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Note

# Pivalates in the selective protection and activation of maltose for the synthesis of sulfated 3-deoxy-maltosyl-(1 → 4)-α,α-trehalose

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**Abstract**

Pivaloylation of maltose gave, in satisfactory yield, 1,2,6,2′,3′,4′,6′-hepta-*O*-pivaloyl-β-maltose which was converted to the 3-deoxygenated analogue in a Barton–McCombie reaction. This compound was used directly in a trimethylsilyl triflate-mediated glycosylation reaction with 2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside to give the corresponding maltosyl-(1 → 4)-α,α-trehalose derivative. After deprotection, the monodeoxygenated tetrasaccharide was sulfated; in the reaction product, one compound fully sulfated at the outer pyranose rings predominated. © 1997 Elsevier Science Ltd.

*Keywords:* Pivalates; Deoxygenation; 3-Deoxy-maltose; Block glycoside synthesis; Sulfates

Reactions of unprotected disaccharides, such as sucrose [1] or trehalose [2], with pivaloyl chloride have led advantageously to regioselective esterifications due to the steric hindrance of the reagent. We have applied the reaction to maltose in order to prepare a 3-deoxy-maltose derivative as a glycosyl donor.

While pivaloylation of maltose in the presence of dimethylaminopyridine over 24 h gave only 46% of 1,2,6,2′,3′,4′,6′-hepta-*O*-pivaloyl-β-maltose (**1**) along with 30% of hexapivalate **2** after chromatography, a prolongation of the reaction time favored the formation of **1** and allowed the direct crystallization of this heptapivalate in 61% yield. A chromatography of the mother liquor furnished another 12% of **1**, a small amount of the α-anomeric **5**, and 17% of hexapivalate **2**. The structures of these derivatives were determined with the help of $^1$H NMR spectra, which were completely assigned (cf. Tables 1 and 2) using H,H-COSY. It is known that the 3-hydroxyl group of maltose is the least reactive in esterification reactions, and the selective preparations of the corresponding non-crystalline heptaacetate [3] and the crystalline heptabenzoate [4,5] have been reported.

Starting from the heptapivalate **1**, with only one free hydroxyl group, we introduced the deoxy function with a Barton–McCombie reaction [6]. Thus, reaction of **1** with 1,1′-thiocarbonyldiimidazole in acetonitrile gave the thiocarbonyl derivative **3** in excellent yield (96%). In the $^1$H NMR spectrum (cf.

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Table 1
$^1$H NMR chemical shifts ($\delta$) for compounds **1–5**

| Proton | **1** | **2** | **3** | **4** | **5** |
|---|---|---|---|---|---|
| H-1 | 5.66 d | 5.66 d | 5.81 d | 5.65 d | 6.25 d |
| H-2 | 4.85 dd | 4.85 dd | 5.30 dd | 4.77 ddd | 4.85 dd |
| H-$3_{eq}$ | 3.79 ddd | 3.78 ddd | 6.16 dd ~ t | 2.81 ddd ~ dt | 4.05 ddd |
| H-$3_{ax}$ | | | | 1.72 $m_c$ | |
| H-4 | 3.70 dd ~ t | 3.66 dd ~ t | 4.17 dd ~ t | 3.75 $m_c$<br>2 H, H-4, H-5 | 3.75 dd |
| H-5 | 3.71 ddd | 3.72 ddd | 3.88 ddd | | 3.93 ddd |
| H-6a | 4.43 dd | 4.40 dd | 4.67 dd | 4.40 dd | 4.42 dd |
| H-6b | 4.21 dd | 4.21 dd | 4.39 dd | 4.26 dd | 4.21 dd |
| H-1′ | 5.65 d | 5.59 d | 5.10 d | 5.23 d | 5.77 d |
| H-2′ | 4.90 dd | 4.83 dd | 4.83 dd | 4.82 dd | 4.90 dd |
| H-3′ | 5.51 dd | 5.33 dd | 5.49 dd | 5.48 dd ~ t | 5.56 dd ~ t |
| H-4′ | 5.17 dd | 3.42 ddd ~ dt | 5.07 dd ~ t | 5.16 dd ~ t | 5.18 dd ~ t |
| H-5′ | 4.15–4.07 | 3.88 ddd ~ dt | 4.09–4.04<br>m (2 H), H-5′, H-6b′ | 4.00 ddd ~ dt | 4.12–4.08 |
| H-6a′ | m (3 H), | 4.51 dd | 4.15 $m_c$ | 4.12 dd | m (3 H), |
| H-6b′ | H-5′, H-6′ | 4.22 dd | | 4.08 dd | H-5′, H-6′ |

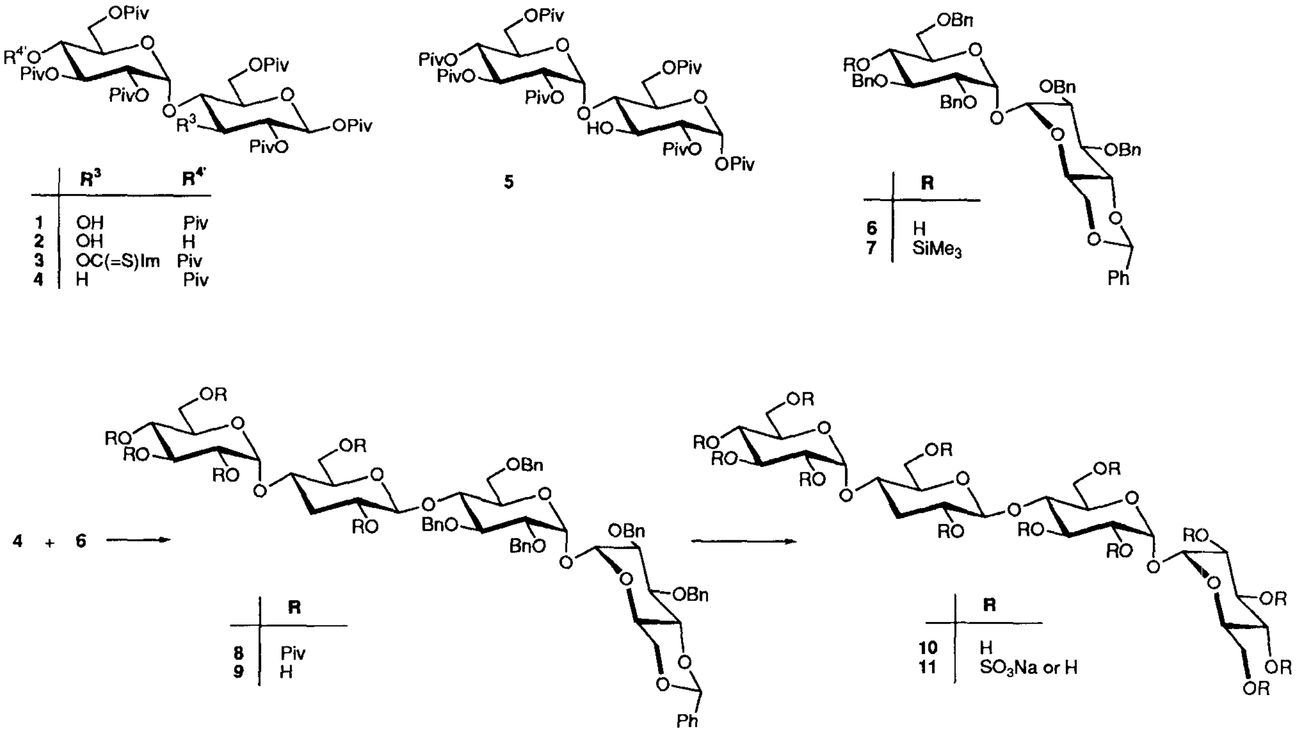
Tables 1 and 2), a strong downfield shift for H-3 was observed ($\Delta\delta = 2.37$ ppm) and a slight upfield shift for three of the pivalate signals. Reduction of **3** with tributyltin hydride in the presence of 2,2′-azobisisobutyronitrile resulted in the 3-deoxy-maltose derivative **4** (94%). This approach to 3-deoxy-maltose competes favourably with the chlorination–reduction sequence [7,8] employed before on the benzoate derivative.

In the context of a program dedicated to evaluating the relative importance of sulfates at various positions of maltosyl-(1 → 4)-$\alpha,\alpha$-trehalose for smooth muscle cell antiproliferative activity [9], we aimed to synthesize monodeoxygenated analogues of this tetrasaccharide [10,11]. Anomeric acetates have been used as glycosyl donors in the presence of trimethylsilyl triflate in the glycosylation of primary alcohols [12] and Paulsen and Paal [13] demonstrated the efficiency of this promoter, especially for unreactive glycosyl acceptors and in block syntheses. Furthermore, anomeric benzoates [14,15] and $p$-nitrobenzoates [16] have been used in trimethylsilyl triflate-mediated glycosylations. We have now employed the anomeric pivalate as glycosyl donor.

Table 2
$^1$H NMR coupling constants in Hz for compounds **1–5**

| Coupling constant | **1** | **2** | **3** | **4** | **5** |
|---|---|---|---|---|---|
| $J_{1,2}$ | 8.3 | 8.0 | 7.9 | 8.2 | 3.7 |
| $J_{2,3}$ | 9.5 | 9.3 | 9.2 | $J_{2,3eq}$ 5.1<br>$J_{2,3ax}$ 11.7 | 10.1 |
| $J_{3,4}$ | 8.2 | 7.7 | 8.8 | $J_{3eq,4}$ 3.7 | 8.8 |
| $J_{4,5}$ | 9.3 | 10.0 | 8.9 | – | 9.9 |
| $J_{5,6a}$ | 1.7 | 1.9 | 2.5 | 1.2 | 2.0 |
| $J_{5,6b}$ | 4.8 | 5.6 | 4.4 | 4.7 | 5.0 |
| $J_{6a,6b}$ | 12.0 | 11.9 | 12.3 | 11.8 | 12.0 |
| $J_{1',2'}$ | 3.9 | 3.9 | 3.5 | 3.9 | 4.1 |
| $J_{2',3'}$ | 10.2 | 10.0 | 10.2 | 10.3 | 10.3 |
| $J_{3',4'}$ | 9.3 | 9.8 | 9.3 | 9.4 | 9.3 |
| $J_{4',5'}$ | 9.2 | 10.0 | 9.4 | 10.3 | 9.8 |
| $J_{5',6a'}$ | – | 3.5 | 4.4 | 3.6 | – |
| $J_{5',6b'}$ | – | 2.4 | – | 2.2 | – |
| $J_{6a',6b'}$ | – | 12.2 | – | 12.6 | – |

The hydroxyl group at C-4 of $\alpha,\alpha$-trehalose is relatively unreactive. Reaction of equimolar amounts of the $\beta$-anomeric pivalate **4**, the established [17–21] $\alpha,\alpha$-trehalose glycosyl acceptor **6**, and trimethylsilyl triflate gave a moderate yield (41%) of the desired tetrasaccharide **8**. The remaining glycosyl donor was recovered unchanged (47%). The tetrasaccharide was characterized by its $^1$H NMR spectrum which could be completely analyzed with the help of 1D TOCSY experiments. It is of interest to note that, compared to acetates in analogous saccharides [10,11], the pivalate at C-2″ did not experience a strong upfield shift due to an interaction with a benzyl group. A by-product of the glycosylation reaction was the trimethylsilyl derivative **7** of the glycosyl acceptor; such a by-product was observed earlier when the reaction was carried out in a basic medium [13]. The $^1$H NMR spectra of **7** and its precursor **6** [17] were very similar, but H-4′ was slightly downfield-shifted, and H-3′, H-5′, and H-6′ significantly upfield ($\Delta\delta = 0.07–0.13$ ppm).



Scheme 1.

Additionally, one benzylic methylene signal changed from a singlet in **6** to two double doublets in **7** with a downfield shift of $\Delta\delta = 0.07$–$0.13$ ppm, so that this methylene group may be at O-6'.

The deblocking of the protected tetrasaccharide proceeded uneventfully. Transesterification of **8** with sodium methanolate furnished **9** (78%); the benzyl and benzylidene groups were removed together by hydrogenation over palladium-on-carbon in 4:1 ethanol–water to yield the free tetrasaccharide **10** quantitatively. With 1D TOCSY $^1$H NMR spectroscopy, the maltosyl protons could be assigned, but, due to heavy signal overlap, those of the trehalose moiety could not. Tetrasaccharide **10** was then sulfated with the sulfur trioxide–trimethylamine complex to give a mixture of 3-deoxy-maltosyl-(1 → 4)-$\alpha,\alpha$-trehalose sulfates **11** (Scheme 1). As opposed to the sulfated parent compound and other analogues [22], however, there was one predominant compound (amounting to ca. 60–70%) according to the $^1$H NMR spectrum. 1D TOCSY spectra of this preparation were of comparably low quality so that the identity of the main compound could not be established. However, most signals of the outer pyranose rings of the trehalose and maltose moieties could be assigned based on the shifts of H-1 and H-4 and H-1''' and H-4''' in one pyranose ring, respectively. A comparison with the data for persulfated $\alpha,\alpha$-trehalose and methyl $\beta$-maltoside [23] suggested that both pyranose moieties were completely sulfated. Further attempts to purify the mixture were not made since the preparation was used for an activity comparison with other comparably sulfated tetrasaccharide mixtures.

In conclusion, the use of pivalates for the selective protection of maltose and the direct employment of an anomeric pivalate in a block glycoside synthesis gave efficient access to 3-deoxy-maltosyl-(1 → 4)-$\alpha,\alpha$-trehalose. The relatively high homogeneity of the sulfated tetrasaccharides **11** seems to indicate that the (here missing) sulfate at C-3'' has contributed to the heterogeneity in the sulfated parent tetrasaccharide and analogues.

## 1. Experimental

*General.*—Solvents and reagents were bought from Fluka. Solutions were evaporated below 50 °C on a Büchi rotary evaporator. Qualitative TLC was performed with precoated Silica Gel 60F-254 plates (E.

Merck); compounds were detected by UV light (254 nm) and spraying with a 10% solution of $H_2SO_4$ in MeOH followed by charring. Melting points were determined with a Büchi 510 capillary apparatus and are uncorrected. Optical rotations were measured on a Perkin–Elmer 241 spectrometer in a 1 dm cell. $^1$H NMR spectra were recorded on Bruker AM-400 (400 MHz) spectrometers with Aspect 3000 and process controller; chemical shifts are given in ppm relative to tetramethylsilane or sodium 2,2,3,3-tetradeutero-3-(trimethylsilyl)-propionate as internal standard. Pulse sequence and experimental conditions for the 1D TOCSY experiments were essentially as described before [17,21]. Mass spectra were recorded on API III Sciex, Perkin–Elmer (ionspray) or MS 902 (FAB) with data system DS 2050 (VG).

*2,3,4,6-Tetra-*O*-pivaloyl-α-*D*-glucopyranosyl-(1 → 4)-1,2,6-tri-*O*-pivaloyl-β-*D*-glucopyranose* (**1**), *2,3,4,6-tetra-*O*-pivaloyl-α-*D*-glucopyranosyl-(1 → 4)-1,2,6-tri-*O*-pivaloyl-α-*D*-glucopyranose* (**5**), *and 2,3,6-tri-*O*-pivaloyl-α-*D*-glucopyranosyl-(1 → 4)-1,2,6-tri-*O*-pivaloyl-β-*D*-glucopyranose* (**2**).—To a solution of maltose monohydrate (36.0 g, 100 mmol) in pyridine (300 mL) containing 4-dimethylaminopyridine (1.22 g, 10 mmol) was added dropwise pivaloyl chloride (175 mL, 1.42 mmol). After 48 h, the solvent was evaporated. The residue was taken up in $CH_2Cl_2$ and washed with aq $NaHCO_3$ and water. The organic phase was dried ($Na_2SO_4$), concentrated, and co-evaporated with toluene. The residue was crystallized from $CH_2Cl_2$–hexane to obtain pure **1** (56.65 g, 61%). The mother liquor was chromatographed on silica gel using 19:1 to 4:1 toluene–EtOAc as eluents to furnish another lot of **1** (11.59 g, 12%) followed by **2** (2.22 g, 2.4%) and **3** (14.0 g, 17%).

**1**: Mp 191–192 °C (EtOAc–hexane); $[\alpha]_D^{20}$ +57° (*c* 0.4, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz; H,H-COSY; cf. Tables 1 and 2): δ 2.82 (d, 1 H, $J_{3,3\text{-OH}}$ 4.8 Hz, 3-OH), 1.22, 1.21 (2 s, 18 H, $^t$Bu), 1.17 (s, 18 H, *tert*-Bu), 1.16, 1.15, 1.13 (3 s, 27 H, *tert*-Bu); FABMS: *m/z* 953.6 ($[M + Na]^+$), 969.5 ($[M + K]^+$). Anal. Calcd for $C_{47}H_{78}O_{18}$: C, 60.63; H, 8.44. Found: C, 60.61; H, 8.48.

**2**: Mp 163 °C (EtOAc–hexane); $[\alpha]_D^{20}$ +38.5° (*c* 0.2, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz; H,H-COSY; cf. Tables 1 and 2): δ 3.06 (d, 1 H, $J_{4',4'\text{-OH}}$ 2.5 Hz, 4′-OH), 2.80 (d, 1 H, $J_{3,3\text{-OH}}$ 4.0 Hz, 3-OH), 1.23, 1.21, 1.20 (3 s, 27 H, *tert*-Bu), 1.17 (3 s, 27 H, *tert*-Bu); FABMS: *m/z* 869.4 ($[M + Na]^+$), 885.4 ($[M + K]^+$). Anal. Calcd for $C_{42}H_{70}O_{17}$: C, 59.56; H, 8.33. Found: C, 59.45; H, 8.28.

**5**: $[\alpha]_D^{20}$ +98.5° (*c* 0.2, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz; cf. Tables 1 and 2): δ 2.54 (d, 1 H, $J_{3,3\text{-OH}}$ 4.8 Hz, 3-OH), 1.26, 1.22, 1.21, 1.19, 1.18, 1.17, 1.14 (7 s, 63 H, *tert*-Bu); FABMS: *m/z* 953.5 ($[M + Na]^+$), 969.5 ($[M + K]^+$). Anal. Calcd for $C_{47}H_{78}O_{18}$: C, 60.63; H, 8.44. Found: C, 60.53; H, 8.41.

*2,3,4,6-Tetra-*O*-pivaloyl-α-*D*-glucopyranosyl-(1 → 4)-3-*O*-(imidazol-1-ylthiocarbonyl)-1,2,6-tri-*O*-pivaloyl-β-*D*-glucopyranose* (**3**).—A solution of the heptapivalate **1** (15.0 g, 16.1 mmol) and thiocarbonyldiimidazole (5.74 g, 32.2 mmol) in MeCN (100 mL) was refluxed for 4 days. After evaporation of solvent, the residue was purified by flash chromatography using 9:1 toluene–EtOAc as eluent to give pure **3** (16.08 g, 96%), $[\alpha]_D^{20}$ +66° (*c* 0.3, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz; cf. Tables 1 and 2): δ 8.31, 7.58, 7.02 (3 ~ s, 3 H, imidazole), 1.25, 1.23, 1.17, 1.16, 1.07, 1.05, 1.01 (7 s, 63 H, *tert*-Bu); FABMS: *m/z* 1041.4 ($[M + H]^+$). Anal. Calcd for $C_{51}H_{80}N_2O_{18}S$: C, 58.83; H, 7.74; N, 2.69. Found: C, 59.37; H, 7.84; N, 2.73.

*2,3,4,6-Tetra-*O*-pivaloyl-α-*D*-glucopyranosyl-(1 → 4)-3-deoxy-1,2,6-tri-*O*-pivaloyl-β-*D-ribo*-hexopyranose* (**4**).—Anhydrous toluene (20 mL) and tributyltin hydride (6 mL, 22.6 mmol) containing a catalytic amount of AIBN (~ 5 mg) were heated to reflux. After 1 h, a solution of **3** (9.938 g, 9.54 mmol) in toluene (40 mL) was added dropwise. Upon cooling, the solvent was evaporated, and the residue was purified by flash chromatography using 24:1 toluene–EtOAc as eluent to give pure **4** (8.21 g, 94%), mp 192–193 °C (EtOH); $[\alpha]_D^{20}$ +67° (*c* 0.4, $CHCl_3$); $^1$H NMR ($CDCl_3$, 400 MHz; cf. Tables 1 and 2): δ 1.23, 1.21, 1.17, 1.16, 1.15, 1.14, 1.12 (7 s, 63 H, *tert*-Bu); FABMS: *m/z* 937.8 ($[M + Na]^+$). Anal. Calcd for $C_{47}H_{78}O_{17}$: C, 61.69; H, 8.59. Found: C, 61.76; H, 8.57.

*2,3,4,6-Tetra-*O*-pivaloyl-α-*D*-glucopyranosyl-(1 → 4)-3-deoxy-2,6-di-*O*-pivaloyl-β-*D-ribo*-hexopyranosyl-(1 → 4)-2,3,6-tri-*O*-benzyl-α-*D*-glucopyranosyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-glucopyranoside* (**8**).—A solution of the glycosyl donor **4** (1.0 g, 1.09 mmol) and the glycosyl acceptor **6** (964 mg, 1.09 mmol) in abs $CH_2Cl_2$ (7 mL) was stirred at room temperature in the presence of molecular sieves (4 Å) for 1 h. Then $Me_3SiOTf$ (0.2 mL, 1.09 mmol) was added at −20 °C. The cooling bath was removed, and after 1.5 h (−3 °C) triethylamine (3 mL) was added. The reaction mixture was filtered over celite, which was washed with $CH_2Cl_2$. The filtrates were evaporated, and the residue was flash-chromatographed using 4:1 EtOAc–hexane as eluent to furnish the starting material **4** (473 mg, 47%), *2,3,6-tri-*O-*benzyl-4-*O-*trimethylsilyl-α-*D-*glucopyranosyl 2,3-di-*O-*benzyl-4,6-*O-*benzylidene-α-*D-*glucopyranoside* (**7**, 182 mg, 17%) and the tetrasaccharide **8** (756 mg, 41%).

**7**: $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.47–7.45 (m, 2 H, Ar), 7.36–7.34 (m, 5 H, Ar), 7.30–7.18 (m, 23 H, Ar), 5.51 (s, 1 H, CHPh), 5.18 (d, 1 H, $J_{1',2'}$ 3.7 Hz, H-1′), 5.14 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1), 4.98, 4.73 (2 d, 2 H, $J_{\mathrm{gem}}$ 11.2 Hz, CH$_2$Ph), 4.93, 4.82 (2 d, 2 H, $J_{\mathrm{gem}}$ 11.2 Hz, CH$_2$Ph), 4.74, 4.67 (2 d, 2 H, $J_{\mathrm{gem}}$ 12.0 Hz, CH$_2$Ph), 4.62, 4.58 (2 d, 2 H, $J_{\mathrm{gem}}$ 11.8 Hz, CH$_2$Ph), 4.47, 4.42 (2 d, 2 H, $J_{\mathrm{gem}}$ 12.0 Hz, CH$_2$Ph), 4.21 (ddd ~ dt, 1 H, $J_{4,5}$ 9.5 Hz, $J_{5,6a}$ 4.9 Hz, H-5), 4.11 (dd ~ t, 1 H, $J_{2,3}$ 9.5 Hz, H-3), 4.05 (dd, 1 H, $J_{6a,6b}$ 10.1 Hz, H-6a), 4.05 (ddd ~ br d, 1 H, H-5′), 3.77 (dd ~ t, 1 H, $\Sigma J$ 18.0 Hz, H-3′), 3.70 (dd ~ t, 1 H, $\Sigma J$ 18.0 Hz, H-4′), 3.61 (dd, 1 H, $J_{5,6b}$ 10.0 Hz, H-6b), 3.59 (dd, 1 H, $J_{3,4}$ 9.0 Hz, H-4), 3.56 (dd, 1 H, H-2), 3.54 (dd, 1 H, H-2′), 3.40 (dd, 1 H, $J_{5',6a'}$ 3.8, $J_{6a',6b'}$ 10.4 Hz, H-6a′), 3.33 (dd, 1 H, $J_{5',6b'}$ 2.0 Hz, H-6b′), −0.01 (s, 9 H, Me$_3$Si); FABMS: *m/z* 953.3 ([M + H]$^+$), 975.3 ([M + Na]$^+$), 991.2 ([M + K]$^+$). Anal. Calcd for C$_{57}$H$_{64}$O$_{11}$Si: C, 71.82; H, 6.77. Found: C, 71.33; H, 6.80.

**8**: Colourless syrup, $[\alpha]_{\mathrm{D}}^{20}$ +80° (*c* 0.1, CHCl$_3$); $^1$H NMR (CDCl$_3$, 400 MHz; 1D TOCSY): $\delta$ 7.50–7.47 (m, 2 H, Ar), 7.41–7.22 (m, 28 H, Ar), 5.52 (s, 1 H, CHPh), 5.50 (dd ~ t, 1 H, $J_{3''',4'''}$ 9.6 Hz, H-3‴), 5.16 (dd ~ t, 1 H, $J_{4''',5'''}$ 10.2 Hz, H-4‴), 5.10 (d, 1 H, $J_{1''',2'''}$ 4.0 Hz, H-1‴), 5.08 (d, 1 H, $J_{1',2'}$ 3.7 Hz, H-1′), 5.05 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 5.02, 4.712 (2 d, 2 H, $J_{\mathrm{gem}}$ 11.3 Hz, CH$_2$Ph), 4.97, 4.84 (2 d, 2 H, $J_{\mathrm{gem}}$ 11.2 Hz, CH$_2$Ph), 4.81 (dd, 1 H, $J_{2''',3'''}$ 10.2 Hz, H-2‴), 4.74, 4.40 (2 d, 2 H, $J_{\mathrm{gem}}$ 12.0 Hz, CH$_2$Ph), 4.705, 4.66 (2 d, 2 H, $J_{\mathrm{gem}}$ 12.0 Hz, CH$_2$Ph), 4.68, 4.58 (2 d, 2 H, $J_{\mathrm{gem}}$ 12.2 Hz, CH$_2$Ph), 4.49 (ddd, 1 H, $J_{1'',2''}$ 7.8 Hz, $J_{2'',3''\mathrm{eq}}$ 5.0 Hz, $J_{2'',3''\mathrm{ax}}$ 11.3 Hz, H-2″), 4.41 (d, 1 H, H-1″), 4.33 (dd, 1 H, $J_{5'',6a''}$ 2.0 Hz, $J_{6a'',6b''}$ 11.6 Hz, H-6a″), 4.29 (ddd ~ dt, 1 H, $J_{5,6\mathrm{eq}}$ 4.7 Hz, $J_{5,6\mathrm{ax}}$ 10.5 Hz, H-5), 4.15 (dd, 1 H, $J_{5''',6a'''}$ 3.8 Hz, $J_{6a''',6b'''}$ 12.5 Hz, H-6a‴), 4.11 (dd ~ t, 1 H, $J_{3,4}$ 10.2 Hz, H-3), 4.10 (ddd ~ br d, 1 H, H-5′), 4.075 (dd, 1 H, H-6a), 4.07 (dd ~ d, 1 H, H-6b‴), 4.05 (ddd, 1 H, H-5‴), 3.98 (dd ~ t, 1 H, $J_{4',5'}$ 10.4 Hz, H-4′), 3.89 (dd, 1 H, $J_{5'',6b''}$ ≈ 7 Hz, H-6b″), 3.88 (dd ~ t, 1 H, $J_{3',4'}$ 8.8 Hz, H-3′), 3.83 (dd, 1 H, $J_{5',6a'}$ 2.3 Hz, $J_{6a',6b'}$ 10.5 Hz, H-6a′), 3.61 (dd ~ t, 1 H, $J_{6a,6b}$ 10 Hz, H-6b), 3.58 (dd ~ t, 1 H, $J_{4,5}$ 9.0 Hz, H-4), 3.56 (dd, 1 H, $J_{5',6b'}$ 1.8 Hz, H-6b′), 3.52 (dd, 1 H, $J_{2,3}$ 9.2 Hz, H-2), 3.50 (ddd ~ dt, 1 H, H-4″), 3.43 (dd, 1 H, $J_{2',3'}$ 9.2 Hz, H-2′), 3.42 (ddd, 1 H, $J_{4'',5''}$ 9.9 Hz, H-5″), 2.36 (ddd ~ dt, 1 H, $J_{3\mathrm{eq}'',4''}$ 5.0 Hz, $J_{3\mathrm{eq}'',3\mathrm{ax}''}$ 11.8 Hz, H-3eq″), 1.20, 1.18, 1.17, 1.13, 1.12, 1.05 (6 s, 54 H, *tert*-Bu), 1.12 (ddd ~ q, 1 H, H-3ax″); FABMS: *m/z* 1716.6 ([M + Na]$^+$), 1731.5 ([M + K]$^+$). Anal. Calcd for C$_{96}$H$_{124}$O$_{26}$: C, 68.07; H, 7.38. Found: C, 67.82; H, 7.42.

*α-*D*-Glucopyranosyl-(1 → 4)-3-deoxy-β-*D-ribo-*hexopyranosyl-(1 → 4)-2,3,6-tri-*O-*benzyl-α-*D*-glucopyranosyl 2,3-di-*O-*benzyl-4,6-*O-*benzylidene-α-*D*-glucopyranoside* (**9**).—To a solution of the protected tetrasaccharide **8** (590 mg, 0.348 mmol) in MeOH (20 mL) was added a catalytic amount of sodium ( ~ 5 mg). After 4 d the reaction mixture was neutralized by addition of acidic ion exchange resin (IR 120 H$^+$) and filtered. The filtrate was concentrated and purified by flash chromatography using 94:3:3 EtOAc–MeOH–water as eluent to furnish pure **9** (322 mg, 78%) as a colourless syrup, $[\alpha]_{\mathrm{D}}^{20}$ +126° (*c* 0.3, CHCl$_3$); $^1$H NMR (Me$_2$SO-$d_6$, 400 MHz): *d* 7.45–7.22 (m, 30 H, aromatic), 5.67 (s, 1 H, CHPh), 5.24 (d, 2 H, $J_{1,2} = J_{1',2'} = 3.5$ Hz, H-1, H-1′), 5.19 (d, 1 H, $J_{\mathrm{OH}}$ 5.3 Hz, CH–O*H*), 4.99 (d, 1 H, $J_{\mathrm{gem}}$ 10.8 Hz, CH$_2$Ph), 4.89 (d, 1 H, $J_{\mathrm{OH}}$ 5.6 Hz, CH–O*H*), 4.79, 4.75 (2 d, 2 H, $J_{\mathrm{gem}}$ 11.8 Hz, CH$_2$Ph), 4.79 (d, 1 H, $J_{1''',2'''}$ 4 Hz, H-1‴), 4.76 (d, 1 H, $J_{\mathrm{OH}}$ 4.8 Hz, CH–O*H*), 4.53 (t, 1 H, $J_{\mathrm{OH}}$ 5.7 Hz, CH$_2$–O*H*), 4.52, 4.48 (2 d, 2 H, $J_{\mathrm{gem}}$ 11.5 Hz, CH$_2$Ph), 4.37 (d, 1 H, $J_{1'',2''}$ 7.5 Hz, H-1″), 4.23 (t, 1 H, $J_{\mathrm{OH}}$ 5.4 Hz, CH$_2$–O*H*), 4.71–4.62 (m, 6 H, 5 CHPh + CH–O*H*),), 2.35 (ddd ~ dt, 1 H, H-3eq″), 1.27 (ddd ~ q, 1 H, H-3ax″); FABMS: *m/z* 1211.4 ([M + Na]$^+$), 1227.3 ([M + K]$^+$). Anal. Calcd for C$_{66}$H$_{76}$O$_{20}$: C, 66.65; H, 6.44. Found: C, 66.36; H, 6.43.

*α-*D*-Glucopyranosyl-(1 → 4)-3-deoxy-β-*D-ribo-*hexopyranosyl-(1 → 4)-α-*D*-glucopyranosyl α-*D*-glucopyranoside* (**10**).—A solution of the tetrasaccharide **9** (269 mg, 0.249 mmol) in 4:1 EtOH–water (20 mL) was hydrogenated in the presence of 10% palladium-on-carbon (240 mg). After 1 h, the reaction mixture was filtered over filter aid and washed with MeOH. The filtrate was concentrated to give pure **10** (161 mg) quantitatively as a colourless syrup, $[\alpha]_{\mathrm{D}}^{20}$ +171° (*c* 0.6, water); $^1$H NMR (D$_2$O, 400 MHz; 1D TOCSY): $\delta$ 5.18, 5.17 (2 d, 2 H, $J_{1a,2a;1b,2b}$ 3.8, 3.7 Hz, H-1a, H-1b), 5.10 (d, 1 H, $J_{1''',2'''}$ 3.8 Hz, H-1‴), 4.51 (d, 1 H, $J_{1'',2''}$ 7.8 Hz, H-1″), 3.92 (dd, 1 H, H-6a″), 3.85 (dd, 1 H, $J_{5''',6a'''}$ 2.0 Hz, H-6a‴), 3.83 (dd ~ t, 1 H, H-3b), 3.78 (ddd, 1 H, H-4″), 3.76 (dd, 1 H, $J_{5''',6b'''}$ 5.0 Hz, $J_{6a''',6b'''}$ 12.5 Hz, H-6b‴), 3.74 (dd, 1 H, $J_{5'',6b''}$ 5.3 Hz, $J_{6a'',6b''}$ 12 Hz, H-6b″), 3.69 (dd, 1 H, $J_{2,3}$ 9.8 Hz, H-2a), 3.66 (ddd, 1 H, H-5″), 3.65 (dd ~ t, 1 H, $J_{3''',4'''}$ 8.8 Hz, H-3‴), 3.63 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-2b), 3.62 (ddd, 1 H, H-5‴), 3.55 (dd, 1 H, $J_{2''',3'''}$ 9.8 Hz, H-2‴), 3.53 (ddd, 1 H, $J_{2'',3''\mathrm{eq}}$ 5.2 Hz, $J_{2'',3''\mathrm{ax}}$ 12.8 Hz, H-2″), 3.43 (dd, 1 H, $J_{4''',5'''}$ 10.5 Hz, H-4‴), 2.61 (ddd ~ dt, 1 H, $J_{3\mathrm{eq}'',4''}$ 4.3 Hz, $J_{3\mathrm{eq}'',3\mathrm{ax}''}$ 11.9 Hz, H-3eq″), 1.51 (ddd q, 1 H, $J_{3\mathrm{ax}'',4''}$ 9.9 Hz, H-3ax″); FABMS: *m/z* 673 ([M + Na]$^+$). Anal. Calcd for $C_{24}H_{42}O_{20}$: C, 44.31; H, 6.51. Found: C, 44.54; H, 6.49.

*Sulfated α-*D*-glucopyranosyl-(1 → 4)-3-deoxy-β-*D*-glucopyranosyl-(1 → 4)-α-*D*-glucopyranosyl α-*D*-glucopyranoside* (**11**).—A solution of the unprotected tetrasaccharide **10** (87 mg, 0.134 mmol) in abs DMF (1 mL) was reacted with the sulfur trioxide trimethylamine-complex (484 mg, 3.48 mmol) at 50 °C. After 20 h, a 10% aq solution of NaOAc was added, and the reaction mixture was concentrated. Additions of water followed by evaporation was repeated to remove trimethylamine. The residue was purified by gel filtration on Sephadex LH20 to give the main product **11** (158 mg) as a colourless solid. $^1$H NMR ($D_2O$, 400 MHz; 1D TOCSY, data of main product): δ 5.58 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 5.56 (d, 1 H, $J_{1',2'}$ 3.9 Hz, H-1′), 5.47 (d, 1 H, $J_{1''',2'''}$ 3.7 Hz, H-1‴), 4.86 (dd ~ t, 1 H, H-3), 4.66 (dd ~ t, 1 H, $J_{3''',4'''}$ 9.7 Hz, H-3‴), 4.52 (dd ~ t, 1 H, H-4), 4.48 (dd, 1 H, H-2′), 4.47 (dd, 1 H, H-2), 4.44 (dd ~ t, 1 H, H-4‴), 4.40 (dd, 1 H, $J_{2''',3'''}$ 9.3 Hz, H-2‴), 4.34 (H-5), 4.31 (H-6a), 4.25 (ddd, 1 H, H-2″), 2.97 (ddd ~ dt, 1 H, $J_{3\mathrm{eq}'',3\mathrm{ax}''}$ 12.2 Hz, H-3eq″), 1.75 (ddd ~ q, 1 H, H-3ax″); ISMS (reconstructs were determined according to the Fenn method [24]): *m/z* 1977 (M), 1875 (M–$SO_3Na$), 1773 (M–2 $SO_3Na$). Anal. Cald for $C_{24}H_{29}Na_{13}O_{20}S_{13}$: S, 21.08. Found: S, 19.98.

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