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Note

Some observations on the reductive ring opening of 4,6-*O*-benzylidene acetals of hexopyranosides with the borane trimethylamine–aluminium chloride reagent

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Dedicated to Professor Dr. András Lipták on the occasion of his 75th birthday

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ABSTRACT

Reductive ring openings of 3-*O*-benzoyl-4,6-*O*-benzylidene-D-glucopyranosides with $BH_3{\cdot}NMe_3$–$AlCl_3$ are accompanied by side reactions, such as debenzoylation and reduction of the benzoate to benzyl ether. This phenomenon was rationalized by aluminium chelate formation between the O-4 acetal and the benzoyl carbonyl group oxygens. It was also shown that these side reactions can be eliminated by using $BH_3{\cdot}THF$ as the reducing agent.

Regioselective protection of hydroxyl groups is an essential step in the synthesis of complex carbohydrates. Benzylidene acetals are formed regioselectively and they are commonly used for the simultaneous protection of O-4 and O-6 of hexopyranosides. The usefulness of benzylidene acetals in carbohydrate chemistry was further increased by the introduction of reductive ring opening,[1] which releases one of the two hydroxyl groups involved in the cyclic acetal while providing the other in protected form as a benzyl ether. The first reagent system used for affecting this transformation was $LiAlH_4$–$AlCl_3$.[1] Reductive ring opening of benzylidene acetals with this reagent was extensively investigated by Lipták and co-workers[2] and the method was widely used for the preparation of 4-*O*-benzyl ethers from 4,6-*O*-benzylidene hexopyranosides. A drawback of the $LiAlH_4$–$AlCl_3$ reagent system is that it is incompatible with the acyl groups. This problem was solved by Garegg and co-workers[3] by introducing borane trimethylamine and aluminium chloride as reagents, as this combination can be used in the presence of acyl groups. The regioselectivity of ring openings with $BH_3{\cdot}NMe_3$–$AlCl_3$ is dependent on the solvent: reactions in tetrahydrofuran give the 6-*O*-benzyl ethers, whereas the 4-*O*-benzyl ethers are produced selectively using toluene as solvent. Though the regioselectivities of these reactions are high, the yields of the 4-*O*-benzyl ethers are generally moderate, as the ring opening in toluene is accompanied by extensive degradation.

To increase the yields of 4-*O*-benzyl ethers we have changed the solvent from toluene to dichloromethane-diethyl ether.[4] In this solvent system the regioselectivity is somewhat compromised, yet the yields of the 4-*O*-benzyl ethers are higher than in toluene, as decomposition of the starting material is significantly reduced. Before the development of our methodology for high-yielding 4-*O*-benzyl selective ring opening,[5] we have been using $BH_3{\cdot}NMe_3$–$AlCl_3$ in dichloromethane-ether routinely in different projects and performed a fairly large number of reductive ring openings on substrates of diverse structures. Over the years, we have noticed that in the case of some acyl-containing substrates, the yields of the 4-*O*-benzyl ethers are significantly reduced. This is not due to the loss of regioselectivity, that is, increased formation of the corresponding 6-*O*-benzyl ethers, as these ring openings tend to give more complex reaction mixtures compared to the regular ones. We have now studied this phenomenon in more detail and report our results.

The effect of protecting groups at positions O-2 and O-3 on the outcome of the reductive ring opening was studied on the derivatives of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside having various combinations of *O*-benzyl and *O*-benzoyl groups

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at O-2, and O-3. The reductive ring openings were performed under identical conditions, by conducting the reactions in dichloromethane-ether (5:1 v/v) at 0 °C using 5 equiv of $BH_3{\cdot}NMe_3$ and 2 equiv of $AlCl_3$. The results are summarized in Table 1.

Reductive ring cleavage of the 2,3-di-*O*-benzyl derivative (**1a**) gave the 4-*O*-benzyl (**2a**) and the 6-*O*-benzyl (**3a)** ethers in 77% and 17% yields, respectively (Table 1, entry 1). In contrast, the ring opening of the 2,3-di-*O*-benzoyl derivative (**1b**) afforded the 4-*O*- (**2b**) and 6-*O*-benzyl (**3b**) ethers in significantly lower yields (Table 1, entry 2).

To find out which of the benzoyl groups is responsible for this effect, the ring opening of the monobenzoylated derivatives (**1c** and **1d**) was studied. Compounds **1c** and **1d** were readily obtained by conventional benzoylation of methyl 3-*O*-benzyl- and 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**1e**), respectively, these latter compounds were obtained by phase transfer-catalyzed benzylation of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside.[6] The yields of the 4-*O*- and 6-*O*-benzyl ethers obtained in the ring opening of the 2-*O*-benzoyl-3-*O*-benzyl derivative (**1c**) were very close to those obtained for the 2,3-di-*O*-benzyl derivative (Table 1, entries 1 and 3). The 3-*O*-benzoyl-2-*O*-benzyl derivative (**1d**), on the other hand, gave the expected derivatives in lower yields, similarly to the 2,3-di-*O*-benzoyl derivative (Table 1, entries 2 and 4). These data clearly support the role of the 3-*O*-acyl group in reducing the yield, and we reasoned that the 3-*O*-benzoyl group is probably involved in some side reactions.

The reductive ring openings of **1b** and **1d** indeed showed a more complex pattern on TLC and various side products could also be isolated from these reaction mixtures (Scheme 1.)

The major by-product isolated from the reaction of **1d** was a dibenzyl ether which contained no benzoyl group, and proved to be methyl 2,6-di-*O*-benzyl-α-D-glucopyranoside (**3e**). An authentic sample of **3e** was readily obtained by reductive opening of methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**1e**) (Table 1, entry 5). Another by-product, isolated in low yield, was **3a** in which the benzoyl was replaced by a benzyl group. The same types of by-products were also found in the ring opening of the 2,3-di-*O*-benzoyl derivative (**1b**): the 3-O-debenzoylated derivative (**4**) was obtained in 13% yield, and, again, a small amount of a derivative containing a 3-*O*-benzyl instead of the 3-*O*-benzoyl group (**3c**), was isolated. The formation of these types of by-products, particularly that of the 3-O-benzylated ones, was unexpected. As far as we know, none of the reagents used for the reductive cleavage of acetals is capable to reduce esters to ethers.

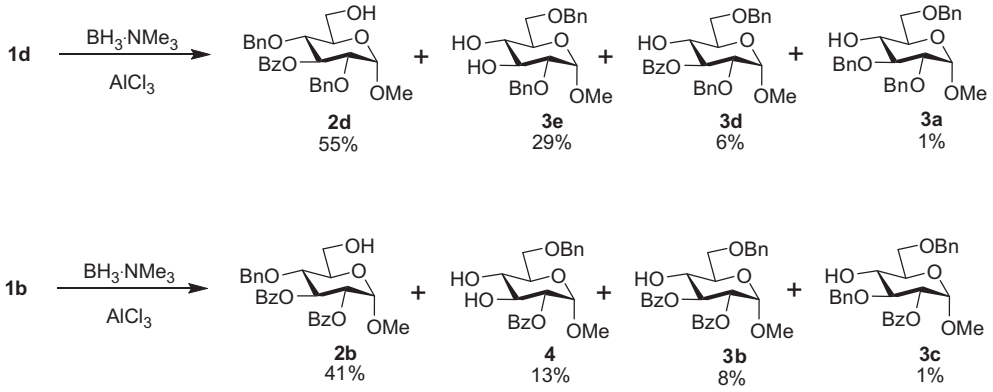
The differences in the ring opening of the 3-*O*-benzyl and 3-*O*-benzoyl derivatives are most probably due to chelation. Coordination of the Lewis acid to the acetal oxygen is the initiating step of the reductive ring cleavage. Complex formation with the acetal oxygen O-4 gives complex **5**, further transformation of **5** then leads to the regular products (**3b** and **3d**) (Scheme 2). In case of the 3-*O*-benzoyl derivatives a chelate (**6**) may be formed with the electron rich oxygen of the benzoyl carbonyl group. Chelate formation polarizes the benzoyl group, cleavage of bond at *a* in **7** leads finally to the debenzoylated derivatives (**3e** and **4**), whereas cleavage of the AlO-CHPh linkage (*b*, Scheme 2) and reduction followed by ring opening of the benzylidene group finally afford the 3-*O*-benzyl derivatives (**3a** and **3c**).

Chelation-controlled cleavage of acetals with various nucleophiles has previously been reported.[7] The exact structure of the Lewis acid involved in the chelation is not completely clear. Aluminium species have been demonstrated to be effective in chelation controlled cleavage of acetals.[7b,e,f] On the other hand, in a series of detailed investigation on the reductive opening of acetals, Ellervik and co-workers came to the conclusion that in $BH_3{\cdot}NMe_3$–$AlCl_3$-mediated ring openings, $AlCl_3$ activates $BH_3{\cdot}NMe_3$ in the presence of acetals, rendering BH_3 to the most electrophilic species.[8] Consequently, the reaction is directed by the complexation of the borane. For this reason we have performed the reductive ring opening of **1d** with $BH_3{\cdot}THF$ and $AlCl_3$ in dichloromethane-ether. The reaction gave the regular product **2d** in almost quantitative yield, with no appreciable amounts of the above by-products (**3e**, **3d** and **3a**) detectable (Table 2, entry 1).

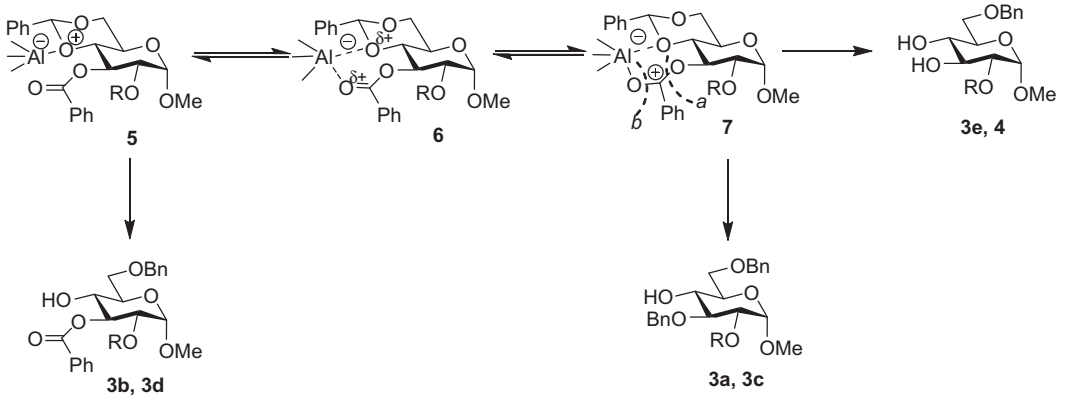
Previously, we have shown that the regioselectivity of ring openings with $BH_3{\cdot}THF$–Lewis acid mixtures is independent of the Lewis acid used.[5] Reductions of the 3-*O*-benzoyl (**1d**) and the 2,3-di-*O*-benzoyl (**1b**) derivatives with $BH_3{\cdot}THF$–TMSOTf gave the normal ring opening products in excellent yields without significant by-product formation (Table 2, entries 2 and 3).[5] These result clearly demonstrate that the active complexing species are

Table 1
Reductive ring openings of methyl 4,6-*O*-benzylidene-α-D-glucopyranosides

Entry	Substrate	Isolated yield (%)	
		4-*O*-Benzyl (**2**)	6-*O*-Benzyl (**3**)
1	**a** R^1 = Bn, R^2 = Bn	77	17
2	**b** R^1 = Bz, R^2 = Bz	41	8
3	**c** R^1 = Bz, R^2 = Bn	76	15
4	**d** R^1 = Bn, R^2 = Bz	55	6
5	**e** R^1 = Bn, R^2 = H	33	22

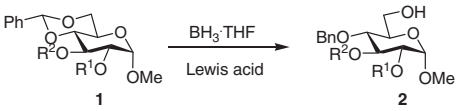


Scheme 1. Products isolated from the reductive ring cleavage of 3-*O*-benzoyl-4,6-*O*-benzylidene-D-glucopyranosides.



Scheme 2. The effect of chelation on the reaction pathway.

Table 2
Reductive ring openings with BH_3·THF



Entry	Substrate	Lewis acid	Yield of **2** (%)
1	**1d** R^1 = Bn, R^2 = Bz	$AlCl_3$	95
2	**1d** R^1 = Bn, R^2 = Bz	TMSOTf	99[a]
3	**1b** R^1 = Bz, R^2 = Bz	TMSOTf	87[a]

[a] Ref. 5.

different in BH_3·NMe_3 and BH_3·THF-mediated ring openings. From the preparative aspect, the same data also support the superiority of BH_3·THF–TMSOTf-mediated reductive ring openings[5] over the BH_3·NMe_3–$AlCl_3$ mediated ones.

In summary, we have found that reductive ring openings of 3-*O*-benzoyl-4,6-*O*-benzylidene-D-glucopyranosides with BH_3·NMe_3–$AlCl_3$ are accompanied by side reactions, such as extensive debenzoylation and reduction of the benzoates to benzyl ethers. We have rationalized this phenomenon by the formation of an aluminium chelate complex with the O-4 acetal and the carbonyl oxygen of the benzoyl group. We have also shown that these side reactions do not occur to any significant extent by using BH_3·THF as the reducing agent.

1. Experimental

1.1. General methods

Evaporations were performed under reduced pressure on rotary evaporators with bath temperatures not exceeding 40 °C. All reactions sensitive to air or moisture were carried out under an argon atmosphere with anhydrous solvents. Air- and moisture-sensitive liquids and solutions were transferred via a syringe. Dichloromethane was distilled from CaH_2, and stored over 4 Å molecular sieves. Solvents used for column chromatography were of technical grade and distilled before use. Thin layer chromatography (TLC) was performed on Silica Gel 60 F254 plates (E. Merck, Darmstadt), the compounds were detected under UV light and by spraying the plates with a 0.02 M solution of resorcinol in 20% methanolic H_2SO_4 followed by heating. For column chromatography, Silica Gel 60 (0.040–0.063 mm) (E. Merck) was employed. Melting points were determined in capillary tubes on a Griffin melting point apparatus and are uncorrected. Optical rotations were measured at room temperature with an Optical Activity P-2000 (Jasco) polarimeter. The NMR spectra were recorded on Varian Unity Inova 3000 (^{1}H: 300 MHz; ^{13}C: 75 MHz) and Varian Unity Inova 2000 (^{1}H: 200 MHz; ^{13}C: 50 MHz) spectrometers at ambient temperature in $CDCl_3$, and assigned using 2D-methods (COSY, HSQC). The chemical shifts were referenced to TMS (0.00 ppm for ^{1}H) and to the central line of $CDCl_3$ (77.0 ppm for ^{13}C). Elemental analyses were performed with an Elementar Vario EL III instrument at the Analytical Department of the Chemical Research Center, Hungarian Academy of Sciences.

1.2. Methyl 2-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (1c)

Benzoyl chloride (1.37 mL, 1.5 equiv) was added to a solution of methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside[6] (2.92 g) in dry pyridine (15 mL) stirred at 0 °C. The mixture was stirred at room temperature for 1 h, then water (1 mL) was added. The mixture was diluted with dichloromethane, washed with 2 M aq HCl, saturated aq $NaHCO_3$ and water, was dried, and concentrated. Recrystallization of the residue from ethyl acetate–hexanes gave **1c** (3.40 g, 91%) as white crystals: mp 132–133 °C, lit.[9] 142–143 °C, lit.[10] 143–145 °C; $[\alpha]_D$ +134 (*c* 0.46, chloroform), lit.[9] +135, lit.[11] +130.1 The ^{1}H and ^{13}C NMR data were in agreement with those published.[10,11]

1.3. Methyl 3-*O*-benzoyl-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (1d)

Benzoylation of **1e**[6] was performed the same way as described above, and afforded **1d** in 89% yield. White crystals: mp 129–130 °C (from ethyl acetate–hexanes), lit.[12] 118–120 °C, lit.[13] 136–137 °C; $[\alpha]_D$ −11.7 (*c* 0.65, chloroform), lit.[13] −6.3. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.43 (s, 3H, OMe), 3.69 (dd, 1H, $J_{3,4}$ 9.6 Hz, $J_{4,5}$ 10.0 Hz, H-4), 3.72 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.6 Hz, H-2), 3.74 (dd, 1H, $J_{5,6a} \sim J_{6a,6b}$ 10.0 Hz, H-6a), 3.97 (ddd, 1H, $J_{4,5} \sim J_{5,6a}$ 10 Hz, $J_{5,6b}$ 4.8 Hz, H-5), 4.29 (dd, 1H, $J_{5,6b}$ 4.8 Hz, $J_{6a,6b}$ 10.0 Hz, H-6a), 4.62 (s, 2H, $PhCH_2$), 4.75 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.46 (s, 1H, PhCH), 5.84 (dd, 1H, $J_{2,3} \sim J_{3,4}$ 9.6 Hz, H-3), 7.20–7.30 (m, 8H, aromatic), 7.36–7.46 (m, 4H, aromatic), 7.52–7.58 (m, 1H, aromatic), 8.02–8.06 (m, 2H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.4 (OMe), 62.4 (C-5), 69.0 (C-6), 71.2 (C-3), 72.8 ($PhCH_2$), 77.4 (C-2), 79.6 (C-4), 98.8 (C-1), 101.4 (PhCH), 126.1, 127.9, 128.1, 128.2, 128.4, 128.8, 129.8, 130.2, 137.0, 137.6 (aromatic), 165.3 (PhCO).

1.4. General procedure for reductive ring openings with $BH_3{\cdot}NMe_3$–$AlCl_3$

A solution of aluminium chloride (1.07 g, 8.0 mmol, 2 equiv) in dry diethyl ether (10 mL) was added during 10 min to a stirred mixture of the benzylidene derivative (**1a**–**1e**) (4.0 mmol) and borane trimethylamine (1.46 g, 20 mmol, 5 equiv) in dry dichloromethane (50 mL) at 0 °C. After completion of the reaction, the mixture was diluted with dichloromethane (100 mL) and stirred with 2 M aq HCl (100 mL) for 2 h. The organic layer was washed with saturated aq $NaHCO_3$ and water, dried ($MgSO_4$), and concentrated. The products were isolated by silica gel column chromatography (toluene–acetone, 98:2→4:1).

1.5. Reductive ring opening of methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (1a)

Eluted first from the column was methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (**3a**) (0.317 g, 17%). Colorless syrup: $[\alpha]_D$ +14 (*c* 0.64, chloroform), lit.[3] $[\alpha]_D$ +9, lit.[6] $[\alpha]_D$ +11, lit.[14] $[\alpha]_D$ +13, lit.[15] $[\alpha]_D$ +14, lit.[16] $[\alpha]_D$ +15.1. MS-ESI: $[M+NH_4]^+$ 482.3, $[M+Na]^+$ 487.3, $[M+K]^+$ 503.2. The ^1H and ^{13}C NMR data were in agreement with those reported.[16,17]

Eluted second was methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (**2a**) (1.432 g, 77%). White crystals: mp 50–51 °C (from ethyl acetate–hexanes), lit.[6] mp 53–54 °C, lit.[16] mp 43–44 °C, lit.[17] oil; lit.[18] mp 65–67 °C, lit.[19] mp 50–51 °C; $[\alpha]_D$ +24 (*c* 0.74, chloroform), lit.[6] $[\alpha]_D$ +22.5, lit.[18] $[\alpha]_D$ +24, lit.[19] $[\alpha]_D$ +22, lit.[20] $[\alpha]_D$ +26.3. The ^1H and ^{13}C NMR data were in agreement with those reported.[16,20]

1.6. Reductive ring opening of methyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (1b)

Eluted first from the column was a fraction, which turned out to be a mixture of two compounds. The components were separated by column chromatography using hexanes–acetone (9:1) as eluent. The first compound proved to be methyl 2-*O*-benzoyl-3,6-di-*O*-benzyl-α-D-glucopyranoside (**3c**) (0.018 g, 1%). Its ^1H, ^{13}C NMR and MS spectra were indistinguishable from the ones described for this compound in Section 1.7. The second component of this mixture was methyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-α-D-glucopyranoside (**3b**) (0.149 g, 8%). Colorless syrup: $[\alpha]_D$ +123 (*c* 0.63, chloroform), lit.[14] $[\alpha]_D$ +113. The ^1H and ^{13}C NMR data were in agreement with those reported.[20]

Continued elution of the original column with toluene–acetone gave next methyl 2,3-di-*O*-benzoyl-4-*O*-benzyl-α-D-glucopyranoside (**2b**) (0.811 g, 41%). White crystals: mp 112–113 °C (from ethyl acetate–hexanes), lit.[3] mp 117–118 °C; $[\alpha]_D$ +133 (*c* 0.80, chloroform), lit.[3] $[\alpha]_D$ +132, lit.[20] $[\alpha]_D$ +140.9. The ^1H and ^{13}C NMR data were in agreement with those reported.[20]

Further elution afforded a compound which proved to be methyl 2-*O*-benzoyl-6-*O*-benzyl-α-D-glucopyranoside (**4**) (0.206 g, 13%). White crystals: mp 87–88 °C; $[\alpha]_D$ +99 (*c* 0.62, chloroform), lit.[20] $[\alpha]_D$ +88.7. MS-ESI: $[M+H]^+$ 389.4, $[M+Na]^+$ 411.2, $[M+K]^+$ 427.0. The ^1H and ^{13}C NMR data were in agreement with those reported.[20]

1.7. Reductive ring opening of methyl 2-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (1c)

Eluted first was methyl 2-*O*-benzoyl-3,6-di-*O*-benzyl-α-D-glucopyranoside (**3c**) (0.288 g, 15%). Colorless syrup: $[\alpha]_D$ +98 (*c* 0.60, chloroform), lit.[9] $[\alpha]_D$ +99. ^1H NMR (300 MHz, $CDCl_3$): δ 2.92 (br s, 1H, OH), 3.42 (s, 3H, OMe), 3.80–3.92 (m, 4H, H-4, H-5, H-6a, H-6b), 4.11 (dd, 1H, $J_{2,3} \sim J_{3,4}$ 9.5 Hz, H-3), 4.63 (d, 1H, *J* 12.0 Hz, 1/2$PhCH_2$), 4.69 (d, 1H, *J* 12.0 Hz, 1/2$PhCH_2$), 4.82 (d, 1H, *J* 11.5 Hz, 1/2$PhCH_2$), 4.91 (d, 1H, *J* 11.5 Hz, 1/2$PhCH_2$), 5.13 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.17 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.5 Hz, H-2), 7.24–7.40 (m, 10H, aromatic), 7.46–7.51 (m, 2H, aromatic), 7.59–7.63 (m, 1H, aromatic), 8.13–8.15 (m, 2H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.1 (OMe), 69.6 (C-6), 69.9 (C-5), 71.3 (C-4), 73.7 (C-2), 73.5 ($PhCH_2$), 75.0 ($PhCH_2$), 79.6 (C-3), 97.1 (C-1), 127.49, 127.53, 127.6, 127.7, 128.3, 129.6, 129.7, 133.1, 137.8, 138.2 (aromatic), 165.7 (PhCO). MS-ESI: $[M-OMe]^+$ 447.2, $[M+H]^+$ 479.2, $[M+Na]^+$ 501.3, $[M+K]^+$ 517.2.

Eluted next was methyl 2-*O*-benzoyl-3,4-di-*O*-benzyl-α-D-glucopyranoside (**2c**) (1.461 g, 76%). White crystals: mp 99–100 °C (from ethyl acetate–hexanes), lit.[21] white solid; $[\alpha]_D$ +148 (*c* 0.67, chloroform). ^1H NMR (300 MHz, $CDCl_3$): δ 2.02 (dd, 1H, $J_{6a,OH}$ 5.5 Hz, $J_{6b,OH}$ 7.3 Hz, OH), 3.35 (s, 3H, OMe), 3.67–3.88 (m, 4H, H-4, H-5, H-6a, H-6b), 4.21 (dd, 1H, $J_{2,3} \sim J_{3,4}$ 9.5 Hz, H-3), 4.69 (d, 1H, *J* 11.0 Hz, 1/2$PhCH_2$), 4.83 (s, 2H, $PhCH_2$), 4.89 (d, 1H, *J* 11.0 Hz, 1/2$PhCH_2$), 5.03 (d, 1H, $J_{1,2}$ 3.6 Hz, H-1), 5.08 (dd, 1H, $J_{1,2}$ 3.6 Hz, $J_{2,3}$ 9.5 Hz, H-2), 7.16–7.32 (m, 10H, aromatic), 7.40–7.46 (m, 2H, aromatic), 7.54–7.59 (m, 1H, aromatic), 8.05–8.07 (m, 2H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.1 (OMe), 61.7 (C-6), 70.9 (C-5), 74.1 (C-2), 75.1 ($PhCH_2$), 75.5 ($PhCH_2$), 77.6 (C-4), 79.9 (C-3), 97.2 (C-1), 127.6, 127.8, 128.0, 128.3, 128.4, 129.6, 129.8, 133.2, 138.0, 138.1 (aromatic), 165.9 (PhCO).

1.8. Reductive ring opening of methyl 3-*O*-benzoyl-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (1d)

Eluted first was a syrup (0.017 g, 1%) which had ^1H, ^{13}C NMR and MS spectra indistinguishable from those of methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (**3a**).

The next compound obtained was methyl 3-*O*-benzoyl-2,6-di-*O*-benzyl-α-D-glucopyranoside (**3d**) (0.107 g, 6%). Colorless syrup: $[\alpha]_D$ +71 (*c* 0.47, chloroform). ^1H NMR (300 MHz, $CDCl_3$): δ 3.06 (br s, 1H, OH), 3.40 (s, 3H, OMe), 3.68 (dd, 1H, $J_{1,2}$ 3.5 Hz, $J_{2,3}$ 9.8 Hz, H-2), 3.70–3.80 (m, 4H, H-4, H-5, H-6a, H-6b), 4.55 (d, 1H, *J* 12.1 Hz, 1/2$PhCH_2$), 4.59 (d, 1H, *J* 12.1 Hz, 1/2$PhCH_2$), 4.61 (d, 1H, *J* 12.6 Hz, 1/2$PhCH_2$), 4.64 (d, 1H, *J* 12.6 Hz, 1/2$PhCH_2$), 4.75 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1), 5.51 (dd, 1H, $J_{2,3} \sim J_{3,4}$ 9.8 Hz, H-3), 7.22–7.32 (m, 10H, aromatic), 7.40–7.45 (m, 2H, aromatic), 7.53–7.58 (m, 1H, aromatic), 8.01–8.03 (m, 2H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$): δ 55.2 (OMe), 69.1 (C-6), 70.2 and 70.3 (C-4 and C-5), 72.8 ($PhCH_2$), 73.5 ($PhCH_2$), 76.1 (C-3), 76.4 (C-2), 97.7 (C-1), 127.5, 127.8, 127.9, 128.3, 129.7, 129.8, 133.1, 137.6, 137.8 (aromatic), 167.4 (PhCO). MS-ESI: $[M+H]^+$ 479.3, $[M+NH_4]^+$ 496.4, $[M+Na]^+$ 501.5, $[M+K]^+$ 517.2. Anal. Calcd for $C_{28}H_{30}O_7$: C, 70.28; H, 6.32. Found: C, 70.19, H, 6.35.

The following compound eluted was methyl 3-*O*-benzoyl-2,4-di-*O*-benzyl-α-D-glucopyranoside (**2d**) (1.062 g, 55%). Colorless syrup: $[\alpha]_D$ +36 (*c* 0.62, chloroform), lit.[5] $[\alpha]_D$ +36. The ^1H and ^{13}C NMR data were in agreement with those reported.[5]

The next fraction proved to be methyl 2,6-di-*O*-benzyl-α-D-glucopyranoside (**3e**) (0.439 g, 29%). White crystals: mp 74–75 °C (from ethyl acetate–hexanes), lit.[18] mp 85–86 °C, lit.[22] mp 80–82 °C; $[\alpha]_D$ +63 (*c* 0.63, chloroform), lit.[18] $[\alpha]_D$ +62.6, lit.[22] $[\alpha]_D$ +58.7, lit.[23] $[\alpha]_D$ +63.2. The ^1H and ^{13}C NMR data were in agreement with those reported.[22,23]

1.9. Reductive ring opening of methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (1e)

Eluted first from the column was methyl 2,4-di-*O*-benzyl-α-D-glucopyranoside (**2e**) (0.488 g, 33%). White crystals: mp 64–65 °C (from ethyl acetate–hexanes), lit.[18] mp 75 °C, lit.[24] mp 71–72 °C, lit.[25] mp 74–75 °C; $[\alpha]_D$ +100 (*c* 0.72, chloroform), lit.[18] $[\alpha]_D$ +87, lit.[24] $[\alpha]_D$ +98.3, lit.[25] $[\alpha]_D$ +88. The ^1H and ^{13}C NMR data were in agreement with those reported.[24]

Eluted second was methyl 2,6-di-*O*-benzyl-α-D-glucopyranoside (**3e**) (0.325 g, 22%) having the same physical constants as described in Section 1.8.

1.10. Reductive ring opening of methyl 3-*O*-benzoyl-2-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (1d) with BH_3·THF–$AlCl_3$

To a solution of **1d** (0.953 g, 2.0 mmol) in dry dichloromethane (30 mL) stirred under argon at 0 °C, a 1 M solution of BH_3·THF (10 mL, 10 mmol, 5 equiv) was added followed by a solution of $AlCl_3$ (0.533 g, 4.0 mmol, 2 equiv) in dry ether (5 mL). The mixture was stirred at room temperature for 1 day, then Et_3N (1 mL) and MeOH (5 mL) were added carefully. The mixture was evaporated; the residue was taken up in dichloromethane. It was subsequently washed with 2 M aq HCl, saturated aq $NaHCO_3$ and water; dried, and concentrated. Column chromatography of the residue (toluene–acetone, 98:2→4:1) afforded **2d** (0.909 g, 95%) having physical constants identical with the product described in Section 1.8.

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