3.2:1	(1:1)
		KH		37	1:11	(1:10)
		KHMDS		44	1:3.3	(1:4.5)
b	R = Me	NaH	NaN_3	59	4.6:1	
		KH		13	1:4.2	
		KHMDS		32	1:5.4	
c	R = Me	NaH	$PhCH_2ONa$	34	3:1	
		KH		19	1:11	
		KHMDS		16	1:5.3	
d	R = Me	NaH	MeOH	29	3.9:1	
		NaHMDS		21	3:1	
		KH		20[d]	1:5.8	
		KHMDS		37[d]	1:3	
		MeONa[c]		66[d]	1:3	
		Cs_2CO_3[c]		51[d]	1:4.1	
e	R = Bn	NaH	PhSNa	29	2.9:1	
		NaHMDS		27	3.2:1	
		KHMDS		22	1:5.3	
f	R = Bn	Cs_2CO_3[c]	MeOH	65[d]	1:4.1	

[a] For NaH and NaHMDS; THF, 5 °C. [b] For KH and KHMDS; toluene, 18-crown-6, –70 °C. [c] Methanol as solvent. [d] Variable amounts (up to 15%) of an aldehyde was also isolated. [e] Crude ratios were determined by ^{1}H NMR spectroscopy. The products were separated by column chromatography to give the isolated yields and ratios. [f] The balance of material was polymeric and could be eluted from the column with methanol.

(7) The ^{1}H NMR spectra of the bromohydrins **4a–d** were obtained in $CDCl_3$, toluene-d_8, and THF-d_8. Comparison of these spectra allowed assignment of the C1-H (anomeric) resonances of each isomer. The ratios were calculated by integration of the anomeric proton signals and ranged from 1.9:1 to 1.4:1. The bromohydrins **4a–d** were acetylated (Ac_2O, pyridine, CH_2Cl_2) to give a mixture of acetates. The manno/gluco ratio for the acetates was 1.44:1.

(8) Stoddart, J. F. *Stereochemistry of Carbohydrates*; Wiley-Interscience: New York, 1971.

(9) The analogous reactions of 2-hydroxy-3-chlorotetrahydropyran (Wakselman, C.; Wartski, L. *Bull. Soc. Chim.* **1967**, 2242) and of *N*-acetylneuraminic acid derivatives have been reported: Okamoto, K.; Kondo, T.; Goto, T. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 631. Okamoto, K.; Goto, T. *Tetrahedron* **1990**, *46*, 5835.

(10) Epoxides have been implicated in the base-catalyzed isomerization of 2-(mesyloxy)arabinose: Jones, J. K. N.; Nicholson, W. H. *J. Chem. Soc.* **1955**, 3050. Smith, D. C. C. *J. Chem. Soc.* **1957**, 2690.

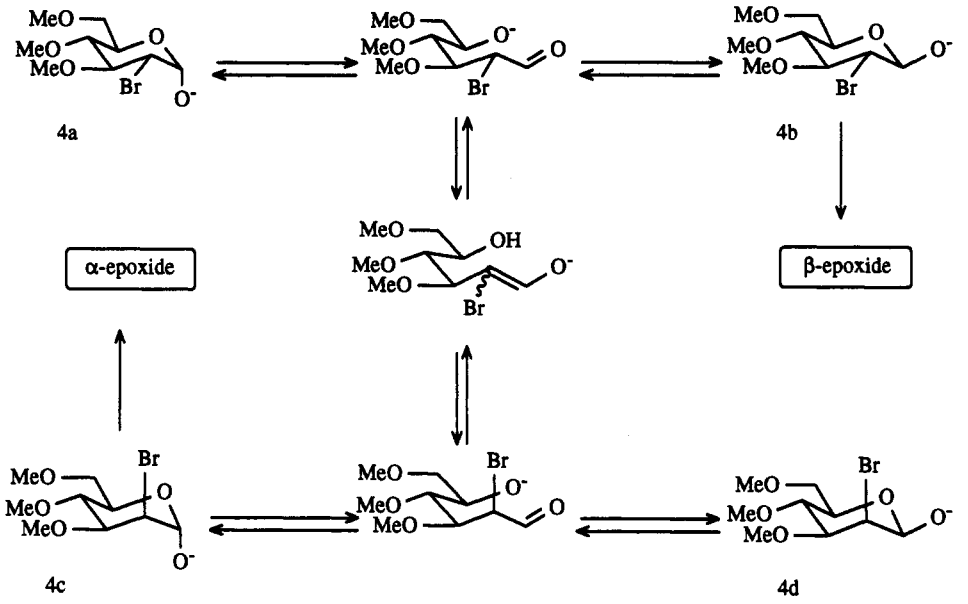
(11) The product ratio was determined by integration of the anomeric proton signals in the crude ^{1}H NMR spectrum. This was compared to the yield of each isomer after chromatographic separation.

(12) The cyclization reaction was performed under variety of conditions. The resulting epoxides were trapped with PhS$^-$, and the ratio of thio glycosides **5a** and **3a** was determined on the crude compounds by ^{1}H NMR spectroscopy.

reaction condns	ratio: α-manno (**5a**): β-gluco (**3a**)
LiH; –78 °C to rt; THF	dec
NaH; 5 °C; THF	3:1
NaH; –72 °C; 15-crown-5; THF	1.1:1
NaH; –68 °C; 15-crown-5; PhMe	1:1.6
KH; –70 °C to rt; THF	1.5:1
KH; –72 °C; 18-crown-6; THF	1:2.6
KH; –72 °C; 18-crown-6; PhMe	1:10

(13) Sun, K. M.; Fraser-Reid, B. *Synthesis* **1982**, 28.

Scheme III



in loss of the epoxide signal and appearance of the anomeric proton signal for the thioglycoside **5a**. The *in situ* cyclization and trapping of the bromohydrins **4** with cesium carbonate was repeated in MeOD. A ^2H NMR spectrum of the isolated compounds indicated deuterium incorporation at C-2 for both the α-manno (**5g**) and β-gluco (**3g**) products at levels of 20 and 77%, respectively.[14]

A combination of two previously observed phenomena is probably responsible. The base-catalyzed epimerization of the C-2 position of *N*-acetylglucosamine has been reported.[15] In this case, equilibrium mixtures of *N*-acetylmannosamine and *N*-acetylglucosamine resulted. Deuterium incorporation into C-2 supports a mechanism involving enolization of the open-chain aldehyde. In addition, changing metal ion and solvent were reported[16] to effect the stereoselectivity of both acylation and alkylation of anomeric alkoxides. The selectivities resulted from a modification of the relative reactivities of the anomeric alkoxides. The selectivities observed in cyclization of the bromohydrins **4a–d** to epoxides **2** could arise[17] from an interconversion of the four bromohydrin isomers (Scheme III) with the cyclization step modified by the metal. The cyclization would be most rapid for the β-gluco bromohydrin **4b** in the presence of sodium and fastest for the α-manno bromohydrin **4c** with potassium/18-crown-6.

In conclusion, the formation and cyclization of bromohydrins is an alternative route for glucal epoxide formation giving access to both epoxide isomers. The application of this method to other carbohydrate substrates is underway and will be reported in due course.

Experimental Section

^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution on a Varian XL-300 spectrometer at 300 and 75 MHz, respectively. The ^1H chemical shifts are reported in ppm downfield from Me_4Si. The ^{13}C chemical shifts are reported in ppm relative to the center line of $CDCl_3$ (77.0 ppm). The ^2H NMR spectra were recorded in $CHCl_3$ at 46 MHz, and chemical shifts are reported relative to $CDCl_3$ (7.24 ppm). Infrared spectra were recorded on a Perkin-Elmer 1600 series FTIR. Melting points were determined on an Electrothermal melting point apparatus and are uncorrected. Mass spectra were determined on a Varian Mat 331A spectrometer, and microanalyses were performed by Atlantic Microlab Inc. Optical rotations were recorded on an Autopol III polarimeter (Rudolph Research) under standard conditions. The THF was distilled from sodium–benzophenone ketyl, CH_2Cl_2 was distilled from CaH_2, and methanol was distilled from Mg. The reactions were performed under argon. *N*-Bromosuccinimide, sodium methoxide/methanol, cesium carbonate, and anhydrous DMF were purchased from Aldrich Chemical Co. *N*-Bromoacetamide was purchased from Sigma Chemical Co. Trimethyl glucal[18] was prepared from triacetyl glucal by methanolysis (MeONa, MeOH) and methylation (NaH, DMF, MeI). Column chromatography was performed on SiO_2 (Merck; 230–400 mesh) eluting with an Et_2O/hexanes mixtures.

Procedure for Dimethyldioxirane Epoxidation and Trapping with Sodium Phenylthiolate. Anhydrous dimethyldioxirane[19] in acetone (0.07 M, 17 mL) was added dropwise to a solution of 3,4,6-tri-*O*-methyl-D-glucal (1) (200 mg, 1.1 mmol) in CH_2Cl_2 (2 mL) at 5 °C. After 90 min, the solution was evaporated to give a white solid (190 mg, 0.93 mmol, 88%) which was redissolved in anhydrous THF (3 mL). The solution was cooled to 5 °C, and sodium phenylthiolate (2.6 mmol) was added. The reaction mixture was stirred overnight and was gradually warmed to room temperature (ca. 15 h). The reaction mixture was diluted with water (50 mL) and extracted with Et_2O (3×, 30 mL). The combined Et_2O were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. SiO_2 chromatography gave **phenyl 3,4,6-tri-*O*-methyl-1-thio-β-D-glucopyranoside (3a)** (139 mg, 0.44 mmol, 47%).

Epoxidation with Dimethyldioxirane and Trapping with Sodium Azide. Anhydrous dimethyldioxirane in acetone (0.06

(14) The level of deuterium incorporation was determined by acetylation of the alcohols **3g** and **5g** to give the d_3 C-2 acetates **3h** and **5h**, respectively (99+% d_6 acetic anhydride in pyridine), and integration of the ^2H NMR spectrum. See ref 15d.

(15) (a) Roseman, S.; Comb, D. G. *J. Am. Chem. Soc.* **1958**, *80*, 3166. (b) Kuhn, R.; Brossmer, R. *Liebigs Ann. Chem.* **1958**, *616*, 221. (c) Carlo, M. J.; Cosmatos, H.; Zimmerman, Jr., K. *Liebigs Ann. Chem.* **1961**, *650*, 187. (d) Szilagyi, L.; Herczegh, P.; Bujtas, G. *Z. Naturforsch.* **1977**, *32B*, 296.

(16) Pfeffer, P. E.; Rothman, E. S.; Moore, G. G. *J. Org. Chem.* **1976**, *41*, 2925. Schmidt, R. R. *Ang. Chem. Int. Ed. Engl.* **1986**, *25*, 212 and references cited therein.

(17) A reviewer commented that it is possible for the halide ion, present in solution, to open the epoxide resulting in a glycosyl halide. However, opening and closing of the epoxide ring is not equilibrating the two epoxides since the same epoxide will always result from an opening–closing sequence. The intermediary glycosyl halides apparently did not react with nucleophile as shown by the absence of 1,2 cis-glycosides.

(18) Flaherty, B.; Overend, W. G.; Williams, N. R. *J. Chem. Soc. C* **1966**, 398–403.

(19) Murray, R. W.; Jeyaraman, R. *J. Org. Chem.* **1985**, *50*, 2847.

M, 35 mL) was added dropwise to a solution of 3,4,6-tri-*O*-methyl-D-glucal (1) (304 mg, 1.6 mmol) in CH_2Cl_2 (5.0 mL) at 5 °C. After 1 h, the solution was evaporated to give a white residue (290 mg, 1.4 mmol, 89%) which was redissolved in anhydrous DMF (4 mL). The solution was cooled to 5 °C, and sodium azide (277 mg, 4.2 mmol) was added. The reaction mixture was stirred at 5 °C for 4 h. The solution was slowly warmed to room temperature (3 h) and then was stirred overnight (15 h). The solution was diluted with water (50 mL) and extracted with Et_2O (3×, 25 mL). The combined Et_2O were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. SiO_2 chromatography gave **3,4,6-tri-*O*-methyl-β-D-glucopyranosyl azide (3b)** (146 mg, 0.6 mmol, 37%).

Hydroxybromination of 3,4,6-Tri-*O*-methyl-D-glucal. A solution of 3,4,6-tri-*O*-methyl-D-glucal (1) (1.3 g, 6.9 mmol) in 10% aqueous THF (26 mL) was cooled to 5 °C, and *N*-bromoacetamide (1.0 g, 7.6 mmol) was added. The reaction progress was followed by thin-layer chromatography (SiO_2, 1:1 hexanes/Et_2O) until the consumption of trimethyl glucal 1 was indicated. The mixture was diluted with water (30 mL) and extracted with Et_2O (3×, 30 mL). The combined Et_2O extracts were washed with water (1×, 50 mL), dried over Na_2SO_4, and concentrated *in vacuo* to give a diastereomeric mixture of bromohydrins **4a–d** (1.7 g, 5.8 mmol, 84%): ^{1}H-NMR (anomeric protons) δ 5.45(s) **4c** (α-manno), 5.30 (d, J = 3.0 Hz) **4a** (α-gluco), 4.75 (d, J = 8.6 Hz) **4b** (β-gluco), 4.58 (d, J = 1.5 Hz) **4d** (β-manno). Crystallization (3×, Et_2O/hexanes) produced a single diastereoisomer, **3,4,6-tri-*O*-methyl-2-deoxy-2-bromo-α-D-glucopyranose (4a)**: mp 149–149.5 °C; $[\alpha]_D$ +145.2° (c = 1.00, $CHCl_3$); IR (KBr) 3401, 2992, 2917, 2842, 1451, 1379, 1189, 1128, 1048, and 1013 cm^{-1}; ^{1}H NMR δ 5.32 (t, 1 H, J = 3.3 Hz), 4.04–3.99 (m, 1 H), 3.80–3.69 (m, 2 H), 3.68 (s, 3 H), 3.66–3.57 (m, 2 H), 3.55 (s, 3 H), 3.41 (s, 3 H), 3.15 (t, 1 H, J = 9 Hz); ^{13}C NMR δ 92.9, 83.0, 81.4, 71.3, 70.4, 61.2, 60.6, 59.2, 51.9; MS (DP/CI) m/z 286, 284, 173, 141, 113, 101, 87, 71. Anal. Calcd for $C_9H_{17}O_5Br$: C, 37.91; H, 6.01. Found: C, 38.00; H, 5.96. Acetylation of the bromohydrin mixture (**4a–d**) with Ac_2O in pyridine and CH_2Cl_2 at 5 °C gave a mixture of acetates (74%). Column chromatography (SiO_2, EtOAc/hexanes (1:4)) gave **3,4,6-tri-*O*-methyl-2-deoxy-2-bromo-α-D-mannopyranosyl acetate** as an oil (13%): IR ($CHCl_3$) 3010, 2932, 2836, 1749, 1373, 1149, and 1110 cm^{-1}; ^{1}H NMR δ 6.32 (d, 1 H, J = 1.9 Hz), 4.37 (dd, 1 H, J = 3.3, 1.8 Hz), 3.81–3.77 (m, 1 H), 3.71–3.52 (m, 4 H), 3.56 (s, 3 H), 3.47 (s, 3 H), 3.43 (s, 3 H), 2.11 (s, 3 H); ^{13}C NMR δ 168.3, 93.9, 78.7, 75.8, 74.3, 71.1, 61.0, 59.5, 57.0, 49.1, 21.0; MS (DP/CI) m/z 327, 325, 269, 267, 237, 235, 155, 89. Further elution yielded **3,4,6-tri-*O*-methyl-2-deoxy-2-bromo-β-D-glucopyranosyl acetate** as a crystalline solid (16%): mp 82–85 °C; IR ($CHCl_3$) 3011, 2937, 2839, 1759, 1117, 1102, and 1061 cm^{-1}; ^{1}H NMR δ 5.68 (d, 1 H, J = 9 Hz), 3.79–3.67 (m, 1 H), 3.70 (s, 3 H), 3.64–3.59 (m, 2 H), 3.56 (s, 3 H), 3.47–3.42 (m, 1 H), 3.41–3.29 (m, 2 H), 3.39 (s, 3 H), 2.13 (s, 3 H); ^{13}C NMR δ 168.7, 93.3, 86.7, 79.9, 75.4, 70.1, 61.3, 60.4, 59.2, 50.9, 20.8; MS (DP/CI) m/z 237, 235 (100).

Hydroxybromination of 3,4,6-Tri-*O*-benzyl-D-glucal. 3,4,6-Tri-*O*-benzyl-D-glucal (**6**) (1.04 g) was treated as above to give a mixture of bromohydrins **7a–d** (100%) as a waxy solid: IR (KBr) 3445, 3030, 2920, 1455, 1120, 1073, and 1042 cm^{-1}; ^{1}H NMR δ 7.40–7.13 (m), 5.45–5.44 (br s), 5.37 (d, J = 3 Hz), 4.99–4.47 (m), 4.36 (dd, J = 3.6, 1.5 Hz), 4.17–3.44 (m); ^{13}C NMR (48 resonances) anomeric carbons δ 96.9, 94.7, 93.0, 91.8; MS (DP/EI) m/z 423, 421, 341, 181, 163, 107, 105, 92, 91, 79, 77, 65, 51. Anal. Calcd for $C_{27}H_{29}O_5$: C, 63.16; H, 5.69. Found: C, 63.14; H, 5.64. Acetylation of the bromohydrin mixture with Ac_2O in pyridine and CH_2Cl_2 at 5 °C gave a mixture of acetates: ^{1}H NMR (anomeric protons) δ 6.31 (s), 5.74 (d), 5.55 (d); (acetate methyls) 2.153 (s), 2.140 (s), 2.035 (s) and 2.025 (s).

Procedure A: Cyclization with NaH. NaH in mineral oil (60%, 208 mg, 5.2 mmol) was washed 3× with hexanes under Ar. The oil-free NaH was suspended in dry THF (10 mL), and the resulting suspension was cooled to 5 °C. A solution of the bromohydrins **4a–d** (5.2 mmol) in anhydrous THF (5 mL) was added in portions to the stirred NaH suspension. The reaction progress was followed by thin-layer chromatography (SiO_2; 1:1 hexanes/Et_2O) until the starting material had been consumed (approximately 4 h). The nucleophile (15.6 mmol) was added, and the reaction mixture was gradually warmed to room temperature (3 h). The reaction mixture was stirred overnight (15 h), diluted with water (25 mL), and extracted with CH_2Cl_2 (3×, 50 mL). The combined CH_2Cl_2 extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The products were purified by SiO_2 chromatography (33–50% Et_2O in hexanes).

Procedure B: Cyclization with NaHMDS. A solution of the bromohydrins **4a–d** (393 mg, 1.4 mmol) in anhydrous THF (9 mL) was cooled to 5 °C. NaHMDS (1.4 mmol, 1.0 M in THF) was added over 5 min. The reaction progress was monitored by TLC until the bromohydrins had been consumed. The nucleophile (4.2 mmol) was added, and the solution was slowly warmed to room temperature (3 h). The reaction mixture was stirred overnight and then was worked up as in procedure A.

Phenyl 3,4,6-Tri-*O*-methyl-1-thio-α-D-mannopyranoside (5a). Bromohydrins **4a–d** (2.13 g, 7.5 mmol), NaH (299 mg, 7.5 mmol), and sodium phenylthiolate (2.97 g, 22.5 mmol) gave **5a** (879 mg, 2.8 mmol, 37%) as a yellow oil (and **3a**, 14%): $[\alpha]_D$ +21.20° (c = 1.0; $CHCl_3$); IR (neat) 3442, 3060, 2918, 1669, 1583, 1574, 1482, 1390, 1344, 1315, and 1087 cm^{-1}; ^{1}H NMR δ 7.49–7.46 (m, 2 H), 7.33–7.25 (m, 3 H), 5.59 (d, 1 H, J = 1.5 Hz), 4.28 (dd, 1 H, J = 3.0, 1.8 Hz), 4.14–4.09 (m, 1 H), 3.66 (dd, 1 H, J = 9, 3.9 Hz), 3.60–3.53 (m, 2 H), 3.54 (s, 3 H), 3.52 (s, 3 H), 3.50 (dd, 1 H, J = 8.1, 4.8 Hz), 3.38 (s, 3 H); ^{13}C NMR δ 133.9, 131.3, 128.9, 127.3, 87.5, 81.8, 75.9, 71.9, 71.1, 69.3, 60.7, 59.2, 57.5; MS (DP/EI) m/z 314 (M^+), 205, 173, 141, 115, 101, 89, 87, 81, 75, 71, 59, 45. Anal. Calcd for $C_{15}H_{22}O_5S$: C, 57.31; H, 7.05. Found: C, 57.28; H, 7.08.

3,4,6-Tri-*O*-methyl-α-D-mannopyranosyl Azide (5b). Bromohydrins **4a–d** (428 mg, 1.5 mmol), NaH (60 mg, 1.5 mmol), and sodium azide (293 mg, 4.5 mmol) gave **5b** (173 mg, 0.7 mmol, 48%) as a yellow oil (and **3b**, 11%): $[\alpha]_D$ +176.3° (c = 0.63, $CHCl_3$); IR (neat) 3443, 2933, 2828, 2113, 1246 and 1123 cm^{-1}; ^{1}H NMR δ 5.43 (d, 1 H, J = 1.8 Hz), 3.90 (dd, 1 H, J = 3.3, 1.8 Hz), 3.76–3.72 (m, 1 H), 3.65–3.63 (m, 2 H), 3.52 (s, 3 H), 3.49 (s, 3 H), 3.50–3.44 (m, 1 H), 3.42 (s, 3 H), 3.38 (d, 1 H, J = 3 Hz), 2.53 (br s, 1 H); ^{13}C NMR δ 89.4, 80.6, 75.2, 72.9, 71.0, 67.6, 60.7, 59.3, 57.6; MS (DP/EI) m/z 205 ($M - N_3$), 172, 101, 88, 87, 86, 75, 74, 71, 59, 45. Anal. Calcd for $C_9H_{17}O_5N_3$: C, 43.72; H, 6.93. Found: C, 44.12; H, 6.89.

Benzyl 3,4,6-Tri-*O*-methyl-α-D-mannopyranoside (5c). Bromohydrins **4a–d** (399 mg, 1.4 mmol), NaH (56 mg, 1.4 mmol), and the sodium salt of benzyl alcohol (4.3 mmol) gave **5c** (115 mg, 0.4 mmol, 26%) as an oil (and **3c**, 8%): $[\alpha]_D$ +88.80° (c = 1.365, $CHCl_3$); IR (neat) 3450, 3031, 2912, 2827, 1456, 1380, 1319, 1186, 1112 and 1060 cm^{-1}; ^{1}H NMR δ 7.34–7.26 (m, 5 H), 4.96 (d, 1 H, J = 1.5 Hz), 4.60 (ABq, 2 H, J = 10.8 Hz), 4.04 (br s, 1 H), 3.71–3.66 (m, 1 H), 3.62–3.60 (m, 2 H), 3.57–3.46 (m, 1 H), 3.52 (s, 3 H), 3.48 (s, 3 H), 3.42 (s, 3 H), 2.48 (br s, 1 H); ^{13}C NMR δ 137.1, 128.3, 127.9, 127.7, 98.5, 81.4, 75.9, 71.4, 70.9, 69.1, 67.7, 60.6, 59.2, 57.4; MS (GC/CI) m/z 311, 205, 173, 141, 91, 71. Anal. Calcd for $C_{16}H_{24}O_6$: C, 61.52; H, 7.74. Found: C, 61.58; H, 7.77.

Phenyl 3,4,6-Tri-*O*-benzyl-1-thio-α-D-mannopyrannoside (5e). Bromohydrins **7a–d** (305 mg, 0.6 mmol) and NaHMDS (0.6 mmol) gave **5e** (65 mg) as an oil (and **3e**, 21 mg): $[\alpha]_D$ +159.9° (c = 2.7, $CHCl_3$); IR ($CDCl_3$) 3444, 3061, 3029, 2868, 1496, 1454, 1365, 1208, 1097, and 1026 cm^{-1}; ^{1}H NMR δ 7.48–7.45 (m, 2 H), 7.37–7.18 (m, 18 H), 5.61 (d, 1 H, J = 1.5 Hz), 4.68 (m, 2 H), 4.71 (s, 2 H), 4.53 (m, 2 H), 4.25 (m, 2 H), 3.97–3.81 (m, 2 H), 3.79–3.65 (m, 2 H), 2.58 (br s, 1H); ^{13}C NMR δ 138.1, 138.0, 137.5, 133.7, 131.5, 128.8, 128.5, 128.3, 128.2, 128.0, 127.8, 127.7, 127.6, 127.4, 127.3, 87.3, 80.3, 75.1, 74.5, 73.3, 72.2, 72.1, 69.8, 68.8; MS (DP/EI) m/z 433 (M – SPh), 181, 110, 109, 92, 91, 79, 77, 65, 51. Anal. Calcd for $C_{33}H_{34}O_5S$: C, 73.04; H, 6.32. Found: C, 72.79; H, 6.41.

Procedure C: Cyclization with KH. A mineral oil suspension of KH (35%, 488 mg, 1.7 mmol) was washed 3× with hexanes under Ar. The washed KH was suspended in a solution of 18-crown-6 (425 mg, 1.7 mmol) in anhydrous $PhCH_3$ (7 mL), and the suspension was cooled to −72 °C. The bromohydrin mixture **4a–d** (1.7 mmol) was dissolved in anhydrous $PhCH_3$ (5 mL) and was added in portions to the KH suspension. The mixture was stirred at −72 °C for 4 h and then was warmed to 5 °C over 30 min. The nucleophile (5.1 mmol) was added, and the mixture was slowly warmed to room temperature and was stirred overnight (18 h). The reaction mixture was worked up and purified as described in procedure A.

Procedure D: Cyclization with KHMDS. A solution of bromohydrins **4a–d** (331 mg, 1.2 mmol) and 18-crown-6 (307 mg,

1.2 mmol) in anhydrous $PhCH_3$ (10 mL) was cooled to −72 °C. KHMDS (1.2 mmol, 0.5 M in $PhCH_3$) was added gradually over 5 min to the bromohydrin mixture. The reaction mixture was stirred at −72 °C for 4 h and then was warmed to 5 °C over 30 min. The nucleophile (3.6 mmol) was added, and the mixture was slowly warmed to room temperature and was stirred overnight. The reaction mixture was worked up as in procedure A.

Phenyl 3,4,6-Tri-*O*-methyl-1-thio-β-D-glucopyranoside (3a). Bromohydrins **4a–d** (399 mg, 1.4 mmol), KHMDS (1.4 mmol, 0.5 M in $PhCH_3$), 18-crown-6 (380 mg, 1.4 mmol), and sodium phenylthiolate (571 mg, 4.3 mmol) gave **3a** (150 mg, 0.5 mmol, 33%) as an oil (and **5a**, 11%): $[\alpha]_D$ −42.3° (c = 1.0; $CHCl_3$); IR (neat) 3416, 3058, 2928, 2834, 1583, 1480, 1439, 1380, 1342, 1264, 1190, and 1084 cm^{-1}; ^1H NMR δ 7.55–7.51 (m, 2 H), 7.32–7.27 (m, 3 H), 4.47 (d, 1 H, J = 9.6 Hz), 3.72–3.57 (m, 2 H), 3.65 (s, 3 H), 3.52 (s, 3 H), 3.41 (s, 3 H), 3.39–3.34 (m, 2 H), 3.24–3.17 (m, 2 H), 2.63 (br s, 1 H); ^{13}C NMR δ 132.5, 128.8, 127.8, 88.3, 87.6, 79.2, 79.1, 72.4, 71.4, 60.9, 60.3, 59.4; MS (DP/EI) m/z 314 (M^+), 205, 173, 141, 115, 109, 101, 89, 87, 75, 71, 59, 45. Anal. Calcd for $C_{15}H_{22}O_5S$: C, 57.31; H, 7.05. Found: C, 57.20; H, 7.09.

3,4,6-Tri-*O*-methyl-β-D-glucopyranoside Azide (3b). Bromohydrins **4a–d** (340 mg, 1.2 mmol), 18-crown-6 (315 mg, 1.2 mmol), KHMDS (1.2 mmol), and sodium azide (232 mg, 3.6 mmol) gave **3b** (80 mg, 0.32 mmol, 27%) as a solid (and **5b**, 5%): mp 79.5–80 °C; $[\alpha]_D$ −26.27° (c = 0.67; $CHCl_3$); IR (KBr) 3420, 2933, 2836, 2116, 1453, 1378, 1256, 1190, and 1087 cm^{-1}; ^1H NMR δ 4.51 (d, 1 H, J = 8.4 Hz), 3.68–3.57 (m, 2 H), 3.66 (s, 3 H), 3.54 (s, 3 H), 3.47–3.38 (m, 1 H), 3.42 (s, 3 H), 3.36–3.17 (m, 3 H); ^{13}C NMR δ 90.2, 86.1, 78.9, 77.4, 73.6, 70.8, 61.0, 60.4, 59.0; MS (DP/EI) m/z 205 ($M - N_3$), 172, 101, 88, 87, 86, 75, 74, 73, 71, 59. Anal. Calcd for $C_9H_{17}O_5N_3$: C, 43.72; H, 6.93. Found: C, 43.88; H, 6.90.

Benzyl 3,4,6-Tri-*O*-methyl-β-D-glucopyranoside (3c). Bromohydrins **4a–d** (494 mg, 1.7 mmol), 18-crown-6 (457 mg, 1.7 mmol), KH (199 mg, 1.7 mmol), and the sodium salt of benzyl alcohol (5.2 mmol) gave **3c** (88 mg, 0.3 mmol, 17%) as an oil (and **5c**, 2%): $[\alpha]_D$ −44.69 (c = 1.6; $CHCl_3$); IR (neat) 3438, 2925, 1731, 1455, 1370, 1263, and 1072 cm^{-1}; ^1H NMR δ 7.37–7.26 (m, 5 H), 4.76 (ABq, 2 H, J = 11.7 Hz), 4.30 (d, 1 H, J = 7.8 Hz), 3.68–3.57 (m, 2 H), 3.64 (s, 3 H), 3.53 (s, 3 H), 3.49–3.44 (m, 1 H), 3.42 (s, 3 H), 3.37–3.29 (m, 1 H), 3.26–3.15 (m, 2 H), 2.55 (br s, 1 H); ^{13}C NMR δ 136.9, 128.3, 128.0, 127.8, 101.5, 85.9, 79.3, 74.9, 74.0, 71.2, 70.9, 60.7, 60.3, 59.3; MS (GC/EI) m/z 267, 177, 115, 101, 91, 71, 45. Anal. Calcd for $C_{16}H_{24}O_6$: C, 61.52; H, 7.74. Found: C, 61.37; H, 7.82.

Phenyl 3,4,6-Tri-*O*-benzyl-1-thio-β-D-glucopyranoside (3e). Bromohydrins **7a–d** (217 mg, 0.4 mmol), KHMDS (0.4 mmol), 18-crown-6 (11 mg, 0.4 mmol), and sodium phenylthiolate (167 mg, 1.3 mmol) gave **3e** (42 mg, 18%) as an oil (and **5e** 8 mg, 4%): $[\alpha]_D$ −11.84° (c = 2.7, $CHCl_3$) [lit.[4c] −11.89°, mp 71–73 °C]; IR ($CDCl_3$) 3447, 3065, 3030, 2865, 1584, 1496, 1454, 1360, 1117, 1056, and 1027 cm^{-1}; ^1H NMR δ 7.58–7.48 (m, 2 H), 7.34–7.19 (m, 18 H), 4.92–4.81 (m, 3 H), 4.63–4.49 (m, 4 H), 3.78–3.74 (m, 2 H), 3.61–3.45 (m, 4 H), 2.40 (br s, 1 H); ^{13}C NMR δ 138.5, 138.3, 138.1, 132.9, 131.8, 129.1, 129.0, 128.5, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 127.6, 127.5, 127.2, 88.0, 85.9, 79.4, 75.1, 73.4, 72.6, 69.0, 65.8; MS (DP/EI) m/z 433 (M − SPh), 181, 110, 109, 92, 91, 65. Anal. Calcd for $C_{33}H_{34}O_5S$: C, 73.04; H, 6.32. Found: C, 73.09; H, 6.37.

General Procedure for Methanol Trapping of the Epoxides. Bromohydrins **4a–d** were cyclized via procedures A–D. The reaction progress was monitored by TLC until consumption of bromohydrins was indicated. Excess anhydrous methanol was added to the reaction mixture at 5 °C. The reaction mixture was slowly warmed to room temperature (3 h), and the solution was stirred overnight (15 h). The mixture was diluted with water (50 mL) and extracted with CH_2Cl_2 (3×, 30 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Methyl glycosides were purified by chromatography (SiO_2, 1:1 hexanes/Et_2O).

Methyl 3,4,6-Tri-*O*-methyl-α-D-mannopyranoside (5d). Bromohydrins **4a–d** (337 mg, 1.2 mmol), NaHMDS (1.2 mmol), and methanol (3 mL) gave **5d** (44 mg, 0.2 mmol, 16%) as an oil (and **3d**, 5%): $[\alpha]_D$ +77.83 (c = 0.6, $CHCl_3$) [The previous lit.[20] value of +8°, c = 1.2 $CHCl_3$, does not agree]; IR [$CDCl_3$) 3454, 2924, 1651, 1454, 1379, 1322, 1260, 1196, 1062, and 1001 cm^{-1}; ^1H NMR δ 4.77 (d, 1 H, J = 1.5 Hz), 4.00 (br s, 1 H), 3.61–3.49 (m, 3 H), 3.52 (s, 3 H), 3.49 (s, 3 H), 3.55–3.39 (m, 2 H), 3.42 (s, 3 H), 3.37 (s, 3 H), 2.50 (d, 1 H, J = 2.4 Hz); ^{13}C NMR δ 100.3, 81.4, 75.8, 71.5, 70.6, 67.6, 60.6, 59.2, 57.4, 54.9; MS (GC/EI) m/z 205, 161, 101, 89, 88, 87, 75, 74, 71, 59, 45. The alcohol was acetylated with Ac_2O in pyridine at 0 °C to give **methyl 2-*O*-acetyl-3,4,6-tri-*O*-methyl-α-D-mannopyranoside** as an oil (80%). Anal. Calcd for $C_{12}H_{22}O_7$: C, 51.79; H, 7.97. Found: C, 51.91; H, 7.96.

Methyl 3,4,6-Tri-*O*-methyl-β-D-glucopyranoside (3d). Bromohydrins **4a–d** (350 mg, 1.2 mmol), 18-crown-6 (325 mg, 1.2 mmol), KHMDS (1.2 mmol), and methanol (3 mL) gave **3d** (81 mg, 0.4 mmol, 28%) as an oil (and **5d**, 9%): $[\alpha]_D$ −6.58 (c = 1.16; $CHCl_3$); IR (neat) 3450, 2935, 2837, 1449, 1380, 1189, and 1070 cm^{-1}; ^1H NMR δ 4.14 (d, 1 H, J = 7.5 Hz), 3.66 (dd, 1 H, J = 10.5, 2.1 Hz), 3.66 (s, 3 H), 3.58 (dd, 1 H, J = 10.5, 4.2 Hz), 3.54 (s, 3 H), 3.53 (s, 3 H), 3.41 (s, 3 H), 3.38–3.30 (m, 2 H), 3.25–3.19 (m, 2 H), 2.57 (d, 1 H, J = 2.7 Hz); ^{13}C NMR δ 103.6, 85.9, 79.3, 74.9, 74.0, 71.2, 60.7, 60.3, 59.3, 57.1; MS (GC/CI) m/z 234 (M) 205, 173, 141, 113, 99, 89, 75, 71. The alcohol was acetylated with Ac_2O in pyridine at 0 °C to give **methyl 2-*O*-acetyl-3,4,6-tri-*O*-methyl-β-D-glucopyranoside** as an oil (80%). Anal. Calcd for $C_{12}H_{22}O_7$: C, 51.79; H, 7.97; Found: C, 51.67; H, 7.95.

Cyclization of the Trimethyl Bromohydrins with Sodium Methoxide and *in Situ* Trapping with Methanol. A solution of the bromohydrins **4a–d** (264 mg, 0.9 mmol) in anhydrous methanol (6 mL) was cooled to 5 °C. Sodium methoxide (25% w/w in MeOH, 0.64 mL, 2.8 mmol) was added gradually (5 min) to the stirred solution. The solution temperature was maintained at 5 °C for 4 h and then was slowly warmed to room temperature (3 h) and stirred overnight (15 h). The mixture was diluted with water (50 mL) and extracted with CH_2Cl_2 (3×, 30 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. SiO_2 chromatography gave **3d** (42%), **5d** (15%), and aldehyde **9a** (9%) as an oil: IR ($CDCl_3$) 3102, 2934, 2828, 1702, 1618, 1176, 1090, 940 cm^{-1}; ^1H NMR δ 9.23 (s, 1 H), 6.10 (d, 1 H, J = 2.7 Hz), 4.71 (dd, 1 H, J = 2.7, 4.7 Hz), 4.65 (m, 1 H), 3.59 (dd, 1 H, J = 4.8, 10.5 Hz), 3.49 (dd, 1 H, J = 4.8, 10.5 Hz), 3.39 (s, 3 H), 3.37 (s, 3 H); ^{13}C NMR δ 182.3 (CH), 157.7 (C), 115.2 (CH), 85.7 (CH), 83.8 (CH), 71.8 (CH_2), 59.4 (CH_3), 55.8 (CH_3); MS (DP/EI) 172 (M^+), 127, 111, 85, 71, 69, 53, 45.

Cyclization of the Trimethyl Bromohydrins with Cesium Carbonate and *in Situ* Trapping with Methanol. A solution of the bromohydrins **4a–d** (230 mg, 0.8 mmol) in anhydrous methanol (6 mL) was cooled to 5 °C, and cesium carbonate (263 mg, 0.8 mmol) was added. The solution was maintained at 5 °C for 4 h and then was gradually warmed to room temperature (3 h) and stirred overnight (15 h). The reaction mixture was worked up as described above. SiO_2 chromatography gave **3d** (41%), **5d** (10%), and the aldehyde **9a** (6%).

Cyclization of the Tribenzyl Bromohydrins with Cesium Carbonate and *in Situ* Trapping with Methanol. Reaction of tribenzyl bromohydrins **7a–d** (413 mg, 0.8 mmol) with cesium carbonate (262 mg, 0.8 mmol) in methanol (6 mL) as above gave **methyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (3f)**[21] (40 mg, 0.09 mmol, 11%) as an oil: IR ($CDCl_3$) 3446, 3030, 2913, 1454, 1104, 1058, and 1028 cm^{-1}; ^1H NMR δ 7.37–7.25 (m, 13 H) 7.19–7.15 (m, 2 H), 4.84–4.48 (m, 8 H), 4.03 (t, 1 H, J = 2.3 Hz), 3.8–3.69 (m, 4 H), 3.36 (s, 3 H), 2.43 (br s, 1 H); ^{13}C NMR δ 138.2, 138.1, 137.8, 128.5, 128.4, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, 127.5, 100.2, 80.2, 75.1, 74.3, 73.5, 72.0, 70.9, 69.0, 68.3, 54.9. The alcohol was acetylated with Ac_2O in pyridine at 0 °C to give **methyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside**[21] as an oil [IR ($CDCl_3$) 3022, 2928, 1746, 1454, 1369, 1236, 1140, and 1079 cm^{-1}; ^1H NMR δ 7.34–7.14 (m, 15 H), 5.35 (d, 1 H, J = 2.4 Hz), 4.87–4.45 (m, 8 H), 3.99–3.70 (m, 5 H), 3.36 (s, 3 H), 2.15 (s, 3 H); ^{13}C NMR δ 170.6, 149.8, 138.4, 137.9, 128.3, 128.2, 128.1, 128.0, 127.8, 127.7, 127.66, 127.60, 127.5, 98.8, 83.6,

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78.2, 77.5, 75.2, 74.4, 73.5, 71.8, 71.3, 68.7, 21.3] and **methyl 3,4,6-tri-*O*-benzyl-β-D-glucopyranoside (5f)**[22] (163 mg, 0.3 mmol, 44%) as a white solid: IR ($CHCl_3$) 3450, 3029, 2866, 1453, 1113, 1061, and 1028 cm^{-1}; ^1H NMR δ 7.39–7.23 (m, 13 H), 7.18–7.15 (m, 2 H), 4.81–4.49 (m, 3 H), 4.65–4.52 (m, 3 H), 4.18 (d, 1H, J = 7.2 Hz) 3.77–3.48 (m, 6 H), 3.56 (s, 3 H), 2.44 (d, 1 H, J = 2.1 Hz); ^{13}C NMR δ 138.4, 138.0, 137.9, 128.4, 128.3, 128.2, 128.1, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 127.2, 103.6, 84.4, 77.6, 75.1, 75.0, 74.9, 74.6, 73.5, 68.8, 57.1. The alcohol was acetylated with Ac_2O in pyridine at 0 °C to give **methyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranoside:**[4a] IR ($CDCl_3$) 3030, 2867, 1748, 1454, 1370, 1233, and 1060 cm^{-1}; ^1H NMR δ 7.34–7.25 (m, 13 H), 7.19–7.16 (m, 2 H) 5.02–4.97 (t, 1 H, J = 8.4 Hz) 4.81–4.54 (m, 6 H) 4.29 (d, 1 H, J = 7.8 Hz), 3.75–3.66 (m, 4 H) 3.51–3.40 (m 1 H), 3.48 (s, 3 H), 1.97 (s, 3 H); ^{13}C NMR δ 169.5, 137.8, 128.4, 128.3, 127.9, 127.8, 127.7, 127.6, 127.5, 101.7, 83.0, 78.0, 77.0, 75.0, 73.5, 73.0, 64.0, 56.6, 21.1. Aldehyde **9b** (40 mg, 0.09 mmol, 11%): IR (neat) 3029, 2856, 1696, 1618, 1174, 1063, 735, and 696 cm^{-1}; ^1H NMR δ 9.50 (s, 1 H), 7.37–7.25 (m, 10 H), 6.02 (d, 1 H, J = 2 Hz), 4.90 (dd, 1 H, J = 3.0, 3.9 Hz), 4.79–4.73 (m, 1 H), 4.69 (br s, 2 H), 4.58–4.53 (m, 2 H), 3.64 (dd, 1 H, J = 4.7, 10.3 Hz), 3.51 (dd, 1 H, J = 4.7, 10.3 Hz); ^{13}C NMR δ 182.3 (CH), 157.6 (C), 137.50 (C), 137.45 (C), 128.5, 128.4, 128.3, 127.9, 127.9, 127.8, 127.7, 126.9 (aromatic CH), 116.1 (CH), 86.3 (CH), 82.3 (CH), 73.6 (CH_2) 70.9 (CH_2), 69.2 (CH_2); MS (DP/EI) m/z 324 (M^+), 295, 233, 203, 92.

Cyclization with Cesium Carbonate and *in Situ* Trapping with Deuterated Methanol. The above reaction was repeated in MeOD (6 mL) with bromohydrins **4a–d** (279 mg) to yield the 2-{^2H} methylglycosides **3g** (28%) and **5g** (6%) and aldehyde (23%). Acetylation of **3g** and **5g** with acetic-d_6 anhydride in pyridine at 5 °C gave the 2-*O*-acetates-d_3 **3h** and **5h**, respectively.

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Supplementary Material Available: The ^1H NMR spectra of the epoxidation reaction in progress and of bromohydrins **4a–d** in toluene-d_8 and $CDCl_3$ and the ^1H and ^2H NMR spectra of the deuterated glycosides **3h** and **5h** (9 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of this journal, and can be ordered from the ACS; see any current masthead page for ordering information.