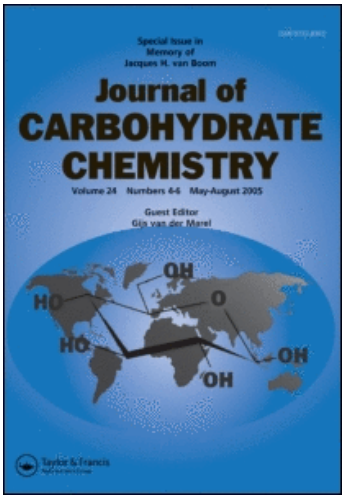

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Huiping Qin[a]; T. Bruce Grindley[a]
[a] Department of Chemistry, Dalhousie University, hali, N.S., Canada

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REGIOSELECTIVE FORMATION OF DI-*O*-BENZYL-SUBSTITUTED HEXOPYRANOSIDES VIA STANNYLENE ACETAL INTERMEDIATES

Huiping Qin and T. Bruce Grindley

Department of Chemistry, Dalhousie University,
Halifax, N.S., Canada B3H 4J3

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ABSTRACT

The reactions of dibutylstannylene acetals derived from several methyl hexopyranosides with benzyl bromide have been investigated. These reactions occur readily in benzyl bromide at 85 °C. At reaction times of one to two days, the major products are di-*O*-benzyl derivatives. In several cases, single di-*O*-benzyl derivatives are the predominant products: methyl α-**D**-glucopyranoside and methyl β-**D**-galactopyranoside gave the 2,6- and 3,6-di-*O*-benzyl ethers in 82 and 70% yields, respectively. The species present in these reactions and the reaction pathway are discussed.

INTRODUCTION

Partially benzylated glycopyranosides are important synthons for the preparation of oligosaccharides. A number of methods are available for the regioselective introduction of benzyl groups: reductive cleavage of benzylidene groups,[1,2] activation of hydroxyl groups through the formation of tributylstannyl ethers,[3,4] phase transfer catalysis,[5] selective activation through copper chelates,[6] activation via electrochemical reduction,[7] and the selective activation of diols with stannylene acetals.[3,8]

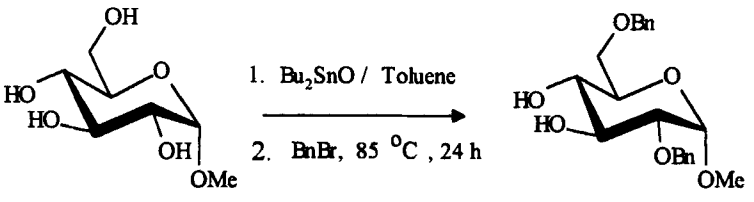
Each of these techniques has its advantages and limitations. Reductive cleavage is limited by the availability of appropriate di-*O*- and mono-*O*- benzylidene derivatives, although when available they can often be transformed into either hydroxy benzyl ether.[1,2]

Phase transfer catalysed alkylation takes place predominantly at the most acidic hydroxyl oxygen atom, normally O-2.[5] Copper chelates require quite basic conditions for formation. Alkylation takes place on the least basic oxygen with selectivity that ranges from excellent (>99:1) to fair (2:1). Results have not been reported for compounds with more than two free hydroxyl groups.[6] Stannyl ethers normally alkylate first on primary hydroxyl groups but yields of di-*O*-alkylated derivatives from pyranoside glycosides are relatively low.[3,4,9]

A number of studies of mono-*O*-alkylation of stannylene acetals derived from pyranoside glycosides have appeared.[3,10,11,12] Products are often obtained regioselectively and vary with the structure of the glycoside. Substitution takes place preferentially on secondary hydroxyl groups. We now report that regioselective di-*O*-benzylation of several methyl hexopyranosides can be achieved by way of stannylene acetal intermediates.

RESULTS AND DISCUSSION

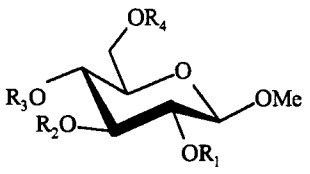
Dibutylstannylene acetals are easily formed from diols by refluxing solutions or mixtures of the diol with equimolar amounts of dibutyltin oxide in benzene or toluene. In the reactions reported here, the tetrol substrates were insoluble in toluene. The initially heterogeneous mixtures in toluene containing 1.5 or 2 equivalents of dibutyltin oxide became clear after being refluxed for about 20 m indicating formation of at least mono-*O*-stannylene acetals; reflux was continued for about 12 h to ensure complete conversion. Toluene was removed and the stannylene acetals were stirred in excess benzyl bromide for 24 to 75 h at about 85 °C to give the benzyl derivatives.

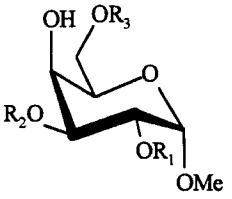


1 **6** (82 %)

Methyl α-D-glucopyranoside (**1**) gave a single product in 82% yield, the known 2,6-di-*O*-benzyl derivative (**6**). A better yield was obtained by using one and one-half rather than two equivalents of dibutyltin oxide.

Methyl β-D-glucopyranoside (**2**) also gave mainly its 2,6-di-*O*-benzyl derivative (**8**). However, compound **8** was obtained in lower yield than compound **6** and it was accompanied by a mixture of products with a composition that was dependent on reaction time. Structures were established by analysis of the ^{1}H NMR spectra of the per-*O*-acetates. The 2,6-di-*O*-benzyl derivative (**8**) was obtained in best yield after 50 h (56%). Also obtained from the 50 h reaction were the 3,6- and 4,6- isomers (**7** and **9**) in 16 and 15% yield, respectively. Compound **9** crystallized from a mixture of two di-*O*-benzyl



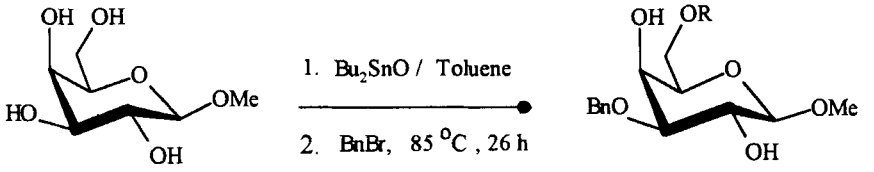


2 $R_1 = R_2 = R_3 = R_4 = H$
7 $R_1 = R_3 = H$ $R_2 = R_4 = Bn$
8 $R_1 = R_4 = Bn$ $R_2 = R_3 = H$
9 $R_1 = R_2 = H$ $R_3 = R_4 = Bn$
10 $R_1 = R_2 = R_3 = H$ $R_4 = Bn$
11 $R_1 = R_2 = Bn$ $R_3 = R_4 = H$
12 $R_1 = R_2 = R_4 = Bn$ $R_3 = H$

3 $R_1 = R_2 = R_3 = H$
13 $R_2 = R_3 = Bn$ $R_1 = H$
14 $R_1 = R_2 = R_3 = Bn$
15 $R_1 = R_3 = H$ $R_2 = Bn$

ethers that had very similar R_Fs. From the chemical shifts of C-2 and C-3 in its ^{13}C NMR spectrum, the other compound was tentatively assigned the 2,3-di-*O*-benzyl structure (**11**). The ratio of **11** to **9** present in the product mixture changed as a function of time, being 2:1 after 22 h (2 eq dibutyltin oxide), 1: 3.4 after 50 h, and 1:11 after 75 h. A significant amount of methyl 2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**12**) was isolated from the 75 h reaction and it seems likely that **7**, **8**, and **11** were slowly transformed into **12** and other products containing more than two benzyl groups as the reaction time increased.

The ratio of 2,6- to 3,6-di-*O*-benzyl products (**8** and **7**) for reaction times up to 50 h is similar to the ratio of 2- to 3- mono-*O*-benzyl ethers obtained by Haque *et al.* in monoalkylation reactions of **2** performed in dioxane.[11]



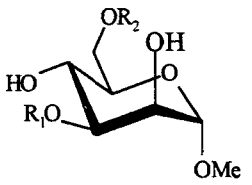
4

16 R = Bn (70 %)

17 R = H (8 %)

Methyl α-**D**-galactopyranoside (**3**) gave the 3,6-di-*O*-benzyl derivative (**13**) in reasonable yield (63%) plus a small amount of the 2,3,6-tri-*O*-benzyl derivative (**14**) (13%). It is probable that compound **14** arises from initial benzylation at O-2, followed by benzylation at O-3. Some 3-*O*-benzyl ether (**15**) was also obtained (2%).

The methyl β-glycoside of **D**-galactose (**4**) also afforded the 3,6-di-*O*-benzyl derivative (**16**) in reasonable yield (70%) but, in this case the only other product was the 3-*O*-benzyl ether (**17**) (8%).



5 $R_1 = R_2 = H$

18 $R_1 = R_2 = Bn$

19 $R_1 = Bn$ $R_2 = H$

Methyl α-**D**-mannopyranoside (**5**) gave the same pattern of substituted products as did **4**, but in lower yields; the 3,6-di-*O*-benzyl- (**18**) and 3-*O*-benzyl- (**19**) ethers were obtained in 35 and 12% yields, respectively. The majority of the product in this case consisted of tri-*O*-benzyl ethers that could not be separated or identified.

The yields of the selectively produced di-*O*-benzyl ethers were influenced by the amount of Bu_2SnO used. For methyl α- and β-**D**-glucopyranoside, methyl β-**D**-galactopyranoside and methyl α-**D**-mannopyranoside, using 1.5 eq. of Bu_2SnO gave higher yields of the major products. For methyl α-**D**-galactopyranoside, using 2.0 eq. of Bu_2SnO afforded a better yield.

Ogawa *et al.*[4] have previously performed benzylation reactions on compounds **1**, **4**, and **5** using tributylstannyl ethers as intermediates and obtained the same di-*O*-benzyl ethers as major products.[4,9] However, the yields of major products were normally lower and more complex product mixtures were obtained; for instance, from compound **1**, the

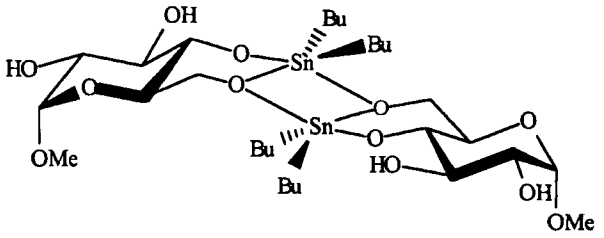


Figure 1. The 6,6-dimer of methyl 4,6-*O*-dibutylstannylene-α-**D**-glucopyranoside.

2,6- (**6**, 31%) , 3,6- (5%), and 4,6- (6%) di-*O*-benzyl ethers and the 6-*O*-benzyl ether (49%) were obtained;[4] from compound **4**, the 3,6-di-*O*-benzyl ether (**16**) (49%) and the 6-*O*-benzyl ether (24%) were obtained.[9] In contrast, compound **5** was benzylated more efficiently under these conditions, giving an 81% yield of **18** and 11% of a tri-*O*-benzyl derivative.

An attempt was made to determine the reaction pathway followed by these disubstitution reactions through an examination of their ^{119}Sn NMR spectra as a function of time for the reaction of the bis(dibutylstannylene acetal) of compound **1** (**1ds**).

The spectra of the dibutylstannylene acetals will be considered before the reaction pathway is discussed. The ^{119}Sn NMR spectrum of a low concentration solution (the saturated solution remaining after the reaction product of **1** with two equivalents of dibutyltin oxide was taken up in anhydrous chloroform-*d* and filtered) of **1ds** in chloroform-*d* at 20 °C contained only two sharp peaks at -126.2 and -223.4 ppm. From its chemical shift, the peak at -223.4 ppm can be assigned to a pentacoordinate tin atom in a dimeric 2,2-dibutyl-1,3,2-dioxastannane ring;[13] the only possible structure that contains this ring is a dimeric 4,6-*O*-dibutylstannylene acetal. Since a single ^{119}Sn NMR signal is observed in this region of the spectrum and three dimer structures are possible, either only one of the C_2-symmetric dimers is populated or there is rapid exchange among the three structures. The rate of exchange for 2,2-dibutyl-1,3,2-dioxastannane, where exchange is expected to be faster, was slow enough that broad lines were observed at room temperature.[13] Thus, it is likely that only a single symmetric dimer of the 4,6-dibutylstannylene acetal is present. It was found that of the three possible dimers, the ones in which tricoordinate oxygen atoms are remote from substituents are favored.[14]

Thus, the populated dimer is probably the one with both primary oxygens tricoordinate, the 6,6-dimer, using nomenclature developed earlier (see Figure 1). The other signal must then be assigned to the 2,3-*O*-dibutylstannylene acetal and, in agreement, its chemical shift, -126.2 ppm, is very similar to that observed for the single dimer present for methyl 4,6-*O*-benzylidene-2,3-*O*-dibutylstannylene-α-**D**-glucopyranoside in chloroform-*d*, -124.9 ppm[14] or -125.4 ppm.[15]

If two sites (the 2,3-*O*- and 4,6-*O*-dibutylstannylene acetals) in each molecule both form dimeric aggregates with other molecules, the result is an infinite polymer. A highly oligomeric structure for compound **1ds** is consistent with its relative insolubility in chloroform-*d*.

Spin-lattice relaxation times are related to molecular motion which in turn is related to molecular size. The spin-lattice relaxation times for the two tin atoms were measured by the inversion-recovery method at 149.2 MHz and 291 K and found to be 42.3 and 35.6 ms, for the peaks at -126.2 and -223.4 ppm, respectively. Relaxation times at 134.6 MHz for ^{119}Sn peaks of carbohydrate-derived dibutylstannylene acetal dimers at this temperature were on the order of 55-70 ms.[16] The relaxation mechanism in these compounds is chemical shift anisotropy for which relaxation times are proportional to $1/(B_o)^2$. T_1 values of 55 to 70 ms at 134.6 MHz are equivalent to 45 to 57 ms at 149.2 MHz. The shorter values measured for **1ds** are consistent with a molecular size larger than a dimer.

A chloroform-*d* solution of the product of reaction of **1** with 1.5 equivalents of dibutyltin oxide contained a small peak at -125.8 with major peaks at -126.7, -142.6, and -223.5 ppm. The signals at -126.7 and -223.5 ppm can be assigned to **1ds**. The other signal at -125.8 ppm is presumably due to methyl 2,3-*O*-dibutylstannylene-α-**D**-glucopyranoside. The ^{119}Sn NMR spectrum of a sample of methyl 2,6-di-*O*-benzyl-3,4-*O*-dibutylstannylene-α-**D**-glucopyranoside in chloroform-*d* contained a single major peak with a chemical shift of -147.3 ppm. Thus, the signal at -142.6 ppm can be assigned to one of the two possible symmetric dimers of the 3,4-dibutylstannylene acetal of **1**. A chloroform-*d* solution of the product of reaction of **1** with 1.0 equivalents of dibutyltin oxide contained only one sharp peak at -142.3 ppm, also consistent with a 3,4-*O*-dibutylstannylene acetal. This observation indicates that five-membered ring stannylene acetals formed from *trans*-diols on pyranose rings are more stable if they are flanked only

by equatorial substituents than if they are flanked by one axial substituent and one equatorial substituent.

A 0.17 M sample of **1ds** was made up in a 2:1 mixture of chloroform-*d* and benzyl bromide. Tin-119 NMR spectra of this sample were run initially and after heating at 85 °C for various intervals of time. The sample was cloudy initially but cleared after heating for five minutes. The results are shown in Figure 2. After heating this sample for 30 h, five sharp peaks were observed in the ^{119}Sn NMR spectrum, at 89.5, -81.0, -110.2 , -130.3 and -147.6 ppm, which had integrals in the ratio 4.1: 1.4 : 1.2: 1.5: 1.5, respectively. The signal at 89.5 ppm was assigned to dibutyltin dibromide by comparison to its literature values, 89.7 ppm neat or 92.1 ppm in chloroform-*d*.[17] The signal at -147.6 ppm was assigned to the pentacoordinate tin atom in a C_2-symmetric dimer of methyl 2,6-di-*O*-benzyl-3,4-*O*-dibutylstannylene-α-**D**-glucopyranoside by comparison with the chemical shift observed for a sample of this compound in chloroform-*d* that was prepared from the pure diol by the normal method, -147.3 ppm. The latter spectrum also contained a second peak at -146.1 ppm having one-tenth the intensity of the major peak, perhaps indicating the presence of a small amount of a second dimer. The chemical shifts of -81.0 and -130.3 ppm are similar to the values -82.8 and -131.3 ppm reported for the tetrameric ladder structure obtained by reaction of dibutyltin dibromide with hydroxide ions.[18] The signal at -110.2 ppm has not been assigned.

The general trends shown in Figure 2 are as follows: the two initial peaks gradually decrease in intensity at approximately equal rates having totally disappeared after 2 h of heating. They are initially replaced by several broad peaks, of which the sharpest are centered at about -102 ppm and near -160 ppm. Finally, the series of peaks mentioned above appears in which that of dibutyltin dibromide is prominent. The broad peaks are attributed to exchanging species; that of dibutyltin dibromide is also broad when it appears initially.

It is evident that the reaction follows a complex course involving many different tin-containing species. The most likely pathway is as follows: initial reaction occurs with one oxygen atom, probably O-2 for **1ds**, to give the 2-*O*-benzyl ether and a 3-*O*-bromodibutyltin ether. The two initial stannylene acetal signals decrease at the same rate to be replaced by broad signals. Therefore, as soon as the 3-*O*-bromodibutyltin ether is formed, it is involved in reversible exchange reactions with the remaining 4,6-*O*-

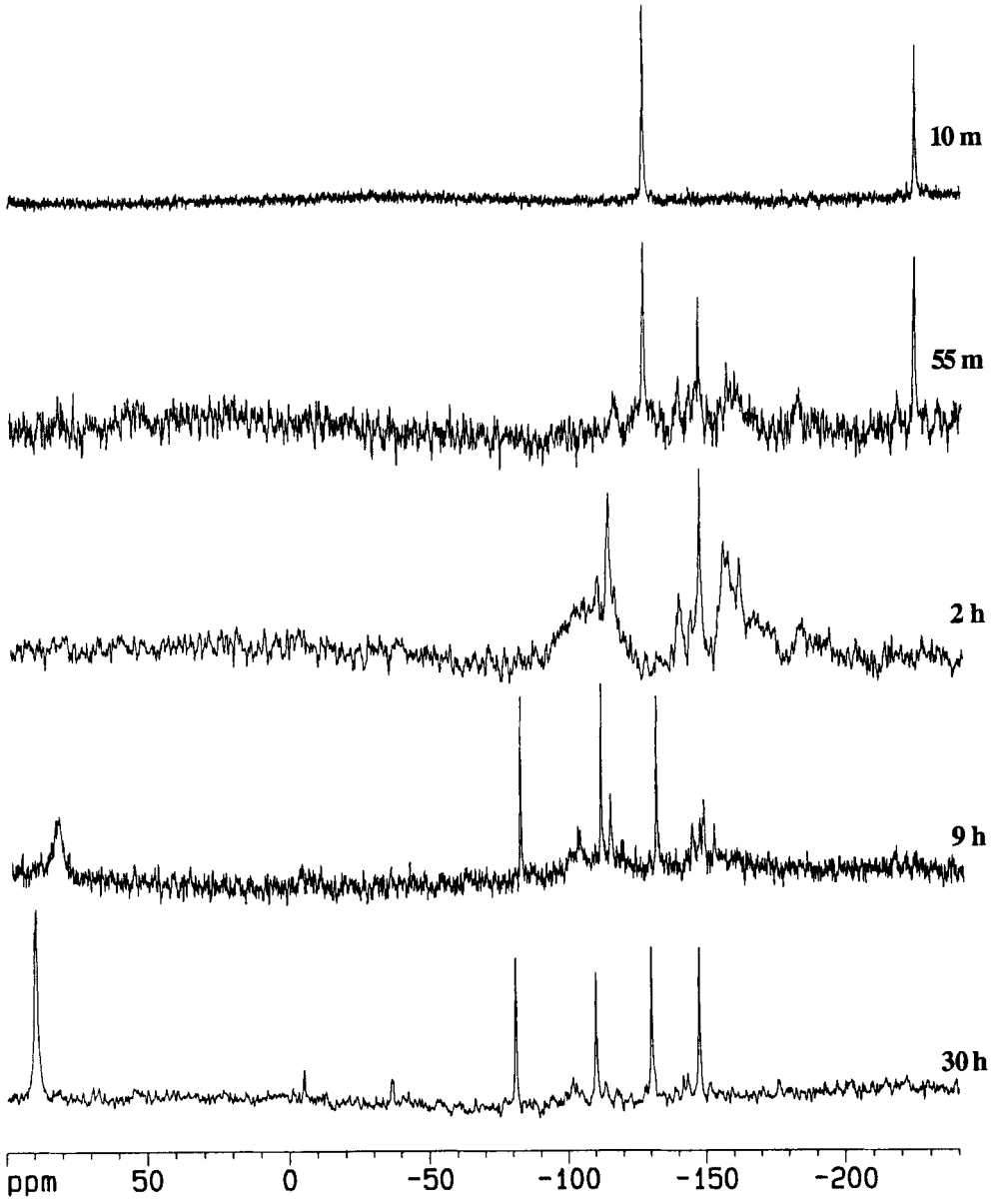


Figure 2. 149.1 MHz ^{119}Sn NMR spectra of a solution of **1ds** in a mixture of 2:1 chloroform-*d*: benzyl bromide after heating at 85 °C for the periods of time indicated. For peak assignments, see text.

dibuylstannylene acetal to give the 6-*O*-bromodibutyltin ether and the 3,4-*O*-dibuylstannylene acetal. Since the signals of the bromodibutyl tin ethers are broad, it is likely that they are involved in monomer-dimer equilibria that occur on the rate of the NMR timescale. Of the oxygen atoms present in this mixture, O-6 is evidently most reactive, probably in the 4,6-*O*-dibutylstannylene acetal. The resulting 2,6-*O*-dibenzyl-3,4-di-*O*-bromodibutyltin derivative is involved in exchange reactions with methyl 2,6-di-*O*-benzyl-3,4-*O*-dibuylstannylene-α-D-glucopyranoside and dibutyltin bromide.

CONCLUSIONS

Synthetically useful yields of di-*O*-benzyl derivatives can be obtained from the reaction of bis(dibutylstannylene) derivatives of most common methyl glycopyranosides with benzyl bromide as solvent at 85 ° C. The reactions follow complex mechanisms.

EXPERIMENTAL

General Methods. Melting points were determined with a Fisher-Johns melting point apparatus and were uncorrected. Specific rotations were measured on a Perkin-Elmer model 141 polarimeter. TLC was performed on 0.20 mm thick Merck silica gel 60F-254 aluminum sheets cut to be approximately 7 cm long. Components were located by spraying with 2% ceric sulfate in 2N sulfuric acid and heating on a hot plate until coloration took place. Flash column chromatography was performed on silica gel 60 PF254 for preparative chromatography. Evaporations were conducted in vacuo. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-250 NMR spectrometer, the ^{119}Sn NMR spectra on a Bruker AMX-400 NMR spectrometer. Solutions for NMR spectra were prepared in chloroform-*d* unless otherwise stated. Chemical shifts are reported in ppm downfield from internal TMS for ^{1}H and ^{13}C NMR spectra and from external tetramethyltin for ^{119}Sn NMR spectra. Most ^{1}H and ^{13}C NMR assignments were confirmed by COSY and HETCOR experiments. Samples for ^{119}Sn NMR spectroscopy were made up under conditions that excluded moisture as much as possible and were sealed under vacuum as previously.[14] Spin-lattice relaxation times were measured at 293 K using the inversion-recovery method with relaxation delays greater than 5 x T_1 and nine variable delays; T_1 values were calculated using a three-parameter fitting procedure available in Bruker software. Acetylation reactions were performed by stirring the

compound in dried pyridine and acetic anhydride (3:2) at 25 °C. Peracetates are given the numbers of the unacetylated precursor followed by **a**.

General Method for Benzylation of Methyl Glycosides. Methyl 2,6-di-*O*-benzyl-α-D-glucopyranoside (6). Methyl α-D-glucopyranoside (**1**) (0.975 g, 5.0 mmol) and dibutyltin oxide (1.862 g, 1.5 eq) were refluxed in toluene (50 mL) for 12 h in an apparatus for the azeotropic removal of water. The solvent was evaporated then benzyl bromide (10 mL) was added. The mixture was stirred at 80-90 °C until TLC indicated that the starting material had disappeared and the concentration of di-*O*-benzyl ether was at a maximum (24 h). The reaction mixture was cooled, diluted with chloroform (20 mL) and the solution was washed with water (50 mL). The organic layer was dried ($MgSO_4$), then concentrated. The remaining liquid residue was fractionated by flash chromatography. Elution was performed using a solvent gradient changing from toluene to ethyl acetate. The title compound (**6**) was obtained as a syrup (1.549 g, 82%) that crystallized from ether-hexane as fine colourless needles; mp 85-87 °C; lit.[4] 80-82 °C; $[\alpha]_D^{24}$ +59.8° (*c* 1.1, chloroform); lit.[4] +58.7°.

Reaction exactly as above using 5 mmol of **1** (0.968 g) except using two equivalents of dibuyltin oxide yielded, in addition to compound **6** (1.125 g, 60 %), a less polar fraction containing a mixture of two unidentified tri-*O*-benzyl derivatives (17%).

In some cases, the initial products were contaminated with dibutyltin derivatives. These compounds were removed by first washing the flash column containing the sample several times with pentane.

Methyl 3,6-di-*O*-benzyl-β-D-glucopyranoside (7), methyl 2,6-di-*O*-benzyl-β-D-glucopyranoside (8), methyl 4,6-di-*O*-benzyl-β-*D*-glucopyranoside (9), and methyl 6-*O*-benzyl-β-D-glucopyranoside (10). Reaction of compound **2** (0.193 g, 1 mmol) with dibutyltin oxide (0.368 g, 1.5 eq) in toluene (40 mL), then with excess benzyl bromide (10 mL) for 50 h as in the general procedure yielded **7** (0.073g, 16%), **8** (0.210g, 56%), a mixture of di-*O*-benzyl derivatives (0.070g, 19%) from which **9** crystallized (0.054g, 15%), and **10** (0.030g, 10%).

Compound **7** was a syrup; $[\alpha]_D^{24}$ -29.5° (*c* 0.76, chloroform); ^{1}H NMR δ 3.35-3.53 (m, 3H, H-3, H-2, H-5), 3.55 (s, 3H, MeO), 3.57-3.65 (m, 1H, H-4), 3.70-3.82 (m, 2H, H-6), 4.22 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1), 4.607, 4.572 (AB q, 2H, $J_{A,B}$ = -12.1 Hz, CH_2Ph), 4.82, 4.94 (AB q, 2H, $J_{A,B}$ = -11.6 Hz, CH_2Ph), 7.10-7.70 (m, 10H, Ar-

H); ^{13}C NMR δ 57.2 (MeO), 70.0 (C-6), 71.5 (C-4), 73.7 (CH_2Ph), 74.1 (C-5), 74.2 (C-2), 74.7 (CH_2Ph), 83.7 (C-3), 103.7 (C-1), 127.1-129.8 (Ar-C).

Anal. Calcd for $C_{21}H_{26}O_6$: C, 67.36; H, 7.00. Found: C, 67.40; H, 6.82.

Acetylation of compound **7** afforded compound **7a**; ^{1}H NMR δ 1.88, 2.02 (2s, 6H, 2Ac), 3.49 (s, 3H, OMe), 3.50-3.617 (m, 3H, H-5, 2 H-6), 3.69 (t, 1H, $J_{2,3} = J_{3,4}$ = 9.5 Hz, H-3), 4.35 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1), 4.54, 4.59 (2s, 4H, 2 CH_2Ph), 5.03, 5.04 (overlapping dd and t, 2H, H-2, H-4), 7.15-7.60 (m, 10H, Ar-H); ^{13}C NMR δ 20.8 and 20.9 (2 Me-Ac), 56.7 (MeO), 69.7 (C-6), 70.8 (C-4), 72.4 (C-2), 73.61 (2C, C-5, CH_2Ph), 73.66 (CH_2Ph), 80.16 (C-3), 101.7 (C-1), 127.6, 127.7, 127.8, 127.9, 128.4, 137.8, 137.9 (Ar-C), 169.4, 169.6 (2 C=O).

Compound **8** was an amorphous solid; mp. 69-70 °C; $[\alpha]_D^{24}$ -5.0° (*c* 3.0, chloroform); ^{1}H NMR δ 3.22 (dd, 1H, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 8.8 Hz, H-2), 3.40-3.58 (m, 3H, H-3, H-4, H-5), 3.56 (s, 3H, OMe), 3.60-3.82 (AB of ABX pattern, 2H, $J_{6,6'}$ = -10.6 Hz, $J_{5,6} + J_{5,6'}$ = 7.9 Hz, 2 H-6), 4.28 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1), 4.584, 4.605 (AB q, 2H, $J_{A,B}$ = -12.1 Hz, CH_2Ph), 4.66, 4.93 (2 d, 2H, J = -11.3 Hz, CH_2Ph), 7.10-7.40 (m, 10H, Ar-H); ^{13}C NMR δ 57.1 (MeO), 70.0 (C-6), 71.2 (C-4), 73.7 (CH_2Ph), 74.1 (C-5), 74.4 (CH_2Ph), 76.0 (C-3), 80.9 (C-2), 104.3 (C-1), 127.1-128.1 (Ar-C).

Anal. Calcd for $C_{21}H_{26}O_6$: C, 67.36; H, 7.00. Found: C, 67.12; H, 6.92.

Acetylation of **8** afforded **8a**; ^{1}H NMR δ 1.89, 1.90 (2s, 6H, 2Ac), 3.40 (dd, 1H, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 9.5 Hz, H-2), 3.48-3.67 (m, 3H, H-5, 2 H-6), 3.59 (s, 3H, OMe), 4.39 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1), 4.52, 4.56 (ABq, 2H, J = -12.1 Hz, CH_2Ph), 4.59, 4.83 (2 d, 2H, J = -12.0 Hz, CH_2Ph), 4.95 (t, 1H, $J_{3,4} = J_{4,5}$ = 9.5 Hz, H-4), 5.15 (t, 1H, $J_{2,3} = J_{3,4}$ = 9.5 Hz, H-3), 7.2-7.5 (m, 10H, Ar-H); ^{13}C NMR δ 20.7 and 20.8 (2 Me-Ac), 57.3 (MeO), 68.8 (C-6), 69.5 (C-4), 73.0 (C-5), 73.6 (CH_2Ph), 74.0 (C-3), 74.3 (CH_2Ph), 78.7 (C-2), 104.5 (C-1), 127.8, 127.9, 128.2, 128.5, 128.6, 129.1, 137.9, 138.3 (Ar-C), 169.4, 169.6 (2 C=O).

Compound **9** crystallized from a mixture of two compounds with the same R_Fs and was recrystallized from ether-hexane to give fine colorless needles; mp 114-115 °C; $[\alpha]_D^{25}$ -11.7° (*c* 0.26, chloroform); ^{1}H NMR δ 2.90 (br s, 1H, OH-3), 2.94 (br s, 1H, OH-2), 3.39-3.58 (m, 2H, H-2, H-5), 3.55 (s, 3H, OMe), 3.60-3.82 (m, 3H, H-4, 2 H-6), 4.17 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1), 4.55, 4.63 (ABq, 2H, J = -12.2 Hz, CH_2Ph), 4.58, 4.80 (2 d, 2H, J = -11.1 Hz, CH_2Ph), 7.18-7.45 (m, 10H, Ar-H); ^{13}C NMR δ 57.2 (MeO),

68.8 (C-6), 73.5 (CH_2Ph), 74.0 (C-5), 74.7 (CH_2Ph), 74.9 (C-3), 76.7, (C-2), 77.5 (C-4), 103.4 (C-1), 127.7, 127.9, 128.0, 128.4, 128.5 138.0, 138.2 (Ar-C).

Anal. Calcd for $C_{21}H_{26}O_6$: C, 67.36; H, 7.00. Found: C, 67.66; H, 7.06.

Acetylation of compound **9** afforded compound **9a**; ^1H NMR δ 1.92, 2.03 (2s, 6H, 2Ac), 3.50 (s, 3H, OMe), 3.49-3.57 (m, 1H, H-5), 3.68-3.81 (m, 3H, H-4, 2 H-6), 4.38 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1), 4.52 (s, 2H, CH_2Ph), 4.57, 4.64 (ABq, 2H, J = 12.1 Hz, CH_2Ph), 4.89 (dd, 1H, $J_{1,2}$ = 7.9 Hz, $J_{2,3}$ = 9.8 Hz, H-2), 5.21 (t, 1H, $J_{2,3}$ = $J_{3,4}$ = 9.8 Hz, H-3), 7.05-7.40 (m, 10H, Ar-H); ^{13}C NMR δ 20.8 (2 Me-Ac), 56.9 (OMe), 68.2 (C-6), 71.9 (C-5), 73.6 (CH_2Ph), 74.7 (CH_2Ph), 74.9 (C-3), 75.0 (C-2), 75.9 (C-4), 101.5 (C-1), 127.7, 127.8, 127.9, 128.4, 128.5, 137.6, 137.9 (Ar-C), 169.9, 170.2 (2 C=O).

Compound **10** was a syrup, $[\alpha]_D^{25}$ -29.4° (*c* 0.28, chloroform), lit.[19] -36°, although it has previously been obtained crystalline;[19] ^1H NMR δ 3.40 (s, 3H, OMe); ^{13}C NMR (dimethylsulfoxide-d_6) δ 55.9 (OMe), 69.8 (C-6), 70.1 (C-4), 72.3 (CH_2Ph), 73.3 (C-2), 75.5 (C-3), 76.6 (C-5), 103.8 (C-1), 126.4, 127.3, 128.9, 138.7 (Ar-C).

Acetylation of compound **10** afforded compound **10a**; ^1H NMR δ 1.91, 2.00, 2.04 (3s, 9H, 3Ac), 3.52 (s, 3H, OMe), 3.55-3.60 (m, 2H, 2 H-6), 3.62-3.72 (m, 1H, H-5), 4.42 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1), 4.518, 4.577 (ABq, 2H, J= -11.8 Hz, CH_2Ph), 4.98 (dd, 1H, $J_{2,3}$ = 9.6 Hz, H-2), 5.07 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 9.7 Hz, H-4), 5.20 (t, 1H, $J_{2,3}$ = $J_{3,4}$ = 9.3 Hz, H-3), 7.20-7.45 (m, 5H, Ar-H); ^{13}C NMR δ 20.62, 20.66, 20.75 (3 Ac Me), 57.0 (OMe), 68.8 (C-6), 69.3 (C-4), 71.4 (C-2), 73.0 (C-3), 73.3 (C-5), 73.6 (CH_2Ph), 101.5 (C-1), 127.8, 127.9, 128.4, 137.8, (Ar-C), 169.5, 169.6, 170.4 (3 Ac C=O).

Reaction as above except that 2.0 eq. of dibutyltin oxide was used and the reaction was allowed to proceed for 22 h produced **7** (14%), **8** (35%), **9** and methyl 2,3-di-*O*-benzyl-β-**D**-glucopranoside (**11**) (26%), and **10** (10%). Compounds **9** and **11** were present in a ratio of 1:2 based on the ^{13}C NMR spectrum of the mixture. From this spectrum, the following peaks could be assigned to **11** (signal assignments by comparison and from J-mod spectrum): δ 57.4 (OMe), 62.4 (C-6), 70.2 (C-4), 74.7 (CH_2Ph), 74.8 (C-5), 75.3 (CH_2Ph), 81.9 (C-2), 83.7 (C-3), 104.9 (C-1), 127-135 ppm (Ph-C).

Reaction as above but for 75 h produced methyl 2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**12**) (6%), **7** (23%), **8** (31%), **9** and **11** (8%), and **10** (5%). Compound

12 was a syrup; $[\alpha]_D^{24}$ -9.0° (*c* 1.05, chloroform); lit.[1] -17°; ^{1}H NMR δ 3.40-3.85 (m, 6H, H-2 to H-6), 3.60 (s, 3H, OMe), 4.36 (d, 1H, $J_{1,2}$ = 7.3 Hz, H-1), 4.603, 4.626 (ABq, 2H, J = -12.1 Hz, CH_2Ph), 4.73, 4.95 (2d, 2H, J = -11.1 Hz, CH_2Ph), 4.77, 4.96 (2d, 2H, J = -11.5 Hz, CH_2Ph), 7.20-7.45 (m, 15H, ArH); ^{13}C NMR δ 57.2 (OMe), 70.2 (C-6), 71.4 (C-4), 73.7, 74.7, 75.3 (3 OCH_2Ph), 81.8 (C-3), 84.0 (C-2), 104.8 (C-1), 127.0-129.1, 138.0, 138.5, 138.6 (Ar-C).

Methyl 3,6-di-*O*-benzyl-α-D-galactopyranoside (13), methyl 2,3,6-tri-*O*-benzyl-α-D-galactopyranoside (14), and methyl 3-*O*-benzyl-α-D-galactopyranoside (15). Reaction of compound **3** (0.191 g, 1 mmol) with dibutyltin oxide (0.498 g, 2 eq) in toluene (30 mL) then with excess benzyl bromide (6 mL) for 34 h was performed as in the general procedure. Flash chromatography first gave compound **14** as a syrup (0.060 g, 13%), $[\alpha]_D^{24}$ +33.4° (*c* 1.67, chloroform), lit.[20] +34°; ^{1}H NMR δ 2.68 (br s, 1H, OH), 3.35 (s, 3H, MeO), 3.65-3.79 (complex m, 2H, H-6,6'), 3.84-3.95 (complex m, 3H, H-2,3,5), 4.07 (br s, 1H, H-4), 4.58, 4.757, 4.762 (3 AB q, 6H, J_{AB} = 11.6, 12.2, and 11.6 Hz, respectively, Δν = 0.040, 0.150, 0.083 ppm, respectively, 3 CH_2Ph), 4.65 (obscured d, 1H, H-1), 7.20-7.45 (m, 15H, ArH); ^{13}C NMR δ 55.4 (OMe), 68.1 (C-4), 68.4 (C-5), 69.6 (C-6), 72.8, 73.58, 73.64 (3 CH_2Ph), 75.7 (C-2), 77.6 (C-3), 98.6 (C-1), 127.7, 127.8, 127.9, 128.1, 128.4, 128.5, 138.0, 138.1, 138.4 (Ar-C).

Acetylation of **14** afforded **14a**; ^{1}H NMR δ 2.07 (s, 3H, Ac), 3.40 (s, 3H, OMe), 3.43-3.54 (AB part of ABX pattern, 2H, 2 H-6), 3.78 (dd, 1H, $J_{2,3}$ = 10.0 Hz, $J_{1,2}$ = 3.7 Hz, H-2), 3.96 (dd, 1H, $J_{3,4}$ = 3.4 Hz, H-3), 4.06 (td, 1H, $J_{5,6} + J_{5,6'}$ = 12.4 Hz, $J_{4,5}$ = 1.1 Hz, H-5), 4.51, 4.66, 4.75 (3 ABq, 6H, J = -11.9, -11.2, -12.1 Hz, and Δν = 0.11, 0.20, and 0.19 ppm, respectively, 3 CH_2Ph), 4.70 (d, 1H, H-1), 5.61 (dd, 1H, H-4), 7.10-7.35 (m, 15H, Ar-H); ^{13}C NMR δ 21.0 (Ac Me), 55.5 (OMe), 67.6 (C-5), 68.3 (C-4), 68.6 (C-6), 72.1, 73.6, 73.7 (3 CH_2Ph), 75.5 (C-2), 76.3 (C-3), 98.9 (C-1), 127.6- 128.5, 137.7, 138.2, 138.5 (Ar-C), 170.4 (C=O).

The second fraction was compound **13**, a syrup (0.231 g, 63%); $[\alpha]_D^{24}$ +94.6° (*c* 3.9, chloroform), lit.[20] +109° (chloroform); ^{1}H NMR δ 2.27, 2.65 (br s, 2H, 2 OH), 3.40 (s, 3H, MeO), 3.62 (dd, 1H, $J_{2,3}$ = 9.6 Hz, $J_{3,4}$ = 3.2 Hz, H-3), 3.71, 3.74 (AB of ABX, 2H, $J_{6,6'}$ = -10.1 Hz, $J_{5,6} + J_{5,6'}$ = 11.6 Hz, H-6,6'), 3.89 (t, 1H, H-5), 4.03 (br dd, 1H, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 9.8 Hz, H-2), 4.05 (dd, 1H, $J_{4,5}$ = 0.9 Hz, H-4),

4.572, 4.606 (ABq, 2H, J = -12.1 Hz, CH_2Ph), 4.71 (s, 2H, CH_2Ph), 4.83 (d, 1H, $J_{1,2}$ = 4.0 Hz, H-1), 7.20-7.45 (m, 10H, ArH); ^{13}C NMR δ 55.4 (OMe), 67.3 (C-2), 68.4 (C-4), 68.9 (C-5), 69.6 (C-6), 72.0 (OCH_2Ph), 73.7 (CH_2Ph), 78.2 (C-3), 99.5 (C-1), 127.8, 128.0, 128.1, 128.6, 137.8, 137.9 (Ar-C).

Acetylation of **13** afforded **13a**; ^1H NMR δ 2.07, 2.09 (2s, 6H, 2Ac), 3.37 (s, 3H, OMe), 3.42-3.60 (m, 2H, 2 H-6), 3.92 (dd, 1H, $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 3.4 Hz, H-3), 4.08 (t, 1H, $J_{5,6} + J_{5,6'}$ = 12.7 Hz, H-5), 4.45, 4.71 (2d, 2H, J = -11.8 Hz, CH_2Ph), 4.46, 4.58 (2d, 2H, J = 11.9 Hz, CH_2Ph), 4.98 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 5.10 (dd, 1H, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ = 10.4 Hz, H-2), 5.64 (d, 1H, $J_{3,4}$ = 3.2 Hz, H-4), 7.10-7.35 (m, 10H, Ar-H); ^{13}C NMR δ 20.8, 21.0 (2 Ac Me), 55.4 (OMe), 67.6 (C-5), 67.7 (C-4), 68.3 (C-6), 70.2 (C-2), 71.7 (OCH_2Ph), 73.5 (C-3), 73.7 (CH_2Ph), 97.3 (C-1), 127.7, 127.8, 127.9, 128.4, 128.9, 137.7, 137.8 (Ar-C), 170.4, 170.5 (2 C=O).

The final compound isolated was **15** (0.006g, 2%), a syrup; $[\alpha]_D^{24}$ +30.8° (*c* 0.039, chloroform containing a trace of dimethylsulfoxide); lit.[21] +95° (chloroform).

Acetylation of **15** afforded **15a**; ^1H NMR δ 2.07, 2.09, 2.14 (3s, 9H, 3Ac), 3.38 (s, 3H, MeO), 3.93 (dd, 1H, $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 3.4 Hz, H-3), 4.05-4.20 (m, 3H, H-5, 2 H-6), 4.45 and 3.94 (ABq, 2H, J = 11.8, CH_2Ph), 4.90 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 5.1 (dd, 1H, $J_{1,2}$ =3.7, $J_{2,3}$ = 10.4 Hz, H-2), 5.56 (d, 1H, $J_{3,4}$ = 3.4 Hz, H-4), 7.10-7.20 (m, 5H, ArH); ^{13}C NMR δ 20.76, 20.82, 20.96 (3Ac), 55.4 (OMe), 62.4 (C-6), 66.5 (C-5), 67.3 (C-4), 70.0 (C-2), 71.8 (OCH_2Ph), 73.2 (C-3), 97.3 (C-1), 127.7, 127.8, 128.4, 137.7 (Ar-C), 170.4 (C=O), 170.6 (2 C=O).

Methyl 3,6-di-*O*-benzyl-β-D-galactopyranoside (16) and methyl 3-*O*-benzyl-β-D-galactopyranoside (17). Reaction of compound **4** (0.204g, 1mmol) with dibutyltin oxide (0.379g, 1.5mmol) in toluene (40mL)then with excess benzyl bromide (10mL)for 26 h as in the general procedure yielded compound **16** as a syrup (0.277g, 70%); $[\alpha]_D^{24}$ -0.9° (*c* 0.7, chloroform); lit.[9] -1.9°; and compound **17** (0.024g, 8%) which was also a syrup; $[\alpha]_D^{24}$ +3.8° (*c* 1.2, chloroform); lit.[21] 0°.

Methyl 3,6-di-*O*-benzyl-α-D-mannopyranoside (18) and methyl 3-*O*-benzyl-α-D-mannopyranoside (19). Reaction of compound **5** (0.200g, 1mmol) with dibutyltin oxide (0.373g, 1.5mmol) in toluene (35mL) then with excess benzyl bromide (10mL) for 26 hours as in the general procedure yielded compound **18** as a syrup (0.135g, 35%); $[\alpha]_D^{24}$ +22.3° (*c* 0.9, chloroform); lit.[4] +20.3°; and compound **19** (0.037g, 12%), a syrup;

$[\alpha]_D^{24}$ +23.2° (*c* 0.7, chloroform). The ^1H and ^{13}C NMR spectra of compound **19** in pyridine-d_5 are identical to those reported by Haque et al.[11]

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