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Diastereoselective Bromination of Allyl Glycosides Using Tetrabutylammonium Tribromide‡

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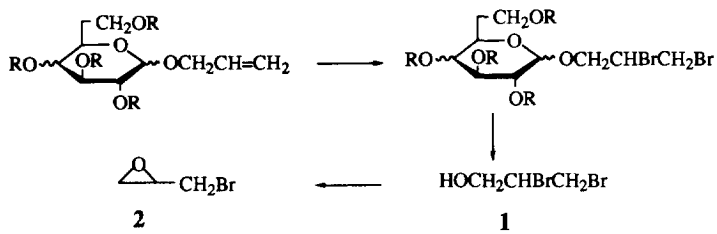
Abstract: Both (R) and (S)-2,3-dibromo-1-propanol with e.e. up to 60% have been obtained by diastereoselective addition of Br_2 to allyl glucosides and galactosides having only one unprotected hydroxyl group at C-2 or C-6 using tetrabutylammonium tribromide, followed by hydrolysis. The absolute configuration is shown to depend on the position of the free hydroxyl and on the configuration at the anomeric centre.

While chiral auxiliary bound derivatives of carbonyl compounds such as ketals,[1] silyl ketene acetals,[2] and imide enolates,[3] have been reported to undergo very successful diastereoselective bromination leading to α bromo substituted products with very high enantiomeric excesses (e.e.), the asymmetric bromination of simple olefins to give 1,2-dibromo derivatives has given much less promising results. Thus, the use of Br_2 complexed to chiral Cinchona alkaloids[4] or to chiral quaternary ammonium bromides[5] under heterogeneous conditions gave low to moderate e.e. in the bromination of prochiral or racemic olefins. Typically, *trans*-1,2-dibromocyclohexane was obtained with a maximum e.e. of *ca.* 10 and 30% respectively.[6] Slightly better results have been obtained by using free Br_2 and a substrate complexed to a chiral host. Thus, a 40% e.e. was reported for the dibromide resulting from the bromination of *trans*-cinnamic acid as an inclusion complex in crystalline β-cyclodextrin.[7] On the other hand, the obtainment of bromohydrins with moderate to very high e.e. by N-bromoacetamide reaction of olefins bound to tartaric acid derivatives has been reported.[8] We therefore thought that dibromides with improved e.e. could be obtained by bromine addition to simple olefins bound to chiral auxiliares.

Sugars, easily available natural compounds, have been increasingly employed in the last few years as chiral auxiliaries for asymmetric synthesis.[9] Although their multiple stereogenic centres and multifunctionality may introduce complications in the selective formation of diastereoisomeric intermediates, proper regio- and stereoselective functionalization allows one to obtain numerous structural variations which can improve the diastereoselection and help in understanding the diastereoselection mechanism. The sugar moiety can be easily removed, especially when bound to an alcohol by an easily hydrolysable glycosyl bond. We therefore decided to investigate the bromination of allyl D-galactopyranosides and D-glucopyranosides in order toobtain, after hydrolysis, optically active 2,3-dibromo-1-propanol (**1**), which can be easily transformed

‡Dedicated to Professor Giancarlo Berti on occasion of his 70th birthday.

to the epibromohydrin **2** of inverted configuration. Considerable attention has been paid recently to the



2 **1**

preparation of optically active **1** by microbial resolution of the racemate.[10]

RESULTS AND DISCUSSION

The suitably functionalized allyl D-galactopyranosides and D-glucopyranosides used in this investigation have been synthesised as reported in Scheme 1.

Allyl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranoside (**3**) was prepared from tetra-O-acetyl-D-galactopyranosyl bromide as previously reported.[11]

Allyl 6-O-benzyl-α-D-galactopyranoside (**5**) was obtained from commercial 1,2:3,4-di-O-isopropylidene-D-galactopyranose by benzylation followed by treatment with hydrogen chloride in anhydrous allyl alcohol. Treatment of **5** with 2,2-dimethoxypropane (DMP) and TsOH gave a mixture of **6** and a by-product containing a labile 1-methoxy-1-methylethyl (MIP) group at the C-2 oxygen, which was selectively removed by treatment with aqueous methanol.

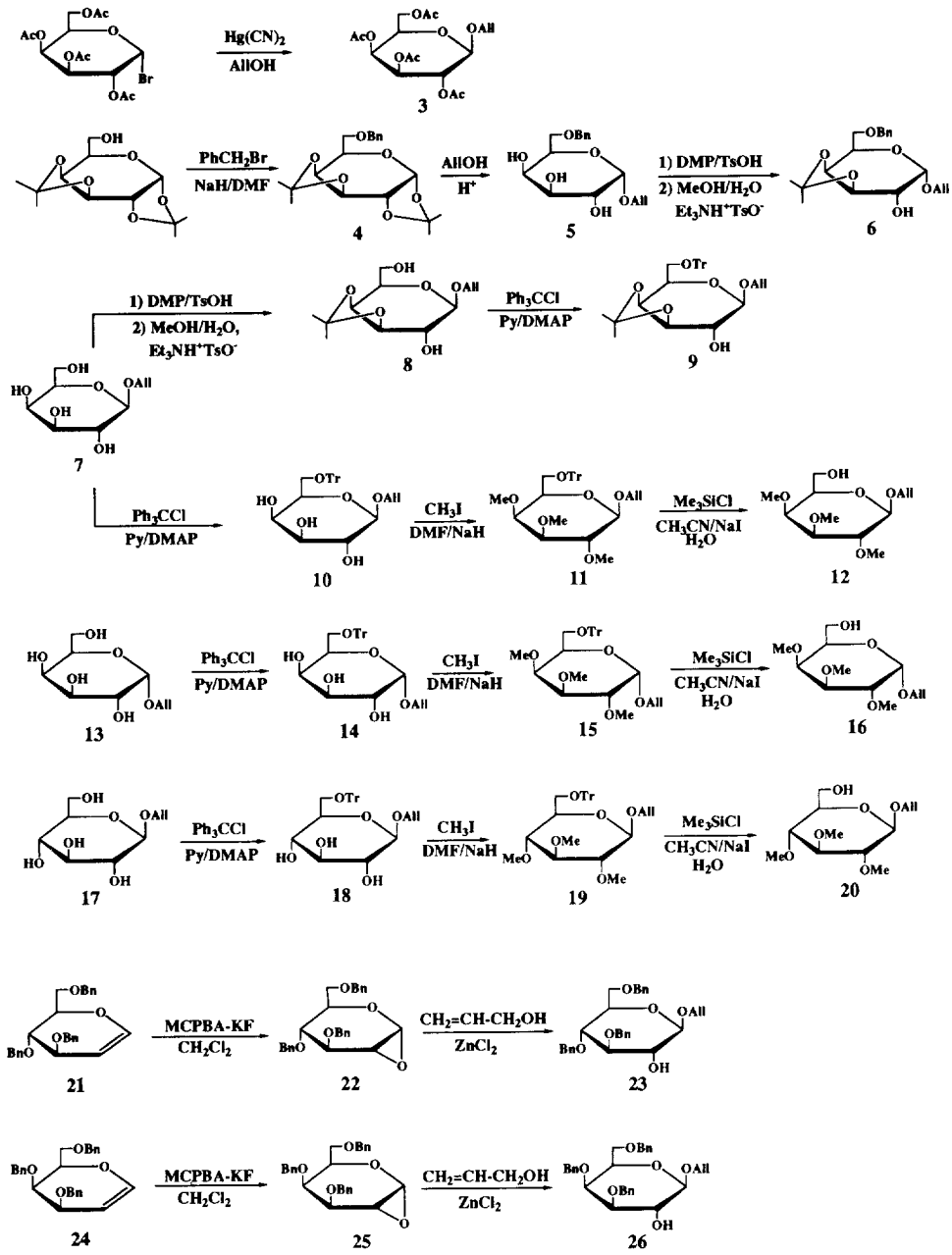
Allyl 3,4-O-isopropylidene-β-D-galactopyranoside (**8**) was analogously obtained from allyl β-D-galactopyranoside (**7**)[11] by DMP treatment followed by removal of the MIP groups present at C-2 and C-6 of by-products. The subsequent tritylation of **8** gave, after purification by column chromatography, pure **9**.

The allyl 2,3,4-tri-O-methyl-β- and α-D-galactopyranosides **12** and **16**, and the corresponding allyl β-D-glucopyranoside **20** were synthesised from the corresponding allyl glycosides **7**, **13** and **17** by tritylation at C-6, followed by exhaustive methylation with CH_3I/NaH in DMF and selective deprotection from the trityl ether with Me_3SiCl.

The 3,4,6-tri-O-benzyl-β-D-glucopyranoside **23** and the analogous galactopyranoside **26** were prepared from the corresponding glycals **21** and **24** by epoxidation with MCPBA-KF in anhydrous CH_2Cl_2,[12] followed by oxirane ring opening with allyl alcohol in the presence of $ZnCl_2$.

These allyl glycosides were subjected to bromination both with molecular Br_2 (with the exception of **6** and **9** which were unstable in the presence of the free halogen) and with tetrabutylammonium tribromide in two moderate polarity aprotic solvents, 1,2-dichloroethane and dichloromethane, at several temperatures. The brominated glycosides were then hydrolysed in acidic medium at 60 °C and the e.e. of the recovered 2,3-dibromo-1-propanol was determined by GLC analysis using a chiral column. Samples of the dibromo alcohol **1** were also subjected to base promoted ring closure to the corresponding epibromohydrin, **2**, whose e.e. was determined by GLC on the same chiral column. Identical e.e's were obtained for both 2,3-dibromo-1-propanoland the resulting epibromohydrin.

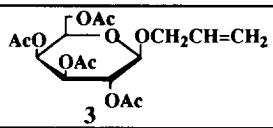
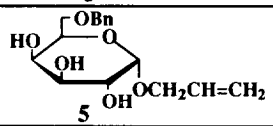
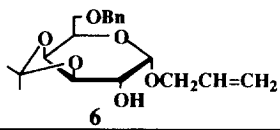
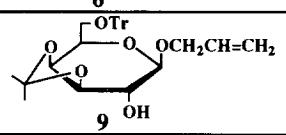
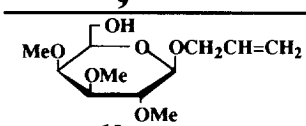
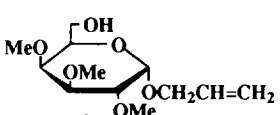
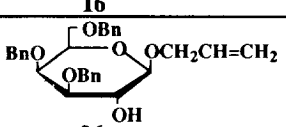
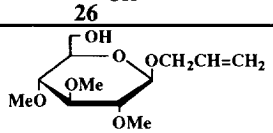
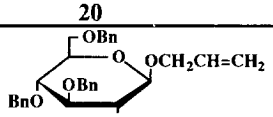
Scheme 1



DMP = 2,2-dimethoxypropane; All =-CH_2-CH=CH_2; Tr=-CPh_3

The absolute configuration of **1** was inferred on the basis of its reported relationship with the specific rotation, R-(+).[10] The obtained e.e. and absolute configurations are reported in the Table.

Table. Bromination of Allyl Glycosides with Br_2 and $Bu_4N^+Br_3^-$.

Compound	Brominating Agent	Solvent	T (°C)	e.e. of 1	Abs. Conf.
 **3**	Br_2	DCE	25	0	
	$Bu_4N^+Br_3^-$	DCE	25	0	
 **5**	Br_2	DCE	25	0	
	$Bu_4N^+Br_3^-$	DCE	25	14	S
 **6**	$Bu_4N^+Br_3^-$	DCE	25	30	S
	$Bu_4N^+Br_3^-$	DCE	-18	50	S
	$Bu_4N^+Br_3^-$	DCM	4	30	S
	$Bu_4N^+Br_3^-$	DCM	-86	50	S
 **9**	$Bu_4N^+Br_3^-$	DCE	-18	40	R
	$Bu_4N^+Br_3^-$	DCM	4	36[a]	R
 **12**	Br_2	DCE	0	16	S
	$Bu_4N^+Br_3^-$	DCE	-18	12	S
	$Bu_4N^+Br_3^-$	DCM	-86	20	S
 **16**	Br_2	DCE	-13	16	R
	$Bu_4N^+Br_3^-$	DCE	-18	50	R
	$Bu_4N^+Br_3^-$	DCM	4	40	R
	$Bu_4N^+Br_3^-$	DCM	-86	60	R
 **26**	Br_2	DCE	0	0	
	$Bu_4N^+Br_3^-$	DCE	-18	40	R
 **20**	Br_2	DCE	0	16	
	$Bu_4N^+Br_3^-$	DCE	-18	30	S
	$Bu_4N^+Br_3^-$	DCM	-86	20	S
 **23**	Br_2	DCE	0	0	
	$Bu_4N^+Br_3^-$	DCE	-18	40	R
	$Bu_4N^+Br_3^-$	DCM	4[a]	36	R

[a] At - 86 °C the unreacted allyl glycoside was recovered even after 7 days.

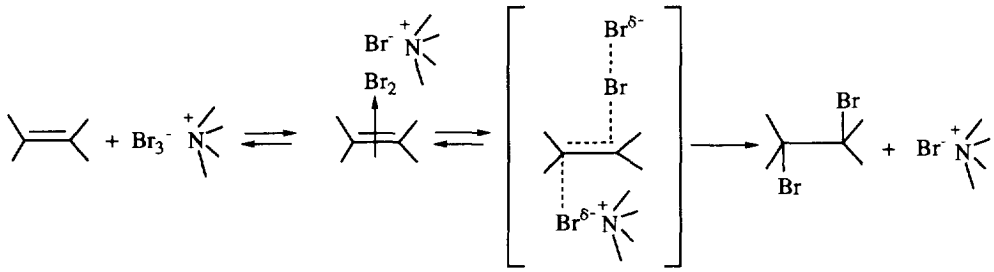
The reactions of molecular Br_2 always exhibited very low, if any, diastereoselctivity. The tribromide reaction of the peracetylated allyl-β-D-galactopyranoside **3** was likewise completely non-diastereoselective and that of derivative **5**, having three free hydroxyl groups, showed very little diasteroselectivity. In contrast, both allyl D-galacto- and D-glucopyranosides having only one free hydroxyl at C-2 or C-6 were brominated by $Bu_4N^+Br_3^-$ with a remarkable diastereoselectivity. However, with D-galactopyranosides having the C-2 free OH the absolute configuration of the excess enantiomer of **1** was inverted on passing from an α to a β anomer (compare **6** and **9**). Furthermore, also the presence of a free OH at C-6 instead of C-2 in both α- and β-D-galactopyranosides and in β-D-glucopyranosides produced an inversion in the configuration of the excess enantiomer of dibromide **1** (compare **6** and **16**, **12** and **26**, and **20** and **23**). Thus, 2,3-dibromo-1-propanol enriched in either the (R) or the (S) enantiomer can be obtained by changing the position of the free hydroxyl from C-2 to C-6 or by inverting the configuration at the anomeric centre. As expected, the e.e. was not affected by the stereochemistry at C-4 (gluco- or galactopyranosides) and by the presence of an isopropylidene bridge in place of two ether functions at C-3 and C-4 (compare **9**, **23** and **26**).

A change in solvent from dichloroethane to the slightly less polar dichloromethane had no relevant effect, while a decrease in temperature produced only a modest increase in the diastereoselectivity. The best results were obtained with the allyl α-D-galactopyranoside derivatives **6** and **16**, from which (S) and (R)-2,3-dibromo-1-propanol with respective 50 and 60% e.e. were obtained at -86 °C in dichloromethane. A dramatic drop in diastereoselection was found when the bromination of all investigated allyl glycosides was carried out in a more polar solvent like acetonitrile, where practically racemic 2,3-dibromo-1-propanol was always obtained.

The lack of any asymmetric induction in the brominations carried out with free Br_2, as opposed to the remarkable diastereoselectivity found with $Bu_4N^+Br_3^-$ for allyl glycosides having one free OH group near to the site of binding of the allyl group, suggests that some kind of hydrogen bonding, occurring during the Br_3^- reaction but not during the free Br_2 addition, may be responsible for these results. This conclusion is consistent with the different bromination mechanisms shown for these two reagents.[13] Both mechanisms involve the pre-equilibrium formation of olefin-Br_2 charge transfer complexes (CTC). The reactions of Br_2 in aprotic solvents proceed through a Br_2 assisted ionization of these complexes to give bromonium-tribromide ion pairs, which then collapse to dibromide products. Hydrogen bonding to the developing counteranion during the CTC ionization is not required, because of the stable charge delocalized nature of the Br_3^- ion. In contrast, when $Bu_4N^+Br_3^-$ is the source of bromine, the olefin-Br_2 CTC present in equilibrium with Br_3^- and the olefin undergoes a slow nucleophilic attack by the bromide that has become detached from Br_2 at the moment of formation of this CTC (or that is present as added salt), while a bromine-bromine bond is being broken and a new bromide ion is formed. (Scheme 2). This process can be assisted by hydrogen bonding to the developing Br^-, as shown by the dependence of the olefin bromination rates on the hydrogen bonding ability of the solvent, and by the solvent kinetic isotope effect measured in $CHCl_3$-$CDCl_3$.[13]

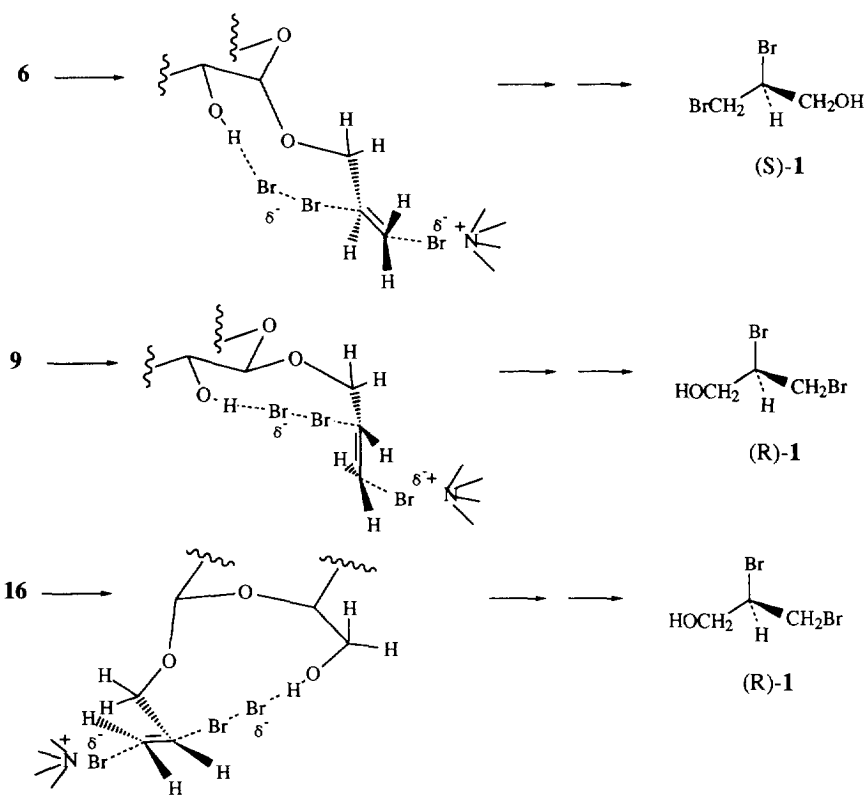
In the Br_3^- reactions of the presently investigated allyl glycosides the breaking of the Br-Br bond in the CTC accompanying the formation the C-Br bonds can be electrophilically assisted by hydrogen bonding of the OH group at C-2 or C-6 and the diastereoselectivity of the addition should be due to a faster reaction of the CTC formed at the face of the double bond which is exposed to the free hydroxyl. Molecular mechanics calculations (MMX) with PCMODEL show that in their more stable conformations the D-galactopyranosides **6** and **9**, taken as models for α and β glycosides having a free OH at C-2, and the α-D-galactopyranoside **16**,

Scheme 2



having the free OH at C-6, expose the *Re*, the *Si*, and the *Si* face of the double bond to the hydroxyl group, respectively. Backside attack by Br^- at the less substituted carbon of the CTC formed at this face, as shown in Scheme 3, is expected to lead respectively to the (S), (R), and (R) dibromo derivative **1**, as actually found. On the other hand, the large drop in diastereoselectivity observed in the bromination of allyl α-D-galactopyranoside **5**, having free OH at C-2, C-3, and C-4, may be due to hydrogen bonding between these hydroxyl groups, preventing the electrophilic solvation of the departing bromide anion in the transition state.

Scheme 3



Work is in progress in order to design, on the basis of the acquired mechanistic information, new asymmetric syntheses of this type which can lead to dibromo alcohols and bromo epoxides with improved enantiomeric excesses.

EXPERIMENTAL

All melting points were measured on a Kofler apparatus and are uncorrected. NMR spectra were registered with a Bruker AC 200 instrument using tetramethylsylane as internal standard. GLC analyses were carried out with a Carlo Erba HRGC 5300 instrument equipped with a 10 m Chiraldex G-TA (ASTEC) column, nitrogen flow 1 ml/min, evaporator and detector 180 °C, at the following temperatures: 95 °C for **1**, and 80 °C for **2**. Optical rotations were measured in chloroform solution (c = 1.0 ± 0.2) with a Perkin Elmer 241 digital polarimeter. All reactions were followed by TLC on Kieselgel 60 F254 with detection by UV or with ethanolic 10% sulphuric acid and heating. Kieselgel 60 (Merk, 70-230 or 230-400 mesh) was used for column and flash chromatography. Reactions in anhydrous conditions were carried out under an argon atmosphere.

Materials: All solvents were RPE grade. Bromine was withdrawn from 1 ml vials (C. Erba, RPE grade) opened immediately before use. Tetrabutylammonium bromide (Aldrich) was crystallized from benzene/AcOEt.

Allyl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranoside (3). Compound **3** was prepared from the corresponding α-glycosyl bromide by $Hg(CN)_2$-catalysed glycosilation.[11]

Allyl 6-O-benzyl-α-D-galactopyranoside (5). Compound **4**, obtained by benzylation[14] of commercial 1,2:3,4-di-O-isopropylidene-D-galactopyranose, was transformed to **5** by treatment with hydrogen chloride in dry allyl alcohol.[15] The product was crystallised from AcOEt-hexane to give pure **5** in a 45% yield as plates. Characterisation data for the final product agreed with published values.[15]

Allyl 6-O-benzyl-3,4-O-isopropylidene-α-D-galactopyranoside (6). A suspension of **5** (750 mg, 2.4 mmol) and TsOH (15 mg) in 2,2-dimethoxypropane (25 ml) was shaken at room temperature for 12 h, during which time the starting material completely disappeared and one major product was formed, accompanyed by a small amount of a side-products, having a 1-methoxy-1-methylethyl (MIP) group at the C-2 oxygen (TLC).[16] Triethylamine (0.2 ml) was then added, the reaction mixture was evaporated under reduced pressure, the residue dissolved in 10:1 methanol/water (15 ml) and the resulting solution was heated at 50 °C for 3 h in order to selectively remove the MIP group in the side-product.[16] After evaporation *in vacuo* and drying by coevaporation of the residue with toluene, chromatography over silica gel (1:1 hexane-AcOEt) gave pure **6** in 95% yield. The ^1H NMR spectrum and other characterisation data for the final product agreed with published values.[15a, 17] ^{13}C NMR ($CDCl_3$) δ: 25.89 and 27.70 (2 dioxolane Me); 68.51 and 69.41 (C-6 and OCH_2); 67.42, 69.49, 73.22 and 76.08 (C-2, C-3, C-4 and C-5); 73.33 (benzylic CH_2); 96.49 (C-1); 109.49 (dioxolane C); 117.80 (=CH_2); 127.53, 128.31 and 128.31 (aromatic CH); 133.58 (=CH); 138.60 (aromatic C).

Allyl 3,4-O-isopropylidene-6-O-trityl-β-D-galactopyranoside (9): Allyl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranoside (**3**) was deacetylated to allyl β-D-galactopyranoside (**7**) as reported by Lee and Lee.[11] Treatment of **7** (800 mg, 3.65 mmol), as reported above for the preparation of **6** from **5**, and chromatography of the crude product over silica gel (1:1 hexane-AcOEt) gave pure **8** (900 mg, 96% yield). Characterisation data for the final product agreed with published values.[18] A solution of **8** (730 mg, 2.8 mmol), and triphenylmethyl chloride (1.32 g, 4.7 mmol) in dry pyridine (10 ml) was kept at room temperature. After 72 h TLC (6:4 hexane-AcOEt) showed that the starting material had completely disappeared and one product had formed. The solvent was removed under reduced pressure, the residue was coevaporated with toluene and finally chromatographed over silica gel (6:4 hexane-AcOEt) to give pure **9** (1.04 g, 74% yield) as solid. R_f 0.36 (6:4 hexane/AcOEt), m.p. 56-58 °C (from hexane), $[\alpha]_D$ -19.4. ^1H NMR ($CDCl_3$) δ: 1.36 and 1.68

(2s, 6H, 2 dioxolane Me); 3.45-4.05 (m, 6H, sugar CH); 4.08 (d, 1H, $J_{1,2}$=8.2 Hz, H-1); 4.29 (m, 2H, OCH_2); 5.12 (m, 2H, $=CH_2$); 5.85 (m, 1H, =CH); 7.00-7.60 (m, 15H, aromatic H). ^{13}C NMR ($CDCl_3$) δ: 26.39 and 28.22 (2 dioxolane Me) 68.37 and 69.72 (C-6 and OCH_2); 72.79, 73.91, 74.07 and 79.36 (C-2, C-3, C-4 and C-5); 86.95 ($C(Ph)_3$); 101.70 (C-1); 109.83 (dioxolane C); 117.48 ($=CH_2$); 127.53-129.00 (aromatic CH); 134.45 (=CH); 144.70 (aromatic C). Anal. Calcd. for $C_{31}H_{34}O_6$: C, 74.08; H, 6.82. Found: C, 74.25; H, 6.93.

Allyl 2,3,4-tri-O-methyl-β-D-galactopyranoside (12). A solution of **7** (980 mg, 4.5 mmol) and triphenylmethyl chloride (1.6 g; 5.7 mmol) in dry pyridine (6 ml) was kept at room temperature for 48 h and then coevaporated with toluene to give **10**. The crude product (2 g) was dissolved in N,N-dimethylformamide (25 ml) and cooled to 0°C. Sodium hydride (0.9 g; 30 mmol), obtained from an 80% dispersion in mineral oil after washing with hexane, and methyl iodide (0.4 ml, 6.5 mmol) were added, and the mixture was allowed to warm to room temperature. After 3 h the excess of sodium hydride was decomposed by addition of methanol, and the bulk of the DMF was removed in a rotary evaporator. The syrup residue was taken up in water, and the product was extracted with dichloromethane. The organic phase was then washed with water, dried ($MgSO_4$) and evaporated to give **11** in near-quantitative yield. Crude **11** (1.2 g) was dissolved in anhydrous acetonitrile (35 ml), and NaI (1.14 g, 7.5 mmol) and trimethylsilyl chloride (0.80 ml) were added. After 5 min, water (50 ml) was added and the reaction mixture was cooled at 0 °C. After 15 min the mixture was filtered and the solution was extracted with CH_2Cl_2. The organic phase was washed with 10% aqueous $Na_2S_2O_3$, dried ($MgSO_4$) and evaporated. Chromatography over silica gel (1:9 hexane-AcOEt) gave pure **12** as syrup in 60% yield. Rf = 0.27 (AcOEt), $[\alpha]_D$ = - 29.1. ^{1}H NMR ($CDCl_3$) δ: 3.22-4.48 (m, 8H, OCH_2 and sugar CH); 3.58, 3.61,and 3.66 (3s, 9H, OCH_3); 4.36 (d, 1H, $H_{1,2}$=7.57 Hz, H-1); 5.30 (m, 2H, $=CH_2$); 5.60 (m, 1H, =CH). ^{13}C NMR ($CDCl_3$) δ: 58.36, 60.76 and 61.10 (3 OCH_3); 61.90 and 69.96 (C-6 and OCH_2); 74.51, 75.36, 80.52 and 83.84 (C-2, C-3, C-4 and C-5); 102.69 (C-1); 116.76 ($=CH_2$); 134.10 (=CH). Anal. Calcd. for $C_{12}H_{22}O_6$: C, 54.95; H, 8.45. Found: C, 54.85; H, 8.52.

Allyl 2,3,4-tri-O-methyl-α-D-galactopyranoside (16). Allyl α-D-galactopyranoside (**13**) was prepared, as reported,[11b] by Lewis acid-catalysed glycosilation with Dowex 50 ion-exchange resin and treated as decribed above for the preparation of **12** from **7**. Pure **16** was obtained as syrup in 64% yield. Rf = 0.27 (AcOEt), $[\alpha]_D$ = + 138.9. ^{1}H NMR (C_6D_6) δ: 3.32, 3.34 and 3.46 (3s, 9H, OCH_3); 3.49-4.00 (m, 6H, sugar CH); 4.17 (m, 2H, OCH_2); 5.00 (d, 1H, $H_{1,2}$=3.56 Hz, H-1); 5.22 (m, 2H, =CH); 5.92 (m, 1H, =CH). ^{13}C NMR (C_6D_6) δ: 58.12, 58.61 and 61.10 (3 OCH_3); 62.12 and 68.45 (C-6 and OCH_2); 71.45, 77.06, 78.54 and 80.52 (C-2, C-3, C-4 and C-5); 96.56 (C-1); 117.14 ($=CH_2$); 134.71 (=CH). Anal. Calcd. for $C_{12}H_{22}O_6$: C, 54.95; H, 8.45. Found: C, 55.02; H, 8.50.

Allyl 2,3,4-tri-O-methyl-β-D-glucopyranoside (20). The allyl β-D-glucopyranoside (**17**), prepared as reported by Lee and Lee,[11] was treated as decribed above for the preparation of **12** from **7**. The pure **20** was obtained as a solid in 60% yield. Rf = 0.48 (AcOEt), m.p. 51-52 °C (from hexane), $[\alpha]_D$ = - 33.6. ^{1}H NMR ($CDCl_3$) δ: 3.00-4.35 (m, 8H, OCH_2 and sugar CH); 3.55, 3.59 and 3.63 (3s, 9H, OCH_3); 4.33 (d, 1H, $J_{1,2}$=7.67 Hz, H-1); 5.27 (m, 2H, $=CH_2$); 5.93 (m, 1H, =CH). ^{13}C NMR ($CDCl_3$) δ: 60.39, 60.39 and 61.00 (3 OCH_3); 61.70 and 70.17 (C-6 and OCH_2); 74.89, 79.14, 83.66 and 86.19 (C-2, C-3, C-4, and C-5); 102.31 (C-1); 117.00 ($=CH_2$); 133.84 (=CH). Anal. Calcd. for $C_{12}H_{22}O_6$: C, 54.95; H, 8.45. Found: C, 54.70; H, 8.50.

Allyl 3,4,6-tri-O-benzyl-β-D-glucopyranoside (23). Commercial tri-O-benzyl-D-glucal (**21**) was epoxidised as follows.[12] A dichloromethane solution (50 ml) containing *m*-chloroperoxybenzoic acid (860 mg, 5 mmol), dried with $MgSO_4$ and filtered, was treated with KF (580 mg, 10 mmol) and stirred for 30 min. Glucal (**21**) (850 mg, 2 mmol) was then added and the mixture was stirred for 24 h at room temperature. The insoluble complexes were then filtered off, and the solvent was removed under reduced pressure to give, in a 95% yield, a 9:1 mixture of **22** and the corresponding diastereoisomeric epoxide, which were identified on the basis of the reported ^{1}H and ^{13}C NMR spectra.[19]

This crude product (850 mg) was dissolved in anhydrous THF (50 ml) and treated with allyl alcohol (600 mg, 10 mmol). The mixture was cooled 0 °C and 1 M $ZnCl_2$ in ethyl ether (2 ml) was added. The reaction mixture was then allowed to warm to room temperature, stirred for 10 h, and finally diluted with water and extracted with ethyl acetate. The organic phase, washed and dried ($MgSO_4$), was evaporated *in vacuo* and the residue was chromatographed over silica gel (7:3 hexane-AcOEt) to give pure **23**[20] in a 55% yield. Rf = 0.25 (8:2, hexane-AcOEt). ^{1}H NMR ($CDCl_3$) δ: 3.48-4.65 (m, 12H, allylic OCH_2, 2 benzylic CH_2 and 6 sugar CH); 4.80-4.97 (m, 3H, benzylic CH_2 and H-1); 5.26 (m, 2H, $=CH_2$); 5.95 (m, 1H, =CH); 7.13-7.40 (m, 15H, aromatic). ^{13}C NMR ($CDCl_3$) δ: 68.72, 70.14 (C-6 and OCH_2); 73.38, 74.90 and 75.08 (3 benzylic CH_2); 74.53, 74.99, 77.44 and 84.42 (C-2, C-3, C-4 and C-5); 101.61 (C-1); 117.84 ($=CH_2$); 127.63- 128.34 (aromatic CH); 133.73 (=CH); 137.96-138.50 (aromatic C). Anal. Calcd. for $C_{30}H_{34}O_6$: C, 73.43; H, 6.99. Found: C, 73.58; H, 7.20.

Allyl 3,4,6-tri-O-benzyl-β-D-galactopyranoside (26). Tri-O-benzyl-D-galactal (**24**), prepared from commercial tri-O-acetyl-D-galactal by deacetylation[21] followed by benzylation according to general alkylation procedure,[22] was subjected to epoxidation with the MCPBA-KF complex,[12] under the same conditions employed for glucal **21**, to give essentially the epoxide **25**.[12] ^{1}H and ^{13}C NMR data for this compound agreed with the published values.[23] Crude **25** was then reacted with allyl alcohol in the presence of $ZnCl_2$, as described above for epoxide **22**. The resulting product was purified by column chromatography over silica gel (8:2 hexane-AcOEt) to give pure allyl 3,4,6-tri-O-benzyl-β-D-galactopyranoside **26** in a 60% yield. Rf = 0.49 (6:4, hexane-AcOEt). ^{1}H NMR (C_6D_6) δ: 3.28-4.72 (m, 13H, allylic OCH_2, 2 benzylic CH_2 and 7 sugar CH); 4.99-5.28 (m, 4H, $=CH_2$ and benzylic CH_2); 5.81 (m, 1H, =CH); 7.04-7.38 (m, 15H, aromatic). ^{13}C NMR (C_6D_6) δ: 69.14 and 69.76 (C-6 and OCH_2);, 72.86, 73.52 and 75.09 (3 benzylic CH_2); 72.19, 73.94, 74.59 and 82.37 (C-2, C-3, C-4 and C-5); 102.99 (C-1); 116.86 ($=CH_2$); 127.53-128.48 (aromatic CH); 134.82 (=CH); 138.75, 139.35 and 139.51 (aromatic C). Anal. Calcd. for $C_{30}H_{34}O_6$: C, 73.43; H, 6.99. Found: C, 73.22; H, 7.15.

Bromination Procedure. 1,2-Dichloroethane or dichloromethane solutions (*ca.* 4 x 10^{-2} M) of the allyl glycosides, prethermostated at the temperature reported in the Table, were mixed with equal volumes of prethermostated solutions of Br_2 or of $(Bu)_4N^+Br_3^-$ (containing a 10% excess of $(Bu)_4N^+Br^-$) in the same solvent at the same concentration. The reaction mixtures were maintained at the proper temperatures in the dark until the colour disappeared (typically 2-3 h for the Br_2 reactions and 3-5 days for the $(Bu)_4N^+Br_3^-$ reactions), and then evaporated *in vacuo* directly for mixtures obtained with free Br_2, or after repeated washing with water, in order to remove the formed $(Bu)_4N^+Br^-$, for those obtained with $(Bu)_4N^+Br_3^-$. The residues were analysed by ^{13}C NMR in order to check the disappearance of the olefinic signals and the appearance of the signals of the bromine bearing carbons at δ around 32.7 and 33.3 (diastereoisomeric CH_2Br) and 49.3 and 49.6 (diastereoisomeric CHBr). A rough preliminary evaluation of the diastereoselectivity of the bromination was given by the ratio of the signals for the diastereoisomeric carbons.

Hydrolysis of the 2,3-dibromopropyl glycosides. 2M Aqueous $HClO_4$ was added to the 2,3-dibromopropyl glycosides (*ca.* 400 mg) and the mixtures were maintained at 60 °C for 4 h. The solutions were then extracted with dichloromethane and the organic phases were dried ($MgSO_4$) and evaporated, and the obtained crude 2,3-dibromo-1-propanol **1** (*ca.* 90% yield) was analysed by GLC in order to determine the e.e. Samples were also occasionally subjected to the measure of the optical rotation in order correlate the GLC reaction times of the two enantiomers with their absolute configuration: (R)-**1** 16.30 min; (S)-**1** 17.30 min.

Dehydrobromination of 2,3-dibromo-1-propanol (1) to epibromohydrin (2.) Samples of **1** (*ca.* 300 mg) were dissolved in isopropyl alcohol (10 ml) and titrated with 1M NaOH in the presence of phenophthalein as indicator. After the end-point the reaction mixtures were left for 30 min at room temperature and then were extracted with ethyl acetate, dried ($MgSO_4$) and evaporated, and the crude epibromohydrin **2** was analysed by

GLC in order to check the e.e.. In all cases two peacks in ratios identical to those found for the parent dibromoalcohol **1** were found.

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