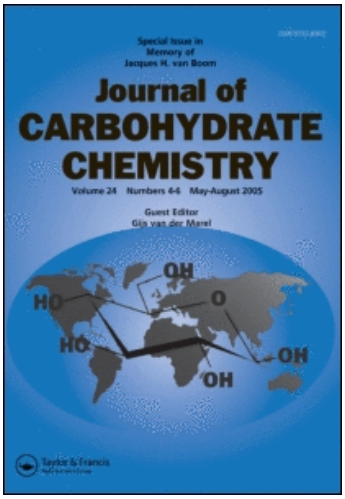

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THE SYNTHESIS OF THE 3'- AND 3'''-MONODEOXYGENATED DERIVATIVES OF β-MALTOSYL-(1→4)-TREHALOSE

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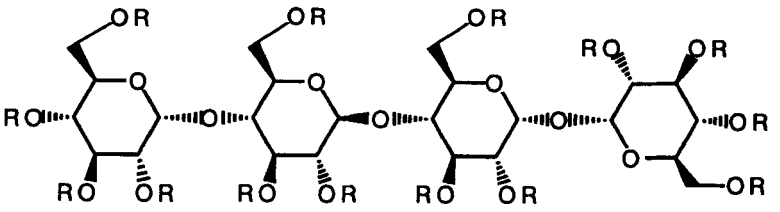
ABSTRACT

Two derivatives of β-maltosyl-(1→4)-trehalose monodeoxygenated at C-3' or C-3''' have been synthesized in [2+2] block syntheses. Starting from 4,6;4',6'-di-*O*-benzylidene-trehalose (**3**) the 3'-hydroxyl group was singled out by selective pivaloylation and reduced by a Barton-McCombie reaction. The benzylidene group in the vicinity of the deoxy function could be reductively opened to supply a suitable monodeoxygenated glycosyl acceptor (**8**). Standard glycosylation with hepta-*O*-acetylmaltosyl bromide and deprotection led to 3'-deoxymaltosyl-(1→4)-trehalose **13**. For the synthesis of a 3'-deoxygenated derivative of maltose we used 1,6-anhydromaltose as starting material. From the tributyltin hydride reduction of the 3,3'-bis-thiocarbonylimidazole derivative **18**, the 3'-monodeoxygenated derivative **20** was obtained in low yield. After opening of the 1,6-anhydro ring, the maltosyl derivative was activated as trichloroacetimidate **24**. Glycosylation followed by standard deprotection furnished the 3'''-deoxymaltosyl-(1→4)-trehalose **28**.

INTRODUCTION

Sulfated β-maltosyl-(1→4)-trehalose (**1**)[1] is an effective inhibitor of the proliferation of smooth muscle cells (SMC), which is a pivotal process in the development of arteriosclerotic lesions.[2,3] The inhibitory effect of **1** compares



1 R = SO_3Na or H, DS ≈ 2.8[4]

2 R = H

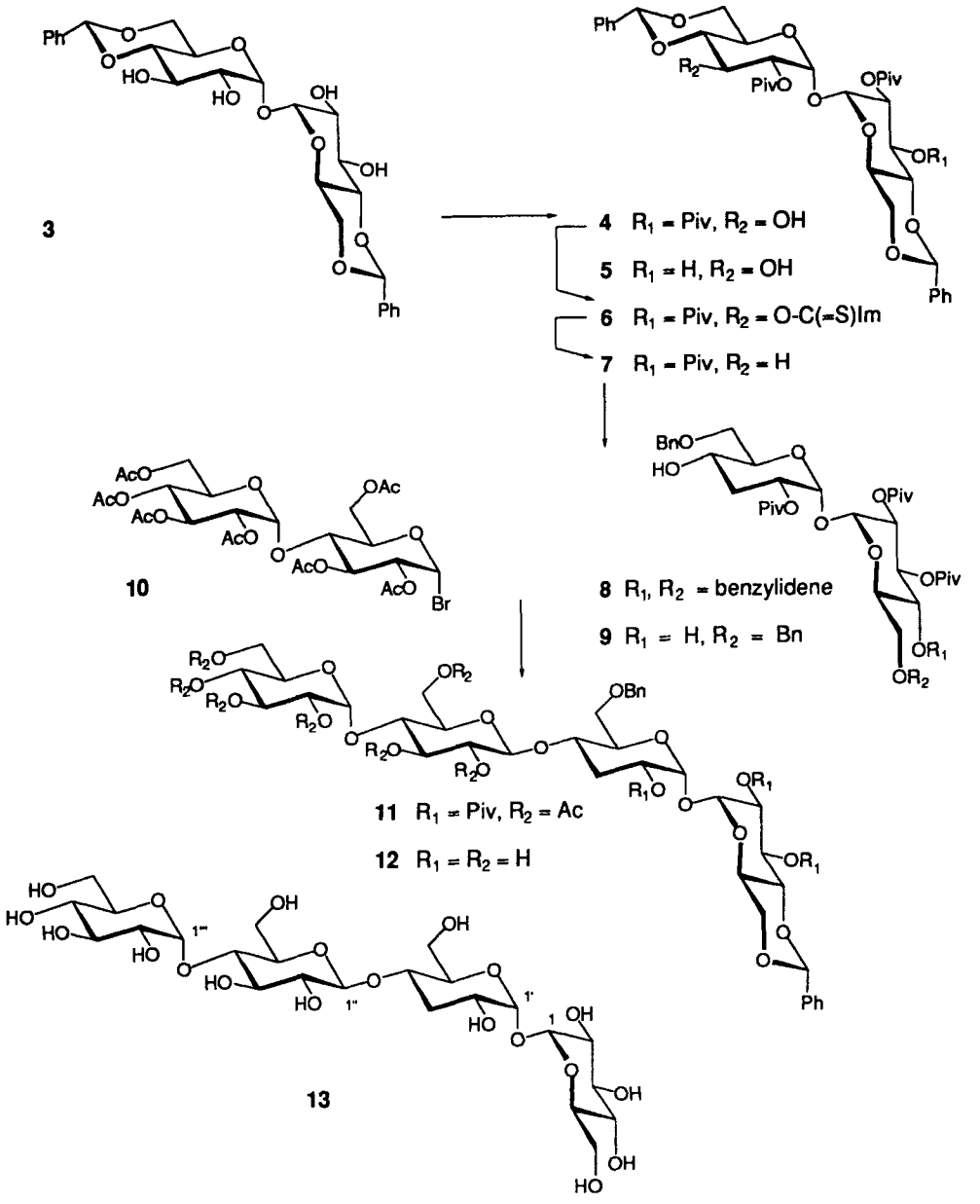
Scheme 1

to the one of heparin[1] and thus seems to mimic the action of heparan sulfate, an endogenous regulator of SMC growth.

Previous investigations have indicated that the biological effect is specific, and close structural analogues were distinctly less active.[1,5] It was therefore of interest to study which of the sulfates are essential for biological activity, and we have embarked on a program to selectively remove individual hydroxyl groups of tetrasaccharide 2 to avoid sulfation at this position. As the disaccharides trehalose and maltose are readily available our synthetic strategy foresaw the introduction of the deoxy function on the di- or tetrasaccharide level. The derivatives deoxygenated at the primary positions have been obtained in block syntheses via the respective iodinated compounds.[6] The syntheses of the tetrasaccharide analogues deoxygenated in positions 4 and 4''' were achieved after Barton-McCombie deoxygenation of the secondary 4-hydroxyl groups.[7] The 3''-hydroxyl group was isolated by selective pivaloylation of maltose and also removed in a Barton-McCombie reaction sequence.[8] In this report our syntheses of the 3'- and 3'''-deoxygenated analogues are detailed.

RESULTS AND DISCUSSION

For the synthesis of 3'-deoxygenated β-maltosyl-(1→4)-trehalose we departed from the partially protected trehalose derivative 4,6;4',6'-di-*O*-

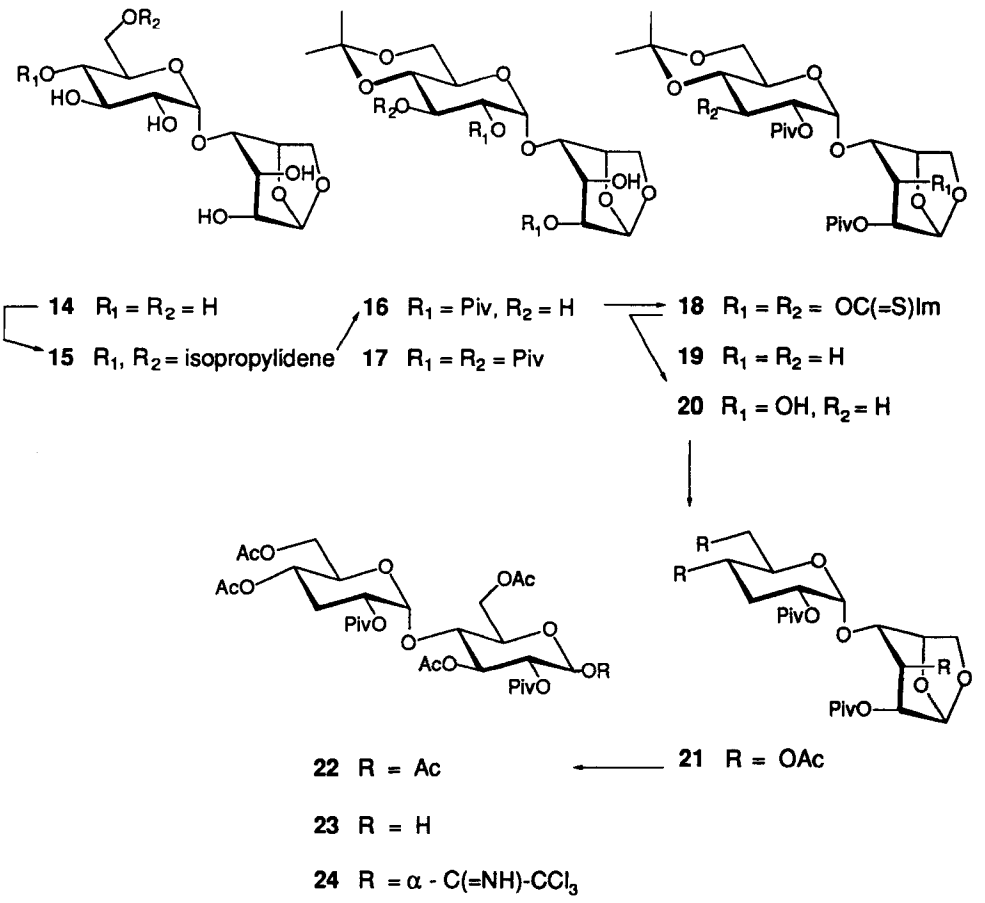


Scheme 2

benzylidenetrehalose (3).[9] As a 'symmetry breaking' reaction of the C_2-symmetrical trehalose we planned to introduce the sterically demanding valate esters which have been employed with advantage for the selective protection of disaccharides such as trehalose[10] or sucrose.[11] Pivaloylation of **3** with six equivalents of pivaloyl chloride afforded the tripivalate **4** in 50 % yield together with the dipivalate **5** (20 %). The sole remaining 3-hydroxyl group in **4** was removed in Barton McCombie reaction sequence:[12] activation with 1,1'-thiocarbonyldiimidazole in refluxing acetonitrile gave the thiocarbonylimidazole derivative **6** in excellent yield (97 %). C_2-Symmetry breaking of the symmetrical dipivalate **5** with 1,1'-thiocarbonyldiimidazole gave inferior overall results (data not shown). Compound **6** was then reduced with tributyltin hydride in toluene in the presence of azoisobutyronitrile (AIBN) as a radical starter to furnish the deoxygenated disaccharide **7** in 83 % yield. For acetal opening, this compound was treated with sodium cyanoborohydride in ether/hydrochloric acid.[13] The acetal in neighbourhood of the deoxy function was as expected more reactive than the other benzylidene group so that the 6'-*O*-benzyl ether **8** was obtained as the major product in 51 % yield along with the dibenzyl ether **9** (22 %).

Glycosylation of the monodeoxygenated disaccharide **8** with hepta-*O*-acetylmaltosyl bromide **10**[14] under Koenigs-Knorr reaction conditions with silver triflate[15] and tetramethylurea as catalyst furnished the tetrasaccharide **11** in 42 % yield. The deblocking of this saccharide followed the usual pattern: transesterification of **11** with sodium methoxide in methanol gave **12** (56 %), and the concomitant removal of the benzyl and benzylidene groups by catalytic hydrogenolysis quantitatively afforded the free tetrasaccharide **13**, the 3'-deoxygenated analogue of tetrasaccharide **2**.

The selective protection of all hydroxyl groups of maltose except the one at the 3'-position is not straightforward since the 3-hydroxyl group is less reactive than the 3'-hydroxyl group. We have therefore investigated the corresponding reactivities of hydroxyl groups in 1,6-anhydro-β-maltose **14**[16] which was prepared according to the well-described method of Kuzuhara and

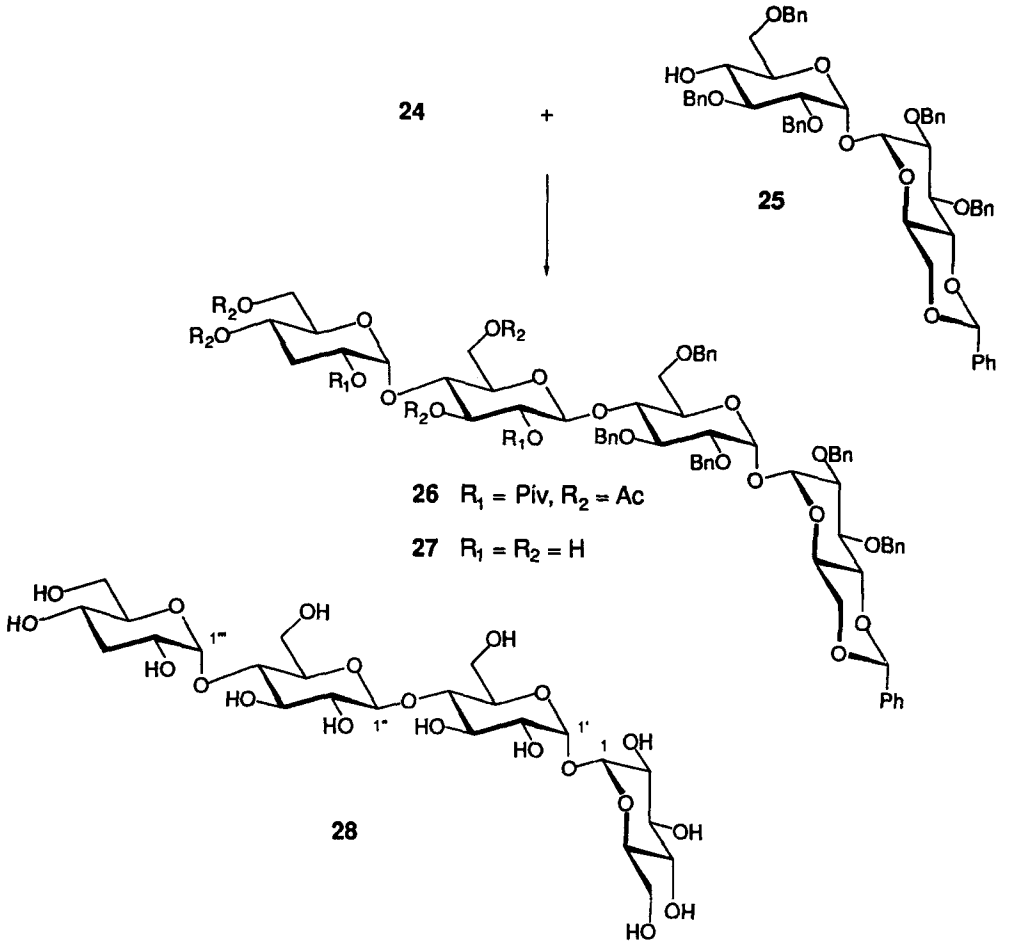


Scheme 3

collaborators.[17] The 4'- and 6'-positions of **14** were protected classically by isopropylidenation with dimethoxypropane to furnish **15**[18] in 96 % yield (Scheme 3). Again, pivaloyl chloride was employed to selectively protect hydroxyl groups. Under these reaction conditions the equatorial 3'-hydroxyl group was more reactive than the axially oriented 3-hydroxyl group; for example with 2.7 equivalents of reagent, the 2,2'-pivalate **16** was formed as the main product and isolated in 65 % yield together with some 5 % of the 2,2',3'-pivalate **17**. The location of the extra pivaloyl group was obvious from the ^{1}H NMR spectrum of **17** which showed the triplet of H-3' downfield

shifted (δ 5.43 ppm). In the ^{1}H NMR spectrum of **16**, the signal of H-3 is broader than usual (half-width ca. 11 Hz), but does not contain any large coupling constants meaning that the 1,6-anhydropyranose ring still mainly occurs in the $^1C_4$ chair conformation instead of a boat conformation which was observed in a related disaccharide derivative with a free 3-hydroxyl group[19] and in which this quasi-equatorial group might be expected to be more reactive. In a program directed towards the preparation of analogous dideoxytetrasaccharides, among others, also the dipivalate **16** had been targeted in order to synthesize the 3,3'-dideoxy derivative of maltose. Thus, in a Barton-McCombie[12] reaction sequence, the two hydroxyl groups of **16** were activated with 1,1'-thiocarbonyldiimidazole in refluxing tetrahydrofuran and 1,2-dichloroethane to give the thiocarbonylimidazole derivative **18** in 76 % yield. The subsequent reduction with tributyltin hydride in toluene in the presence of azoisobutyronitrile (AIBN) as a radical starter afforded the dideoxy derivative **19** (83 %). In this reaction the 3'-monodeoxy derivative **20** was obtained as a by-product in low yield (15 %). It is worth noting that in the ^{1}H NMR spectrum of **19**, the 6-H with the small coupling constant $J_{5,6'}$ in this case H-6b, is significantly shifted upfield, obviously a consequence of the missing interaction with the hydroxyl group in position 3.

Since only small amounts of monodeoxygenated tetrasaccharides were required for their use as biological probes, it was decided not to invest into the exploration of the selective activation of the 3'-hydroxyl group of **16** or alternative reaction sequences but to use the small amount of 3'-monodeoxy derivative **20** for further reactions. Following our experience in related cases, the 1,6-anhydro ring of **20** was not opened with concomitant cleavage of the 4',6'-*O*-isopropylidene group but in a two-step process. Thus, treatment of **20** with 80 % acetic acid followed by acetylation afforded **21** in excellent yield (95 %). 1,6-Anhydro ring opening with acetic anhydride/ acetic acid/ sulfuric acid then furnished **22** in 86 % yield. The anomeric acetates were obtained in a 3:1 α/β-mixture so that the direct employment as a glycosyl donor was not advisable since only the β-acetates are sufficiently activated for a trimethylsilyl



Scheme 4

triflate mediated glycosylation.[20] Therefore, the anomeric acetates were hydrolyzed selectively with hydrazinium acetate to give **23** in 90% yield and the free anomeric center was then activated by reaction with sodium hydride and trichloroacetonitrile[21] to yield the α-trichloroacetimidate **24** after chromatography (48 %).

The deoxygenated maltosyl donor **24** was reacted with the established trehalose glycosyl acceptor **25** to afford the tetrasaccharide derivative **26** in good yield (69 %) using trimethylsilyl triflate as a catalyst and dichloro-

methane as solvent. These conditions, initially employed in α-D-glycosylation reactions,[22] are also successful in β-D-glycosylations with glycosyl acceptors of low reactivity.[23] Regarding the ^{1}H NMR spectrum it is interesting to note that one of the pivalate tert. butyl groups has experienced an up-field shift of ca. 0.1 ppm (δ 1.03 ppm); characteristic up-field shifts for 2''-*O*-acetates in the range of 0.3 ppm have been observed before and attributed to an interaction with the 6'-*O*-benzyl group. The deprotection of **26** including deacetylation with sodium methoxide in methanol to give **27** and catalytic hydrogenolysis gave quantitatively the free tetrasaccharide **28**, the 3'''-deoxygenated analogue of tetrasaccharide **2**.

The investigation of the antiproliferative activities of the highly sulfated derivatives of the deoxygenated tetrasaccharides **13** and **28** has shown that the removal of sulfates at C-3' and C-3''' leads only to a relatively small reduction in activity.[24]

EXPERIMENTAL

General Procedures. Experimental conditions were essentially as described before.[6] MPLC = medium pressure liquid chromatography. Specific rotations were measured at 20 °C. Mass spectra were recorded on API III Sciex, Perkin Elmer (ionspray), VG 7070 F (CI) with data system SS 300, or MS 902 (FAB) with data system DS 2050 (VG).

4,6-*O*-Benzylidene-2-*O*-pivaloyl-α-D-glucopyranosyl 4,6-*O*-Benzylidene-2,3-di-*O*-pivaloyl-α-D-glucopyranoside (**4**) and **4,6-*O*-Benzylidene-2-*O*-pivaloyl-α-D-glucopyranosyl 4,6-*O*-Benzylidene-2-*O*-pivaloyl-α-D-glucopyranoside** (**5**). To a soln of **3** (51.8 g, 0.10 mol) in pyridine (518 mL) and abs dichloromethane (518 mL) was added at 0 - 5 °C within 4 h a soln of pivaloyl chloride (72.5 g, 0.60 mol) in abs dichloromethane (145 mL). The reaction mixture was stirred for 2 h at 0 - 5 °C, then at rt over night. The reaction mixture was concentrated under vacuum. The residue was taken up in ethyl acetate, washed with dil sulfuric acid/ice, saturated sodium bicarbonate soln,

and brine, dried over magnesium sulfate and concentrated. The residue was purified over silica gel (2 kg) using ethyl acetate/ hexane/ chloroform 1:4:2 and 1:2:2 as eluent to furnish pure **4** (39.4 g, 51 %) as a colourless solid and, after crystallization from acetone/ hexane, pure **5** (12.8 g, 19.6 %) as colourless crystals.

Data for **4**: Mp 259 - 261 °C; $[\alpha]_D$ +89.6 ° (*c* 0.5, chloroform); MS (ionspray) *m/z* 788 (100 %, $[M + NH_4]^+$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.44 - 7.42 (m, 2H, aromat), 7.38 - 7.32 (m, 8H, aromat), 5.67 (dd ~ t, 1H, $J_{3,4}$ = 9.7 Hz, H-3), 5.52 (s, 1H, CHPh), 5.49 (s, 1H, CHPh), 5.43, 5.42 (2 d ~ t, 2H, H-1, H-1'), 5.01 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 9.9 Hz, H-2), 4.86 (dd, 1H, $J_{1',2'}$ = 3.8 Hz, $J_{2',3'}$ = 9.6 Hz, H-2'), 4.28 (dd ~ t, 1H, $J_{3',4'}$ = 9.5 Hz, H-3'), 4.23 (dd, 1H, $J_{5,6a}$ = 4.8 Hz, $J_{6a,6b}$ = 10.3 Hz, H-6a), 4.19 (dd, 1H, $J_{5',6a'}$ = 4.5 Hz, $J_{6a',6b'}$ = 10.0 Hz, H-6a'; assignments for H-6a and H-6a' may be interchanged), 3.88 (ddd ~ dt, 1H, H-5), 3.82 (ddd ~ dt, 1H, $J_{5',6b'}$ = 10.2 Hz, H-5'), 3.74, 3.74, 3.70 (3 dd ~ t, 3H, H-6b, H-6b', H-4), 3.59 (dd ~ t, 1H, $J_{4',5'}$ = 9.1 Hz, H-4'), 2.40 (br s, 1H, 3'-OH), 1.28 (s, 9H, 2'-^{t}Bu), 1.26 (s, 9H, 2-^{t}Bu), 1.16 (s, 9H, 3-^{t}Bu).

Anal. Calcd for $C_{41}H_{54}O_{14}$ (770.87): C, 63.88; H, 7.06. Found: C, 63.98; H, 6.96.

Data for **5**: Mp 232 - 236 °C; $[\alpha]_D$ +109.8 ° (*c* 0.5, chloroform); MS (ionspray) *m/z* 709 (75 %, $[M + Na]^+$), 704 (30 %, $[M + NH_4]^+$), 687 (80 %, $[M + H]^+$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45 - 7.43 (m, 2H, aromat), 7.38 - 7.36 (m, 8H, aromat), 5.52 (s, 1H, CHPh), 5.40 (d, 1H, $J_{1,2}$ = 3.9 Hz, H-1), 4.88 (dd, 1H, $J_{2,3}$ = 9.9 Hz, H-2), 4.23 (ddd ~ dt, 1H, $J_{3,4}$ = 9.9 Hz, $J_{3,3\text{-OH}}$ = 1.9 Hz, H-3), 4.20 (dd, 1H, $J_{6a,6b}$ = 10.2 Hz, H-6a), (ddd ~ dt, 1H, $J_{4,5}$ = 8.8 Hz, $J_{5,6a}$ = 4.7 Hz, H-5), 3.72 (dd, 1H, $J_{5,6b}$ = 10.4 Hz, H-6b), 3.59 (dd ~ t, 1H, H-4'), 2.44 (d, 1H, 3-OH), 1.13 (s, 9H, 3-^{t}Bu).

Anal. Calcd for $C_{36}H_{46}O_{13}$ (686.75): C, 62.96; H, 6.75. Found: C, 62.76; H, 6.66.

4,6 - *O*- Benzylidene-2-*O*-pivaloyl-3-*O*-thiocarbonylimidazolyl -α-D-gluco-pyranosyl 4,6-*O*-Benzylidene-2,3-di-*O*-pivaloyl-α-D-glucopyranoside (6). To a soln of **4** (15.4 g, 20.0 mmol) in acetonitrile (400 mL) was added 1,1'-

thiocarbonyldiimidazole (10.7 g, 60.0 mmol) and 4-dimethylaminopyridine (0.015 g, 0.13 mmol) at rt. The reaction mixture was heated under reflux for 20 h, then concentrated under reduced pressure. The residue was chromatographed over silica gel (400 g) using hexane/ acetone 2:1 and 1:1 as eluent to obtain **6** (17.2 g, 97 %) as a beige amorphous powder: $[\alpha]_D$ +65.0 ° (*c* 0.4, chloroform); MS (ionspray) *m/z* 881 (100 %, $[M + H]^+$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.29 (s, 1H, imidazole), 7.58 (~t, 1H, imidazole), 7.38 - 7.31 (m, 10H, aromat), 7.01 (~t, 1H, imidazole), 6.57 (dd ~ t, 1H, $J_{3',4'}$ = 9.4 Hz, H-3'), 5.69 (dd ~ t, 1H, $J_{3,4}$ = 9.8 Hz, H-3), 5.51, 5.49 (2 d ~ t, 2H, H-1, H-1'), 5.50 (2 s, 2H, CHPh), 5.25 (dd, 1H, $J_{1',2'}$ = 3.7 Hz, $J_{2',3'}$ = 9.9 Hz, H-2'), 5.02 (dd, 1H, $J_{1,2}$ = 3.9 Hz, $J_{2,3}$ = 9.8 Hz, H-2), 4.27 (dd, 1H, $J_{5',6a'}$ = 3.3 Hz, H-6a'), 4.23 (dd, 1H, $J_{5,6a}$ = 4.7 Hz, H-6a), 3.99 - 3.91 (m, 2H), 3.88 - 3.71 (m, 4H), 1.28 (s, 9H, 2-^{t}Bu), 1.18 (s, 9H, 3-^{t}Bu), 1.09 (s, 9H, 2'-^{t}Bu).

Anal. Calcd for $C_{45}H_{56}N_2O_{14}S$ (881.01): C, 61.35; H, 6.41; N, 3.18; S, 3.64. Found: C, 61.52; H, 6.35; N, 3.05; S, 3.52.

4,6-*O*-Benzylidene-2-*O*-pivaloyl-3-deoxy-α-D-glucopyranosyl 4,6-*O*-Benzylidene-2,3-di-*O*-pivaloyl-α-D-glucopyranoside (**7**). To a soln of **6** (17.2 g, 19.5 mmol) in abs toluene (950 mL) was added α,α'-azodiisobutyronitrile (2.5 g, 15.2 mmol). At reflux temperature, a soln of tributyltin hydride (30 mL, 104 mmol) in toluene (50 mL) was added dropwise within 10 min. The reaction mixture was refluxed for 16 h and then concentrated. The residue was purified over silica gel (1000 g) using toluene/ ethyl acetate 19:1 and 9:1 as eluent to furnish, after crystallization from acetone/ hexane, pure **7** (12.4 g, 84%) as a colourless solid: mp 257-259 °C; $[\alpha]_D$ +76.6 ° (*c* 0.5, chloroform); MS (FAB) *m/z* 755 (40 %, $[M + H]^+$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.43 - 7.40 (m, 2H, aromat), 7.39 - 7.32 (m, 8H, aromat), 5.70 (dd ~ t, 1H, $J_{3,4}$ = 9.6 Hz, H-3), 5.51, 5.50 (2 s, 2H, 2 CHPh), 5.48 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 5.30 (d, 1H, $J_{1',2'}$ = 3.5 Hz, H-1'), 5.03 (dd, 1H, $J_{2,3}$ = 10.1 Hz, H-2), 4.93 (ddd, 1H, $J_{2',3'eq}$ = 4.8 Hz, $J_{2',3'ax}$ = 11.9 Hz, H-2'), 4.23 (dd, 1H, $J_{5,6a}$ = 4.9 Hz, $J_{6a,6b}$ = 10.3 Hz, H-6a), 4.17 (dd, 1H, $J_{5',6a'}$ = 4.3 Hz, $J_{6a',6b'}$ = 9.8 Hz, H-6a'), 3.98 (ddd ~ dt, 1H, $J_{5,6b}$ = 10.2 Hz, H-5), 3.77 (ddd ~ dt, 1H, H-5'), 3.75 (dd ~ t, 1H, H-6b), 3.71 (dd ~ t, 1H, $J_{4,5}$ = 9.7 Hz, H-4),

3.70 (dd ~ t, 1H, $J_{5',6b'}$ = 10.3 Hz, H-6b), 3.67 (ddd, 1H, $J_{3'eq,4'}$ = 4.1 Hz, $J_{4',5'}$ = 9.1 Hz, H-4'), 2.30 (ddd ~ dt, 1H, $J_{3'eq,3'ax}$ = 11.2 Hz, H-3'eq), 2.17 (ddd ~ q, 1H, $J_{3'ax,4'}$ = 11.7 Hz, H-3'ax), 1.27 (s, 9H, 2'-^{t}Bu), 1.24 (s, 9H, 2-^{t}Bu), 1.16 (s, 9H, 3-^{t}Bu).

Anal. Calcd for $C_{41}H_{54}O_{13}$ (754.87): C, 65.24; H, 7.21. Found: C,65.50; H, 7.02.

6-*O*-Benzyl-3-deoxy-2-*O*--pivaloyl-α-D-glucopyranosyl 4,6-*O*-(*R*)-Benzylidene-2,3-di-*O*-pivaloyl-α-D-glucopyranoside (8) and 6-*O*-Benzyl-3-deoxy-2-*O*-pivaloyl-α-D-glucopyranosyl 6-*O*-Benzyl-2,3-di-*O*-pivaloyl-α-D-glucopyranoside (9). To a soln of **7** (4.58 g, 6.0 mmol) in abs tetrahydrofuran (90 mL) were added pulverized 3Å molecular sieves (2.6 g) at 0 °C followed by sodium cyanoborohydride (2.6 g, 40 mmol) and a few crystals of methyl orange. Stirring was continued for 30 min, then hydrogen chloride in diethyl ether (30 mL of a 1.0 m soln, 30 mmol) was added dropwise over 2 h at 0 °C to the milky reaction mixture. After stirring for 3 h at 0 °C, the orange-red reaction mixture was poured into sodium bicarbonate soln, and tetrahydrofuran was evaporated under reduced pressure. The aqueous residue was extracted twice with ethyl acetate. The organic phases were washed with ice water and brine, dried over magnesium sulfate, and concentrated. The residue was chromatographed on silica gel (440 g) using ethyl acetate/ toluene 1:9 containing 1 %, 2 %, and 5 % methanol as eluent to give **8** (2.35 g, 51 %) as a colorless powder and **9** (1.05 g, 22 %) as a glassy syrup.

Data for **8**: $[\alpha]_D$ +77.8 ° (*c* 0.5, chloroform); MS (ionspray) *m/z* 795 (10 %, $[M + K]^+$), 779 (40 %, $[M + Na]^+$), 774 (100 %, $[M + NH_4]^+$); ^{1}H NMR ($CDCl_3$, 400 MHz, H,H-COSY) δ 7.37 - 7.28 (m, 10H, aromat), 5.67 (dd ~ t, 1H, $J_{3,4}$ = 9.7 Hz, H-3), 5.48 (s, 1H, CHPh), 5.41 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 5.24 (d, 1H, $J_{1',2'}$ = 3.4 Hz, H-1'), 5.02 (dd, 1H, $J_{2,3}$ = 9.9 Hz, H-2), 4.82 (ddd, 1H, $J_{2',3'eq}$ = 4.8 Hz, $J_{2',3'ax}$ = 12.3 Hz, H-2'), 4.57, 4.52 (2 d, 2H, J_{gem} = 11.9 Hz, CH_2Ph), 4.23 (dd, 1H, $J_{5,6a}$ = 4.9 Hz, $J_{6a,6b}$ = 10.1 Hz, H-6a), 3.95 (ddd ~ dt, 1H, $J_{4,5}$ = 10.0 Hz, H-5), 3.79 (br ddd, 1H, H-4'), 3.74 (dd ~ t, 1H, $J_{5,6b}$ = 10.0 Hz, H-6b), 3.69 (dd ~ t, 1H, H-4), 3.68 (dd, 1H, H-6a'), 3.65 (ddd, 1H, $J_{5',6a'}$ = 4.0 Hz, $J_{4',5'}$ = 9.8 Hz, H-5'), 3.57 (dd,

1H, $J_{5',6b'}$ = 6.1 Hz, $J_{6a',6b'}$ = 8.8 Hz, H-6b'), 2.76 (br s, 1H, 4'-OH), 2.21 (ddd ~ dt, 1H, $J_{3'eq,4'}$ = 4.6 Hz, $J_{3'eq,3'ax}$ = 11.5 Hz, H-3'eq), 2.00 (ddd ~ q, 1H, $J_{3'ax,4'}$ = 11.4 Hz, H-3'ax), 1.23 (s, 9H, 2-^{t}Bu), 1.21 (s, 9H, 2'-^{t}Bu), 1.15 (s, 9H, 3-^{t}Bu).

Anal. Calcd for $C_{41}H_{56}O_{13}$ (756.89): C, 65.06; H, 7.46. Found: C, 64.90; H, 7.60.

Data for **9**: $[\alpha]_D$ +97.8 ° (*c* 0.5, chloroform); MS (ionspray) *m/z* 781 (35 %, $[M + Na]^+$), 776 (100 %, $[M + NH_4]^+$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37 - 7.27 (m, 10H, aromat), 5.40 (dd ~ t, 1H, $J_{3,4}$ = 9.1 Hz, H-3), 5.39 (d, 1H, H-1), 5.19 (d, 1H, $J_{1',2'}$ = 3.4 Hz, H-1'), 4.98 (dd, 1H, $J_{1,2}$ = 3.6 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 4.82 (ddd, 1H, $J_{2',3'eq}$ = 4.7 Hz, $J_{2',3'ax}$ = 12.2 Hz, H-2'), 4.58, 4.53 (2 d, 2H, J_{gem} = 12.0 Hz, CH_2Ph), 4.56, 4.51 (2 d, 2H, J_{gem} = 11.9 Hz, CH_2Ph), 3.86 (ddd ~ dt, 1H, $J_{4,5}$ = 9.8 Hz, H-5), 3.78 (br ddd and dd ~ t, 2H, H-4', H-4), 3.73 (dd, 1H, $J_{5,6a}$ = 4.2 Hz, $J_{6a,6b}$ = 10.4 Hz, H-6a), 3.69 (dd, 1H, $J_{5',6a'}$ = 4.0 Hz, H-6a'), 3.66 (dd, 1H, $J_{5,6b}$ = 3.8 Hz, H-6b), 3.62 (ddd, 1H, $J_{4',5'}$ = 9.3 Hz, H-5'), 3.55 (dd, 1H, $J_{5',6b'}$ = 6.4 Hz, $J_{6a',6b'}$ = 8.9 Hz), 2.84, 2.81 (2 br s, 2H, 4-OH, 4'-OH), 2.20 (ddd ~ dt, 1H, $J_{3'eq,4'}$ = 4.7 Hz, $J_{3'eq,3'ax}$ = 11.5 Hz, H-3'eq), 1.96 (ddd ~ q, 1H, $J_{3'ax,4'}$ = 11.4 Hz, H-3'ax), 1.21 (s, 18H, 2 ^{t}Bu), 1.20 (s, 9H, ^{t}Bu).

Anal. Calcd for $C_{41}H_{58}O_{13}$ (758.90): C, 64.89; H, 7.70. Found: C, 64.78; H, 7.76.

***O*-(2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl)- (1→4) -*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→4)-6-*O*-benzyl-3-deoxy-2-O-pivaloyl-α-D-glucopyranosyl 4,6-*O*-(*R*)-Benzylidene-2,3-di-*O*-pivaloyl-α-D-glucopyranoside (11).** To a soln of glycosyl acceptor **8** (1.66 g, 2.2 mmol) and acetobromomaltose **10** (2.94 g, 4.2 mmol) in abs dichloromethane (20 mL) was added tetramethylurea (0.96 mL, 8.0 mmol) and silver triflate (1.03 g, 4.0 mmol) at -10 °C. The reaction mixture was stirred at rt for 18 h, and then filtered through a pad of filter aid. The filtrate and dichloromethane washings were combined and washed twice with aq sodium bicarbonate soln. The organic phases were dried over magnesium sulfate and concentrated. The residue was chromatographed on silica gel using ethyl acetate/ hexane 1:2 and 1:1 as eluent to furnish **11** (1.27 g,

42 %) as a colorless foam: $[\alpha]_D$ +101.5 ° (*c* 0.2, chloroform); MS (FAB) *m/z* 1413.6 (84 %, $[M + K]^+$), 1397 (100 %, $[M + Na]^+$).

Anal. Calcd for $C_{67}H_{90}O_{30}$ (1375.43): C, 58.51; H, 6.60. Found: C, 58.76; H, 6.44.

***O*-α-D-Glucopyranosyl- (1→4) -*O*-β-D-glucopyranosyl-(1→4)-6-*O*-benzyl-3-deoxy-α-D-glucopyranosyl 4,6-*O*-(*R*)-Benzylidene-α-D-glucopyranoside (12).** To a soln of **11** (1.10 g, 0.80 mmol) in dimethoxyethane (2 mL) and methanol (20 mL) was added a soln of sodium methanolate (10 mL of 2.0 g Na/ 100 mL methanol) at rt. The reaction mixture was kept for 5 days at rt, neutralized with Amberlite IR 120 (H^+), and filtered. After addition of a few drops of triethylamine, the filtrate and methanol washings were concentrated. The residue was chromatographed on silica gel using ethyl acetate/ methanol/ water 17:2:1 and 8:1:1 as eluent to obtain **12** (0.37 g, 56 %) as a colorless foam: $[\alpha]_D$ +114.0 ° (*c* 0.1, water); MS (FAB) *m/z* 867 (20 %, $[M + K]^+$), 851 (47 %, $[M + Na]^+$); 829 (40 % $[M + H]^+$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.56 - 7.54 (m, 2H, aromat), 7.48 - 7.43 (m, 8H, aromat), 5.75 (s, 1H, CHPh), 5.33 (d, 1H, $J_{1''',2'''}$ = 3.8 Hz, H-1'''), 5.26 (d, 1H, $J_{1,2}$ = 3.9 Hz, H-1), 5.10 (d, 1H, $J_{1',2'}$ = 3.4 Hz, H-1'), 4.69, 4.53 (2 d, 2H, J_{gem} = 11.8 Hz, CH_2Ph), 4.31 (dd, 1H, $J_{5,6a}$ = 4.8 Hz, $J_{6a,6b}$ = 10.2 Hz, H-6a), 4.27 (d, 1H, $J_{1'',2''}$ = 8.0 Hz, H-1''), 2.37 (ddd ~ dt, 1H, H-3'eq), 2.01 (ddd ~ q, 1H, H-3'ax).

Anal. Calcd for $C_{38}H_{52}O_{20}$ (828.81): C, 55.07; H, 6.32. Found: C, 44.97; H, 6.40.

***O*-α-D-Glucopyranosyl- (1→4) -*O*-β-D-glucopyranosyl- (1→4) -3-deoxy-α-D-glucopyranosyl α-D-Glucopyranoside (13).** A soln of **12** (320 mg, 0.386 mmol) in ethanol (15 mL) and water (5 mL) was hydrogenated in the presence of 10% palladium on charcoal (200 mg) at 1.1 bar and rt for 18 h. The reaction mixture was filtered over a pad of celite and washed with ethanol/ water 1:1. After addition of a few drops of triethylamine, the filtrate was concentrated. The aqueous residue was filtered through a column of RP-18 (30 g). Product fractions were concentrated and lyophilized to obtain **13** (255 mg, 100 %) as an

amorphous colourless powder: $[\alpha]_D$ +127.8 ° (*c* 0.1, water); MS (ionspray) *m / z* 673 (100 %, $[M + Na]^+$); ^1H NMR (D_2O, 400 MHz) δ 5.41 (d, 1H, $J_{1''',2'''}$ = 3.9 Hz, H-1'''), 5.23 (d, 1H, $J_{1,2}$ = 3.9 Hz, H-1), 5.10 (d, 1H, $J_{1',2'}$ = 3.3 Hz, H-1'), 4.58 (d, 1H, $J_{1'',2''}$ = 8.1 Hz, H-1''), 2.42 (ddd ~ dt, 1H, H-3'eq), 2.02 (ddd ~ q, 1H, H-3'ax).

Anal. Calcd for $C_{24}H_{42}O_{20}$ (650.58): C, 44.31; H, 6.51. Found: C, 44.21; H, 6.45.

***O*-(4,6-*O*-Isopropylidene-α-D-glucopyranosyl)- (1→4)-1,6-anhydro-β-D-glucopyranose (15).** To a soln of dried 1,6-anhydro-β-maltose **14** (11.3 g, 35 mmol) in abs DMF (43 mL) and α,α-dimethoxytoluene (22 mL, 0.18 mol) was added camphor sulfonic acid (450 mg). After stirring at rt for 6.5 h triethylamine (2 mL) was added, and the soln was concentrated. The residue was purified by chromatography using ethyl acetate/ methanol 6:1 as eluents. From the main fraction pure **15** (13.1 g, 96 %) was obtained by crystallization from ethyl acetate/ ether: mp 154 - 156 °C; $[\alpha]_D$ +54.4 ° (*c* 0.2, dioxane); MS (CI) *m/z* 382 (100 %, $[M + NH_4]^+$), 365 (78 %, $[M + H]^+$); ^1H NMR (Me_2SO, 250 MHz) δ 5.14 (d, 1H, J = 4.0 Hz, OH), 5.06 (d, 1H, J = 5.0 Hz, OH), 4.69 (d, 1H, $J_{2,2\text{-OH}}$ = 7.6 Hz, 2-OH), 4.65 (d, 1H, $J_{2',2'\text{-OH}}$ = 8.8 Hz, 2'-OH); ^1H NMR (Me_2SO, trace D_2O, 250 MHz) δ 5.20 (br s, 1H, H-1), 4.92 (d, 1H, $J_{1',2'}$ = 3.6 Hz, H-1'), 4.53 (dd ~ br d, 1H, $J_{5,6b}$ = 5.2 Hz, H-5), 3.94 (d, 1H, $J_{6a,6b}$ = 7.0 Hz, H-6a), 3.78 - 3.36 (m, 8H, H-3, H-4, H-6b, H-3' - H-6'), 3.24 (dd, 1H, $J_{2',3'}$ = 9.0 Hz, H-2'), 3.20 (br s, 1H, H-2), 1.43, 1.32 (2 s, 6H, 2 CH_3).

Anal. Calcd for $C_{15}H_{24}O_{10}$ (364.35): C, 49.45; H, 6.64. Found: C, 49.08; H, 6.74.

***O* -(4,6-*O*-Isopropylidene-2-*O*-pivaloyl-α-D-glucopyranosyl)-(1→4)-1,6-anhydro-2-*O*-pivaloyl-β-D-glucopyranose (16)** and ***O*-(4,6-*O*-isopropylidene-2,3-di-*O*-pivaloyl-α-D-glucopyranosyl)- (1→4) -1,6-anhydro-2-*O*-pivaloyl-β-D-glucopyranose (17).** To a soln of isopropylidene derivative **15** (8.6 g, 24 mmol) in pyridine (10 mL) was added pivaloyl chloride (8 mL, 65 mmol) at -14 °C. After 2.5 h at -14 - -10 °C the reaction mixture was poured into ice water and

extracted with ethyl acetate. Organic solutions were combined, concentrated, and dried on vacuum. The solid residue was treated with ether to leave crystalline **16** (6.0 g, 48 %) which was filtered off. The mother liquor was purified by MPLC using ethyl acetate/ hexane as eluent to furnish pure tripivalate **17** (710 mg, 4.8 %) followed by another lot of dipivalate **16** (2.2 g, 17 %).

Data for **16**: Colourless crystals, mp 168 - 170 °C; $[\alpha]_D$ +44.0 ° (*c* 0.5, dioxane); MS (CI) *m/z* 533 (5 %, $[M + H]^+$), 287 (non-reducing end pyranose, 100 %); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.42 (br s, 1H, H-1), 5.27 (d, 1H, $J_{1',2'}$ = 3.9 Hz, H-1'), 4.73 (d, 1H, $J_{5,6b}$ = 5.3 Hz, H-5), 4.68 (dd, 1H, $J_{2',3'}$ = 9.6 Hz, H-2'), 4.45 (br s, 1H, H-2), 4.04 (ddd ~ dt, 1H, $J_{3',4'}$ = 9.4 Hz, $J_{3',3'\text{-OH}}$ = 2.0 Hz, H-3'), 4.02 (dd, 1H, $J_{5,6a} \approx 1$ Hz, H-6a), 4.01 (ddd ~ dt, 1H, $J_{5',6b'}$ = 11.5 Hz, H-5'), 3.88 (dd, 1H, $J_{5',6a'}$ = 5.2 Hz, $J_{6a',6b'}$ = 10.8 Hz, H-6a'), 3.75 (dd ~ t, 1H, H-6b'), 3.72 (dd ~ t, 1H, $J_{6a,6b}$ = 8.0 Hz, H-6b), 3.69 (~ ddd, 1H, H-3), 3.61 (dd ~ t, 1H, $J_{4',5'}$ = 9.5 Hz, H-4'), 3.49 (br s, 1H, H-4), 2.73 (d, 1H, $J_{3,3\text{-OH}}$ = 5.0 Hz, 3-OH), 2.29 (d, 1H, 3'-OH), 1.53, 1.43 (2 s, 6H, 2 CH_3), 1.25, 1.22 (2 s, 18H, 2 ^{t}Bu).

Anal. Calcd for $C_{25}H_{40}O_{12}$ (532.58): C, 56.38; H, 7.57. Found: C, 56.39; H, 7.64.

Data for **17**: Colourless solid, $[\alpha]_D$ +36.2 ° (*c* 0.5, dioxane); MS (CI) *m/z* 634 (100 %, $[M + NH_4]^+$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.43 (br s, 1H, H-1), 5.43 (dd ~ t, 1H, $J_{3',4'}$ = 9.6 Hz, H-3'), 5.29 (d, 1H, $J_{1',2'}$ = 4.0 Hz, H-1'), 4.81 (dd, 1H, $J_{2',3'}$ = 9.9 Hz, H-2'), 4.76 (br d, 1H, $J_{5,6b}$ = 5.0 Hz, H-5), 4.46 (br s, 1H, H-2), 4.10 (ddd ~ dt, 1H, $J_{4',5'}$ = 9.8 Hz, H-5'), 4.02 (dd, 1H, $J_{5,6a} \leq 1$ Hz, $J_{6a,6b}$ = 7.2 Hz, H-6a), 3.91 (dd, 1H, $J_{5',6a'}$ = 5.2 Hz, $J_{6a',6b'}$ = 10.4 Hz, H-6a'), 3.74 (dd ~ t, 1H, $J_{5',6b'}$ = 10.6 Hz, H-6b'), 3.73 (dd, 1H, H-6b), 3.71 (~ s, 1H, H-3), 3.69 (dd ~ t, 1H, H-4'), 2.77 (br s, 1H, 3-OH), 1.43, 1.32 (2 s, 6H, 2 CH_3), 1.30 (s, 9H, ^{t}Bu), 1.16 (s, 18H, 2 ^{t}Bu).

Anal. Calcd for $C_{30}H_{48}O_{13}$ (616.70): C, 58.43; H, 7.85. Found: C, 58.83; H, 7.81.

***O* - (4,6-*O*-Isopropylidene-2-*O*-pivaloyl-3-*O*-thiocarbonylimidazole-α-D-glucopyranosyl)-(1→4)-1,6-anhydro-2-*O*-pivaloyl-3-*O*-thiocarbonylimidazolyl-**

β-D-glucopyranose (18). A soln of disaccharide **16** (8.0 g, 15.0 mmol) in tetrahydrofuran (65 mL) and 1,2-dichloroethane (65 mL) was refluxed under argon in the presence of 1,1'-thiocarbonyldiimidazole (11.0 g, 61.7 mmol) for 17 h. The reaction mixture was cooled, poured into ice/ dilute hydrochloric acid, and extracted with ethyl acetate. The organic phases were washed with bicarbonate soln and water, dried, and concentrated. The residue was purified by chromatography on silica gel using ethyl acetate/ hexane 5:1 as eluent to afford pure **18** (8.6 g, 76 %) as a colourless solid: $[\alpha]_D$ +14.2 ° (*c* 0.5, dioxane); ^{1}H NMR ($CDCl_3$, 400 MHz; H,H-COSY) δ 8.34 (~ s, 1H, imidazole), 8.30 (~ s, 1H, imidazole), 7.61 (dd ~ t, 1H, imidazole), 7.59 (dd ~ t, 1H, imidazole), 7.08 (dd ~ t, 1H, imidazole), 7.05 (dd ~ t, 1H, imidazole), 6.33 (dd ~ t, 1H, $J_{3',4'}$ = 9.5 Hz, H-3'), 5.57 (br s, 1H, H-1), 5.48 (br s, 1H, H-3), 5.31 (d, 1H, $J_{1',2'}$ = 3.9 Hz, H-1'), 5.11 (dd, 1H, $J_{2',3'}$ = 9.9 Hz, H-2'), 4.83 (ddd ~ br d, 1H, H-5), 4.75 (~ d, 1H, H-2), 4.32 (ddd ~ dt, 1H, $J_{5',6a'}$ = 5.3 Hz, $J_{5',6b'}$ = 10.2 Hz, H-5'), 3.99 (dd ~ t, 1H, $J_{4',5'}$ = 9.9 Hz, H-4'), 3.96 (dd, 1H, H-6a'), 3.92 (dd, 1H, $J_{5,6a}$ = 1.0 Hz, H-6a), 3.87 (dd, 1H, $J_{5,6b}$ = 5.6 Hz, $J_{6a,6b}$ = 7.2 Hz, H-6b), 3.81 (dd ~ t, 1H, $J_{6a',6b'}$ = 10.6 Hz, H-6b'), 3.73 (br s, 1H, H-4), 1.49, 1.38 (2 s, 6H, 2 CH_3), 1.36, 1.08 (2 s, 18H, 2 ^{t}Bu).

Anal. Calcd for $C_{33}H_{44}N_4O_{12}S_2$ (752.85): C, 52.65; H, 5.89; N, 7.44; S, 8.52. Found: C, 52.43; H, 5.99; N, 7.35; S, 8.43.

***O* - (3-Deoxy - 4,6-*O*-isopropylidene - 2-*O*-pivaloyl - α-D-glucopyranosyl)-(1→4)-1,6-anhydro-3-deoxy-2-*O*-pivaloyl-β-D-glucopyranose (19)** and ***O*-(3-Deoxy-4,6-*O*-isopropylidene-2-*O*-pivaloyl-α-D-glucopyranosyl)- (1 → 4) -1,6-anhydro-2-*O*-pivaloyl-β-D-glucopyranose (20).** A soln of tributyltin hydride (8.0 mL, 30.2 mmol) in toluene (30 mL) was refluxed for 1 h in the presence of AIBN (250 mg). Then a soln of the thiocarbonylimidazole derivative **18** (5.68 g, 7.54 mmol) in toluene (20 mL) was added to the refluxing solution. After another 15 min at reflux the solvent was evaporated. The crude reaction mixture was purified by chromatography over silica gel using toluene/ ethyl acetate 4:1 as eluents to afford **19** (3.1 g, 83 %) as a colourless foam followed by **20** (515 mg, 15 %).

Data for **19**: $[\alpha]_D$ +25.0 ° (*c* 0.2, dioxane); MS (CI) *m/z* 518 (30 %, $[M + NH_4]^+$), 271 (100 %, non-reducing end pyranose); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 5.41 (br s, 1H, H-1), 5.03 (d, 1H, $J_{1',2'}$ = 3.7 Hz, H-1'), 4.79 (m_c, 1H, H-2), 4.77 (dd, 1H, $J_{2',3'eq}$ = 6.1 Hz, $J_{2',3'ax}$ = 11.1 Hz, H-2'), 4.61 (ddd ~ dt, 1H, $J_{5,6a}$ = 5.3 Hz, H-5), 4.17 (ddd ~ dt, 1H, $J_{4',5'}$ = 9.7 Hz, H-5'), 3.87 (dd, 1H, $J_{5',6a'}$ = 5.1 Hz, $J_{6a',6b'}$ = 10.2 Hz, H-6a'), 3.79 (dd, 1H, $J_{6a,6b}$ = 7.7 Hz, H-6a), 3.72 (dd, 1H, $J_{5,6b}$ = 1.4 Hz, H-6b), 3.69 (dd ~ t, 1H, $J_{5',6b'}$ = 10.6 Hz, H-6b'), 3.68 (ddd, 1H, $J_{3'ax,4'}$ = 8.0 Hz, H-4'), 3.42 (br d, 1H, $J_{3ax,4}$ = 5.0 Hz, H-4), 2.22 (ddd ~ dt, 1H, $J_{3'eq,3'ax}$ = 15.8 Hz, $J_{3'eq,4'}$ = 4.1 Hz, H-3'eq), 2.05 (ddd, 1H, 3'ax), 2.04 (m_c, 1H, H-3a), 1.81 (br d, 1H, $J_{3a,3b}$ = 16.0 Hz, H-3b), 1.50, 1.40 (2 s, 6H, 2 CH_3), 1.30, 1.17 (2 s, 18H, 2 ^{t}Bu).

Anal. Calcd for $C_{25}H_{40}O_{10}$ (500.59): C, 59.98; H, 8.05. Found: C, 59.81; H, 8.17.

Data for **20**: MS (CI) *m/z* 534 (60 %, $[M + NH_4]^+$), 517 (38 %, $[M + H]^+$); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 5.43 (br s, 1H, H-1), 5.14 (d, 1H, $J_{1',2'}$ = 3.7 Hz, H-1'), 4.80 (dd, 1H, $J_{2',3'eq}$ = 5.6 Hz, $J_{2',3'ax}$ = 11.5 Hz, H-2'), 4.76 (ddd ~ dt, 1H, $J_{5,6b}$ = 5.3 Hz, H-5), 4.46 (~ ddd, 1H, ΣJ ≈ 4.5 Hz, H-2), 4.03 (dd, 1H, $J_{5,6a}$ = 0.7 Hz, $J_{6a,6b}$ = 7.4 Hz, H-6a), 3.94 (ddd ~ dt, 1H, $J_{5',6a'}$ = 5.0 Hz, H-5'), 3.84 (dd, 1H, $J_{6a',6b'}$ = 10.5-Hz, H-6a'), 3.77 - 3.70 (m, 3H, H-6b, H-6b', H-3), 3.69 (m_c, 1H, H-4'), 3.53 (~ ddd, 1H, H-4), 2.69 (br. s, 1H, 3-OH), 2.03 (m_c, 1H, H-3'eq), 1.97 (m_c, 1H, H-3'ax), 1.50, 1.37 (2 s, 6H, 2 CH_3), 1.27, 1.18 (2 s, 18H, 2 ^{t}Bu).

Anal. Calcd for $C_{25}H_{40}O_{11}$ (516.58): C, 58.13; H, 7.81. Found: C, 58.04; H, 7.84.

***O*-(4,6-Di-*O*-acetyl-3-deoxy-2-*O*-pivaloyl-α-D-glucopyranosyl)- (1→4) -1,6-anhydro-3-*O*-acetyl-2-*O*-pivaloyl-β-D-glucopyranose (21).** Isopropylidene derivative **20** (540 mg, 1.05 mmol) was dissolved in 80 % aqueous acetic acid (10 mL) at 50 °C and then kept at rt. After 16 h the solution was concentrated, and the residue was co-evaporated with toluene. The crude product was acetylated with acetic anhydride (0.5 mL) in pyridine (1 mL) at rt. After 1 d the solution was concentrated, and the residue was co-evaporated with toluene. The crude product was purified by MPLC using ethyl acetate/ hexane 1:1 as

eluent to afford pure **21** (600 mg, 95 %) as a colourless solid: $[\alpha]_D$ +50.0 ° (*c* 0.2, dioxane); MS (FAB) *m/z* 641 (30 %, $[M + K]^+$), 625 (30 %, $[M + Na]^+$), 602 (45 %, $[M]^+$), 315 (100 %); ^{1}H NMR ($CDCl_3$, 400 MHz; H,H-COSY) δ 5.43 (br s, 1H, H-1), 5.15 (d, 1H, $J_{1',2'}$ = 3.5 Hz, H-1'), 4.94 (ddd ~ dt, 1H, $J_{5,6b}$ = 5.3 Hz, H-5), 4.83 (ddd ~ dt, 1H, $J_{3'eq,4'}$ = 5.0 Hz, $J_{3'ax,4'}$ = 11.0 Hz, H-4'), 4.80 (dddd ~ m_c, 1H, H-3), 4.76 (dd, 1H, $J_{2',3'eq}$ = 5.0 Hz, $J_{2',3'ax}$ = 12.2 Hz, H-2'), 4.56 (br s, 1H, H-2), 4.38 (ddd, 1H, $J_{4',5'}$ = 10.2 Hz, H-5'), 4.25 (dd, 1H, $J_{5',6a'}$ = 2.0 Hz, $J_{6a',6b'}$ = 12.2-Hz, H-6a'), 4.15 (dd, 1H, $J_{5',6b'}$ = 5.8 Hz, H-6b'), 4.01 (dd, 1H, $J_{5,6a}$ = 0.9 Hz, H-6a), 3.77 (dd, 1H, $J_{6a,6b}$ = 7.8 Hz, H-6b), 3.46 (br d, 1H, H-4), 2.30 (ddd ~ dt, 1H, H-3'ax), ~2.08 (m, 1H, H-3'eq), 2.08, 2.05, 2.02 (3 s, 9H, 3 OAc), 1.27, 1.19 (2 s, 18H, 2 ^{t}Bu).

Anal. Calcd for $C_{28}H_{42}O_{14}$ (602.63): C, 55.81; H, 7.03. Found: C, 55.89; H, 7.07.

***O*-(4,6-Di-*O*-acetyl-3-deoxy-2-*O*-pivaloyl-α-D-glucopyranosyl)-(1→4)-1,3,6-tri-*O*-acetyl-2-*O*-pivaloyl-D-glucopyranose (22).** 1,6-Anhydro derivative **21** (370 mg, 0.61 mmol) was dissolved in an acetylation mixture (2 mL) composed of acetic anhydride (14 mL), acetic acid (6 mL), and concd sulfuric acid (0.1 mL). After 6 d at 11 °C anhydrous sodium acetate was added, and the mixture was stirred for 1.5 h, poured into ice/ dilute sodium bicarbonate soln, and extracted with ethyl acetate. Organic phases were washed with water, dried over sodium sulfate, and concentrated. The residue was purified by chromatography over silica gel using ethyl acetate/ hexane 1:2 as eluent to afford pure **22** (372 mg, 86 %) as a mixture of anomers: MS (FAB) *m/z* 743 (25 %, $[M + K]^+$), 727 (25 %, $[M + Na]^+$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.30 (d, 0.75H, $J_{1,2}$ = 3.7 Hz, H-1α), 5.77 (d, 0.25H, $J_{1,2}$ = 8.0 Hz, H-1β), 5.49 (dd, 0.75H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 9.0 Hz, H-3α), 5.42 (d, 0.75H, $J_{1',2'}$ = 3.5 Hz, H-1'α), 5.38 (d, 0.25H, $J_{1',2'}$ = 3.5 Hz, H-1'β), 5.21 (dd ~ t, 0.25H, $J_{3,4}$ = 8.8 Hz, H-3β), 5.00 (dd, 0.25H, $J_{2,3}$ = 9.2 Hz, H-2β), 4.89 (dd, 0.75H, H-2α), 4.83 (ddd ~ dt, 0.75H, $J_{3'eq,4'}$ = 4.8 Hz, H-4'α), 4.81 (ddd ~ dt, 0.25H, $J_{3'eq,4'}$ = 4.9 Hz, H-4'β), 2.21 (ddd ~ dt, 1H, H-3'eq), 2.15, 2.14, 2.11, 2.06, 2.03 (5 s, 3.75H, 5 OAc α), 2.13, 2.07, 2.06, 2.05, 2.02 (5 s, 1.25H, 5 OAc β), 1.90 (ddd ~ q, 1H, H-3'ax), 1.21, 1.12 (2 s, 13.5H, 2 ^{t}Bu α), 1.19, 1.13 (2 s, 4.5H, 2 ^{t}Bu β).

Anal. Calcd for $C_{32}H_{48}O_{17}$ (704.72): C, 54.54; H, 6.87. Found: C, 54.65; H, 6.93.

***O*-(4,6-Di-*O*-acetyl-3-deoxy-2-*O*-pivaloyl-α-D-glucopyranosyl)-(1→4)-3,6-di-*O*-acetyl-2-*O*-pivaloyl-D-glucopyranose (23).** To a soln of **22** (470 mg, 0.67 mmol) in DMF (1 mL) was added hydrazinium acetate (67 mg, 0.73 mmol) which slowly dissolved during stirring for 4 h at rt. Then the reaction mixture was diluted with ethyl acetate and poured into ice/ water. The aqueous phase was extracted with ethyl acetate repeatedly. The organic phases were washed with water, dried over sodium sulfate, and concentrated. The residue was purified by chromatography over silica gel using toluene/ ethyl acetate 2:1 as eluent to afford pure **23** (399 mg, 90 %) as a colourless solid: MS (FAB) *m/z* 701 (30 %, $[M + K]^+$), 685 (25 %, $[M + Na]^+$), 663 (17 %, $[M + H]^+$), 645 (60 %, $[M + H - H_2O]^+$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.56 (dd, 1H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 9.0 Hz, H-3), 5.43 (d, 1H, $J_{1',2'}$ = 3.6 Hz, H-1'), 5.39 (dd ~ t, 1H, $J_{1,2}$ = 3.4 Hz, H-1), 4.83 (ddd ~ dt, 1H, $J_{3'eq,4'}$ = 4.8 Hz, $J_{3'ax,4'}$ = 11.0 Hz, H-4'), 4.75 - 4.59 (m, 3H, H-2', H-2, H-6a), 4.30 (dd, 1H, $J_{5',6a'}$ = 4.0 Hz, $J_{6a',6b'}$ = 12.0-Hz, H-6a'), 3.80 (ddd, 1H, $J_{4',5'}$ = 10.0 Hz, $J_{5',6b'}$ = 2.0 Hz, H-5'), 2.90 (dd, 1H, $J_{1,1\text{-OH}}$ = 3.7 Hz, $J_{2,1\text{-OH}}$ = 1.0-Hz, 1-OH), 2.20 (ddd ~ dt, 1H, H-3'eq), 1.91 (ddd ~ q, 1H, H-3'ax), 2.15, 2.11, 2.06, 2.03 (4 s, 12H, 4 OAc), 1.20, 1.17 (2 s, 18H, 2 ^{t}Bu).

Anal. Calcd for $C_{30}H_{46}O_{16}$ (662.68): C, 54.37; H, 7.00. Found: C, 54.29; H, 7.03.

***O* - (4,6-Di-*O*-acetyl-3-deoxy-2-*O*-pivaloyl-α-D-glucopyranosyl)- (1 → 4) -*O*-(3,6-di-*O*-acetyl-2-*O*-pivaloyl-α-D-glucopyranosyl) Trichloroacetimidate (24).** To a soln of **23** (380 mg, 0.57 mmol) in abs dichloromethane (4 mL) and trichloroacetonitrile (0.36 mL, 3.6 mmol) was added sodium hydride (80 % suspension in oil, 64 mg, 2.65 mmol). After 24 h at rt and under argon the reaction mixture was filtered over a pad of Speedex and concentrated. The residue was purified by chromatography over silica gel using ethyl acetate/ hexane 1:2 as eluent; the main fraction consisted of pure **24** (220 mg, 48 %): MS (FAB) *m/z* 846 (10 %, $[M + K]^+$), 828 (8 %, $[M + Na]^+$), 645 (100 %, $[M + H - NH_2\text{-}CO\text{-}CCl_3]^+$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.64 (s, NH), 6.49 (d, 1H, $J_{1,2}$ =

3.4 Hz, H-1), 5.64 (dd, 1H, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 8.8 Hz, H-3), 5.47 (d, 1H, $J_{1',2'}$ = 3.7 Hz, H-1'), 4.96 (dd, 1H, H-2), 4.82 (ddd ~ dt, 1H, $J_{3'eq,4'}$ = 4.8 Hz, $J_{3'ax,4'}$ = 11.1 Hz, H-4'), 4.71 82 (ddd ~ dt, 1H, $J_{2',3'eq}$ = 4.9 Hz, $J_{2',3'ax}$ = 12.5 Hz, H-2'), 4.58 (dd, 1H, $J_{5,6a}$ = 1.8 Hz, $J_{6a,6b'}$= 12.0-Hz, H-6a), 4.30 (dd, 1H, $J_{5',6a'}$ = 4.1 Hz, $J_{6a',6b'}$ = 12.0-Hz, H-6a'), 4.23 (dd, 1H, $J_{5,6b}$ = 4.0 Hz, H-6b), 4. (dd ~ t, 1H, $J_{4,5}$ = 9.6 Hz, H-4), 4.15 (ddd, 1H, H-5), 4.06 (dd, 1H, $J_{5',6b'}$ = 2.1 Hz, H-6b'), 3.74 (ddd, 1H, H-5'), 2.21 (ddd ~ dt, 1H, H-3'eq), 2.13, 2.11, 2.06, 2.04 (4 s, 12H, 4 OAc), 1.91 (ddd ~ q, 1H, $J_{3'eq,3'ax}$ = 11.7 Hz, H-3'ax), 1.19, 1.11 (2 s, 18H, 2 ^{t}Bu).

***O* - (4,6-Di-*O*-acetyl-3-deoxy-2-*O*-pivaloyl-α-D-glucopyranosyl)- (1 → 4) -*O*-(3,6-di-*O*-acetyl-2-*O*-pivaloyl-β-D-glucopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl 2,3-Di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (26).** A soln of imidate **24** (200 mg, 0.27 mmol) and glycosyl acceptor **25** (238 mg, 0.27 mmol) in abs dichloromethane (1 mL) was stirred at rt in the presence of 4 Å molecular sieves for 1 h. A soln of trimethylsilyl triflate (50 µL) in dichloromethane (1 mL) was added at -30 °C, and the mixture was stirred for 1 h. Then the reaction mixture was poured into ice/ aqueous sodium bicarbonate soln and extracted with ethyl acetate. The organic phases were washed with ice/ water, dried over sodium sulfate, and concentrated. The residue was purified by MPLC using ethyl acetate/ hexane 1:2 as eluent to afford pure tetrasaccharide **26** (263 mg, 69 %) as a colourless syrup; MS (FAB) *m/z* 1564 (30 %, $[M + K]^+$), 1548 (30 %, $[M + Na]^+$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.49 - 7.47 (m, 2H, aromat), 7.44 - 7.23 (m, 28H, aromat), 5.50 (s, 1H, CHPh), 5.25 (d, 1H, $J_{1''',2'''}$ = 3.6 Hz, H-1'''), 5.09, 5.04 (2 d, 2H, J = 3.8 Hz, J = 3.7 Hz, H-1, H-1'), 5.04, 4.78 (2 d, 2H, J_{gem} = 12.0 Hz, CH_2Ph), 4.97 (dd ~ t, 1H, H-3''), 4.96, 4.84 (2 d, 2H, J_{gem} = 10.7 Hz, CH_2Ph), 4.83 (dd, 1H, $J_{2'',3''}$ = 9.6 Hz, H-2''), 4.81 (ddd ~ dt, 1H, H-4'''), 4.73, 4.39 (2 d, 2H, J_{gem} = 12.0 Hz, CH_2Ph), 4.72 (ddd ~ dt, 1H, H-2'''), 4.71, 4.65 (2 d, 2H, J_{gem} = 13.0 Hz, CH_2Ph), 4.69, 4.61 (2 d, 2H, J_{gem} = 12.0 Hz, CH_2Ph), 4.39 (d, 1H, $J_{1'',2''}$ = 8.0 Hz, H-1''), 4.34 (dd, 1H, $J_{5''',6a'''}$ = 2.5 Hz, $J_{6a''',6b'''}$ = 11.7 Hz, H-6a'), 4.24 (dd, 1H, $J_{5'',6a''}$ = 4.3 Hz, $J_{6a'',6b''}$ ≈ 11.5 Hz, H-6a'), 4.22 (ddd ~ dt, 1H, $J_{5,6a}$ = 5.0 Hz, H-5), 4.10 - 3.94 (m, 7H, H-3, H-6b'', H-6a, H-5', H-6b''', H-3', H-4'), 3.86 (dd ~ t, 1H, H-4''?), 3.74 (ddd, 1H, $J_{5''',6b'''}$ = 3.8 Hz,

$J_{4''',5'''}$ = 9.8 Hz, H-5'''), 3.72 (dd, 1H, $J_{5',6a'}$ = 2.0 Hz, H-6a'), 3.59, 3.56 (2 d, 2H, H-6b, H-4), 3.53, 3.50 (2 dd, 2H, H-2, H-2'), 3.53 (dd, 1H, H-6b'), 3.26 (ddd, 1H, $J_{5'',6b''}$ = 2.9 Hz, H-5''), 2.19 (ddd ~ dt, 1H, H-3'''eq), 2.06, 2.04, 1.96, 1.90 (4 s, 12H, 4 OAc), 1.89 (ddd ~ q, 1H, H-3'''ax), 1.22, 1.03 (2 s, 18H, 2 ^{t}Bu).

Anal. Calcd for $C_{84}H_{100}O_{26}$ (1525.70): C, 66.13; H, 6.61. Found: C, 66.04; H, 6.67.

O-(3-Deoxy-α-D-glucopyranosyl)-(1→4)-O-α-D-glucopyranosyl-(1→4)-2,3,6-tri-O-benzyl-α-D-glucopyranosyl 2,3-Di-O-benzyl-4,6-O-benzylidene-α-D-glucopyranoside (27). To a soln of **26** (250 mg, 0.16 mmol) in cyclohexane (1 mL) and methanol (3 mL) was added a soln of sodium methanolate (0.98 mL of 2 g Na/ 100 mL methanol) at rt. The reaction mixture was stirred for 16 h at rt, neutralized with Amberlite IR 120 (H^+), and filtered. After addition of a few drops of triethylamine, the filtrate and methanol washings were concentrated. The residue was purified by MPLC using ethyl acetate/ methanol/ water 185:10:5 as eluent to obtain **27** (195 mg) quantitatively as a colourless foam: MS (FAB) *m/z* 1227 (30 %, $[M + K]^+$), 1211 (45 %, $[M + Na]^+$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.51 - 7.49 (m, 2H, aromat), 7.41 - 7.26 (m, 28H, aromat), 5.56 (s, 1H, CHPh), 5.14, 5.13 (2 d, 2H, H-1', H-1), 4.98 (d, 1H, $J_{1''',2'''}$ = 3.4 Hz, H-1'''), 4.89, 4.85 (2 d, 2H, J_{gem} = 11.1 Hz, CH_2Ph), 4.95, 4.90 (2 d, 2H, J_{gem} = 11.4 Hz, CH_2Ph), 4.81, 4.63 (2 d, 2H, J_{gem} = 11.8 Hz, CH_2Ph), 4.72, 4.68 (2 d, 2H, J_{gem} = 12.0 Hz, CH_2Ph), 4.59, 4.43 (2 d, 2H, J_{gem} = 12.1 Hz, CH_2Ph), 4.39 (d, 1H, $J_{1'',2''}$ = 7.7 Hz, H-1''), 4.26 (ddd ~ dt, 1H, $J_{5,6a}$ = 4.9 Hz, $J_{5,6b}$ = 10.0 Hz, H-5), 4.13 (dd ~ t, 1H, H-3), 4.12 (ddd ~ br d, 1H, H-5'), 4.11 (dd ~ t, 1H, $J_{6a,6b} \approx$ 10 Hz, H-6a), 3.97, 3.92 (2 dd ~ t, 2H, H-3', H-4'), 3.77 (dd, 1H, $J_{5'',6a''}$ = 3.1 Hz, $J_{6a'',6b''}$ = 11.4 Hz, H-6a'' or 6a'''), 3.72 - 3.49 (m, 12H), 3.45 (dd ~ t, 1H), 3.34 (dd, 1H, $J_{5',6b'}$ = 1.5 Hz, $J_{6a',6b'}$ = 11.2 Hz, H-6b'), 3.23 (d ~ t, 1H, $J_{2'',3''}$ = 9.2 Hz, H-2''), 2.97 (dd, 1H, $J_{4'',5''}$ = 9.4 Hz, $J_{5'',6b''}$ = 2.4 Hz, H-5''), 2.12 (ddd ~ dt, 1H, H-3'''eq), 1.72 (ddd ~ q, 1H, H-3'''ax).

Anal. Calcd for $C_{66}H_{76}O_{20}$ (1189.31): C, 66.65; H, 6.44. Found: C, 66.48; H, 6.47.

***O*-(3-Deoxy-α-D-glucopyranosyl)- (1→4) -*O*-β-D-glucopyranosyl-(1→4)-α-D-glucopyranosyl β-D-Glucopyranoside (28).** A soln of **27** (182 mg, 0.15 mmol) in ethanol/water 3:1 (8 mL) was hydrogenated in the presence of 10 % palladium on charcoal (80 mg) at 1.1 bar for 3 d. The reaction mixture was filtered through a pad of filter aid which was washed with ethanol/ water 1:1. The filtrates were concentrated and filtered over Sephadex LH 20 using water as eluent to obtain pure **23** (101 mg) quantitatively as a colourless solid: $[\alpha]_D$ +150.5 ° (*c* 0.2, water); MS (ionspray) *m/z* 689 (30 %, $[M + K]^+$), 673 (60 %, $[M + Na]^+$); ^1H NMR (D_2O, 400 MHz) δ 5.32 (d, 1H, $J_{1''',2'''}$ = 3.5 Hz, H-1'''), 5.20, 4.91 (2 d, 2H, H-1, H-1'), 4.55 (d, 1H, $J_{1'',2''}$ = 8.0 Hz, H-1''), 2.20 (ddd ~ dt, 1H, H-3'''eq), 1.75 (ddd ~ q, 1H, H-3'''ax).

Anal. Calcd for $C_{24}H_{42}O_{20}$ (650.58): C, 44.31; H, 6.51. Found: C, 44.20; H, 6.55.

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