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SYNTHESIS OF A METHYL HEPTAGLUCOSIDE: ANALOGUE OF THE PHYTOALEXIN ELICITOR FROM *PHYTOPHTORA MEGASPERMA*

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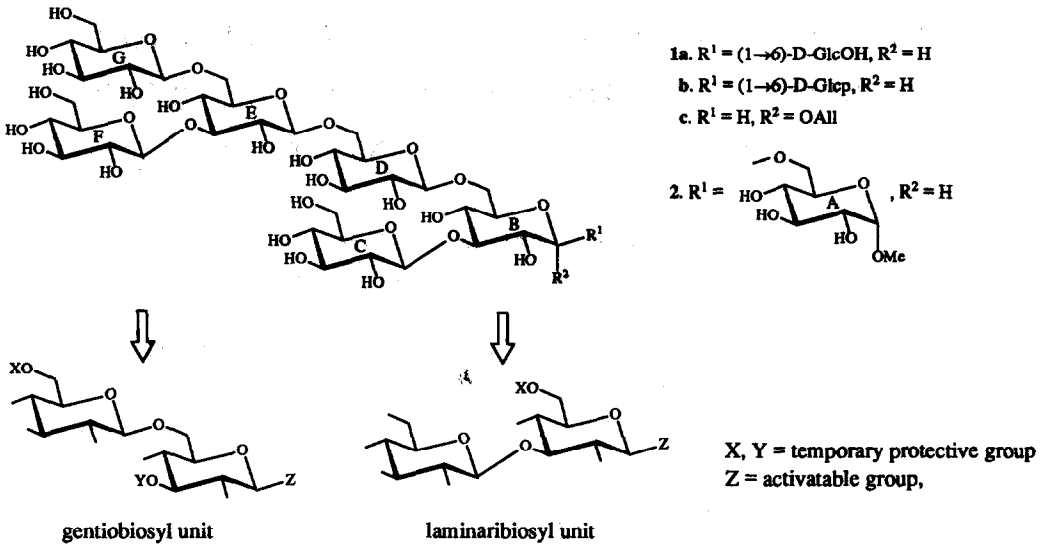
Abstract

The ethylthio-laminaribioside **29**, prepared by regiospecific glycosylation of ethyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (**9**) with 2,3,4,6-tetra-*O*-benzoyl-D-glucopyranosyl imidate **17** and subsequent benzoylation, could be elongated in a step-wise fashion by consecutive iodonium ion promoted condensations with methyl 2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (**5**), ethyl 2,3,4-tri-*O*-benzoyl-6-*O*-*tert*-butyldimethylsilyl-1-thio-β-D-glucopyranoside (**7**), the laminaribioside **29** and ethyl 2,3,4,6-tetra-*O*-benzoyl-1-thio-β-D-glucopyranoside (**8**), and intermittent protective group manipulations, to yield the partially acylated heptasaccharide **36**. Finally, one-step deacylation of branched heptamer **36** afforded the target compound α-methyl 3^2,3^4-di-β-D-glucopyranosylgentiopentaoside (**2**).

Introduction

In 1984, *Albersheim et al.*[1] reported that the branched β-D-glucohexaosyl glucitol **1a**, isolated from the mycelial walls of *Phytophtora Megasperma* f.sp. *glycinea*, showed phytoalexin elicitor activity[2] in soybean. The proposed structure was firmly established through an unambiguous synthesis[3] of the unreduced 3^2,3^4-di-β-D-glucopyranosylgentiopentaose **1b**, having the same biopotency as its isolated congener **1a**. It was also established[4] that **1b** recognizes high-affinity binding sites of a receptor tethered in soybean membranes. In addition, earlier structure-activity studies indicated[5] that the glucosyl units **C**, **F** and **G** (see Figure 1) are essential for maximal elicitor activity. However, elicitor activity was reduced considerably if two side-chain glucosyl residues were attached to adjacent backbone glucosyl residues (*e.g.* isomeric 3^3,3^4-di-β-glucopyranosylgentiopentaose). On the other hand, modification of the reducing terminal glucosyl unit **A** in **1b** by conjugation with tyramine or replacement by an allyl group (*i.e.* α-allyl-hexa-β-glucoside **1c**[6]) did not alter its biological activity.

Figure 1

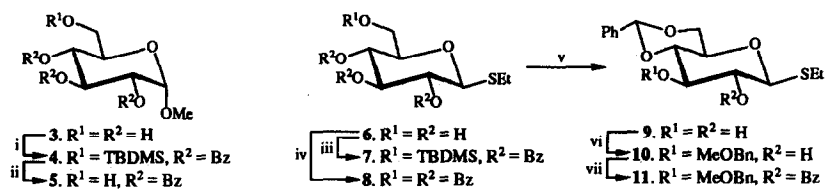


With the objective to gain a more detailed insight into the structural requirements for optimal interaction of the phytoalexin elicitor with the plant receptor, we here report a versatile and convergent route of synthesis to α-methyl 3^2,3^4-di-β-D-glucopyranosylgentiopentaoside (*i.e.* compound **2** in Figure 1).

Results and discussion

Retrosynthetic analysis reveals (see Figure 1) that the assembly of the target molecule **2** can be realized following a gentiobiosyl or laminaribiosyl approach. In addition, our heuristic knowledge[7] of sugar chemistry indicated that the use of alkyl 1-thioglycosides building units would be desirable. Consequently, we prepared (see Scheme 1) the two non-terminal ethyl 1-thioglucosides **7** and **11**, and the terminal ethylthio and methyl glucosides **8** and **5**, respectively. Thus, the methyl 2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (**5**) is easily accessible by regioselective silylation of the methyl α-D-glucopyranoside (**3**) with *tert*-butyldimethylsilyl

Scheme 1



Reagents and conditions: i. TBDMSCl (1.1 eq.), pyridine then BzCl; ii. *p*TsOH, CH_3CN/H_2O (2 steps: 85%); iii. TBDMSCl (1.1 eq.), pyridine then BzCl (89%); iv. BzCl, pyridine (92%); v. $PhCH(OMe)_2$, *p*TsOH, CH_3CN (81%); vi. Bu_2SnO, MeOH, Δ then *p*MeOBnCl, Bu_4NBr, toluene, Δ; vii. BzCl, pyridine (2 steps: 72%).

chloride (TBDMS-Cl) followed by benzoylation of **4** and subsequent acidolysis of the silyl group. Similarly, silylation of ethyl 1-thio-β-D-glucopyranoside[8] (**6**) with TBDMS-Cl gave, after benzoylation, the ethyl 2,3,4-tri-*O*-benzoyl-6-*O*-*tert*-butyldimethylsilyl-1-thio-β-D-glucopyranoside (**7**). On the other hand, exhaustive benzoylation of **6** yielded the ethyl 2,3,4,6-tetra-*O*-benzoyl-1-thio-β-D-glucopyranoside (**8**). The key non-terminal ethyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-*para*-methoxybenzyl-1-thio-β-D-glucopyranoside (**11**) was obtained by regioselective benzylation[9] of the *in situ* prepared stannylidene[10] derivative of ethyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside[11] (**9**) with *para*-methoxybenzyl chloride and subsequent benzoylation of **10**.

At this stage, we first explored whether the construction of heptamer **2** could be accomplished *via* the gentiobiosyl route which entails a sequential build up of the linear gentiopentaosyl backbone (**ABDEG**) followed by a one-step introduction of the side-chain units **C** and **F**. The sequence of reactions of this linear approach is delineated in Scheme 2 and commences with the synthesis of the gentiobioside **12**. Thus, glycosylation of acceptor **5** with donor **11** in the presence of the promoter *N*-iodosuccinimide and catalytic triflic acid[12] (NIS/TfOH) resulted in dimer **12**. Transacetalation of the benzylidene group in **12** gave the corresponding diol **13** in 72% overall yield.

Prior to the scheduled step-wise elongation of dimer **13** with the non-terminal donor **7**, we examined first whether trimer **16**, obtained by regioselective iodonium promoted condensation of dimer **13** with the terminal thioglucosyl donor **8**, followed by benzoylation of the resulting trimer **14** and oxidative removal[13] of the *para*-

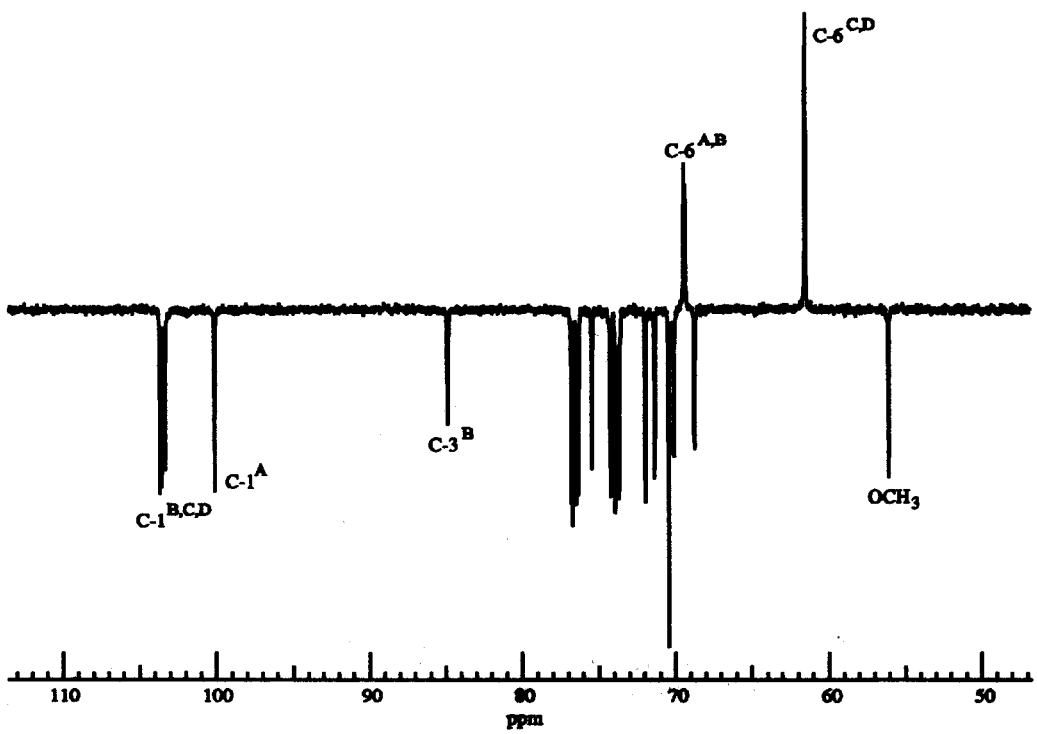
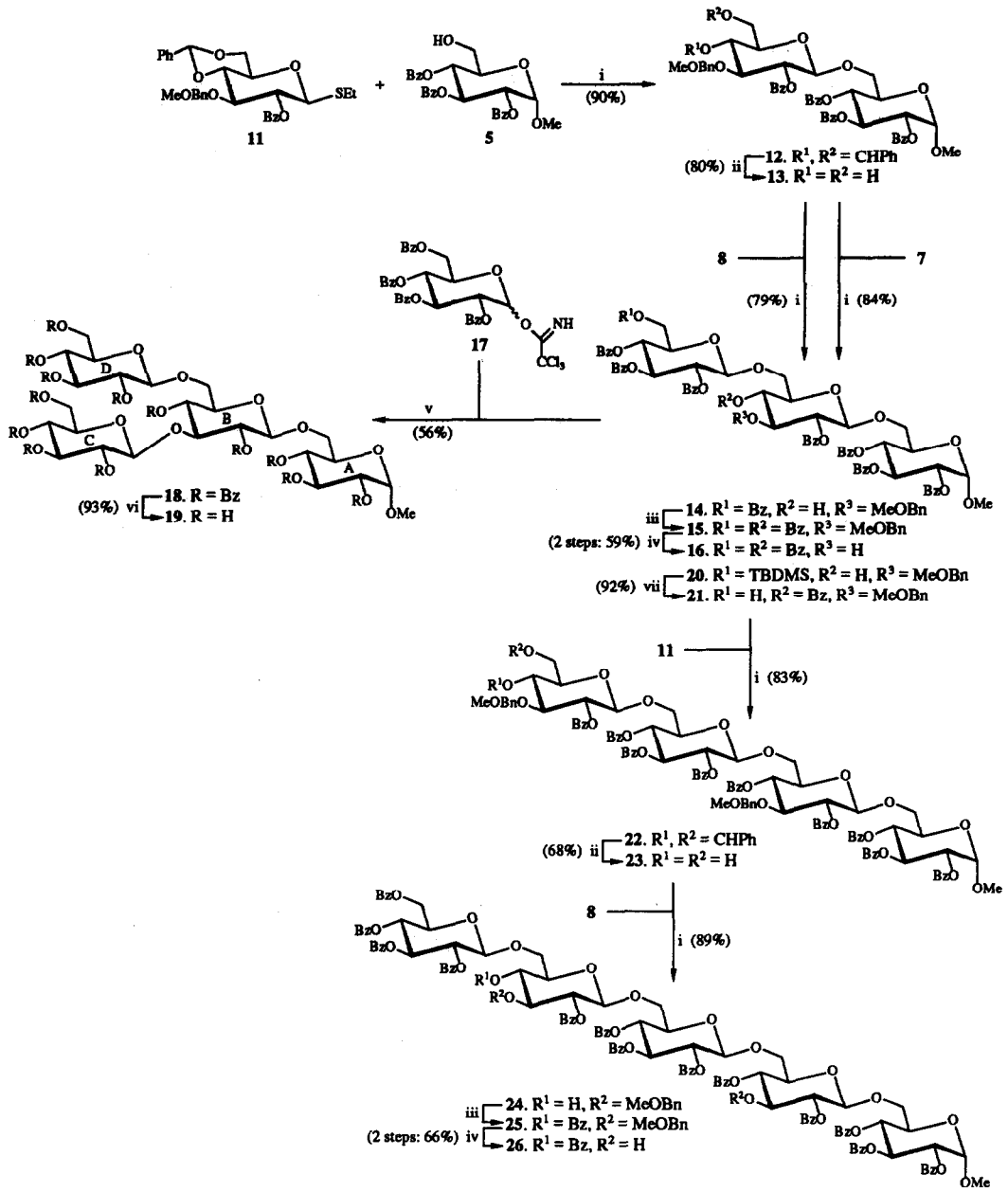


Figure 2. ^{13}C-APT spectrum (D_2O) of tetramer **19**

Scheme 2



Reagents and conditions: i. NIS/cat.TfOH, $ClCH_2CH_2Cl/Et_2O$, MS(0.4 nm), 0°C; ii. HCl, $MeOH/CH_2Cl_2$; iii. BzCl, pyridine; iv. DDQ, CH_2Cl_2/H_2O; v. TMSOTf (0.1 eq.), CH_2Cl_2, MS(0.4 nm), 0°C; vi. NaOMe, $MeOH/CH_2Cl_2$; vii. BzCl, pyridine then *p*TsOH, CH_3CN/H_2O.

methoxybenzyl (MeOBn) group from **15** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), could be extended at the C-O-3' branch-postion with the terminal ethylthioglucosyl donor **8**. Unfortunately, NIS/TfOH mediated condensation of the secondary hydroxyl in **16** with donor **8** was abortive. However, an acceptable yield of the expected tetramer **18** was obtained by condensing **16** with the known[14] trichloroacetimidate derivative **17** using trimethylsilyl triflate[15] (TMSOTf) as the catalyst. The presence in **18** of the expected three β-linkages [*i.e.* two (1→6) and one (1→3)] was unambiguously ascertained by NMR spectroscopy (see Figure 2) of the corresponding debenzoylated tetramer **19**. The latter result stimulated us to prepare the gentiopentaoside **26** which will serve as acceptor in the final *bis*-glycosylation with donor **17**. Thus, condensation of dimer **13** with the non-terminal synthon **7** gave, after benzoylation and desilylation of the initially formed product **20**, the partially protected trimer **21** which in turn was elongated with the non-terminal unit **11**. Transacetalation of the resulting tetramer **22**, followed by condensation of **23** with the terminal unit **8**, led, after benzoylation of **24** and subsequent removal of the MeOBn group from fully protected **25**, to the isolation of partially benzoylated pentamer **26**. Surprisingly, *bis*-glycosylation of **26** with excess **17** under the conditions mentioned earlier for the synthesis of the branched tetramer **18** did not proceed as expected: no trace of the fully benzoylated precursor of **2** could be detected.

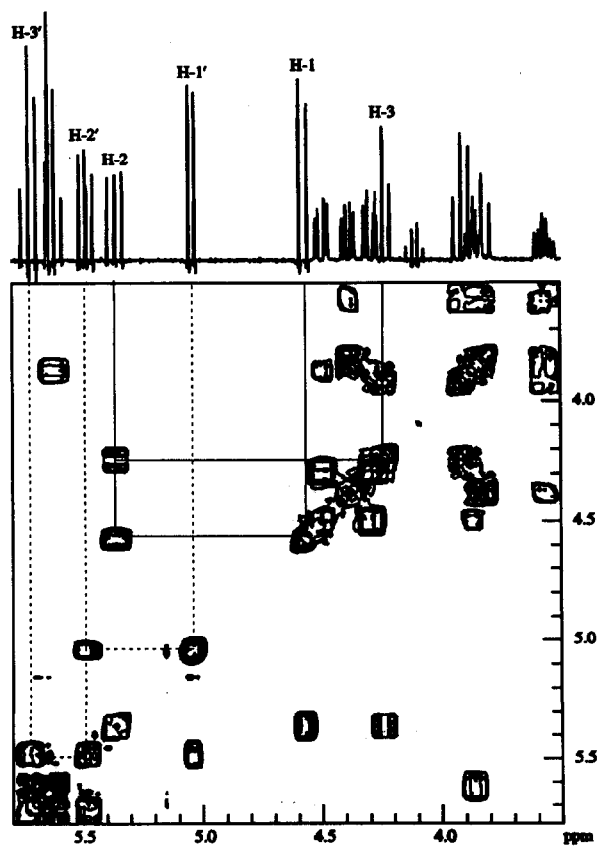


Figure 3. ^{1}H-COSY spectrum ($CDCl_3$) of dimer **29**

The latter disappointing result urged us to pursue the laminaribiosyl approach followed earlier[6,16,17] by other groups in the synthesis of the phytoalexin elicitors **1b,c**. For example, *Fügedi et al.*[16] prepared the key laminaribioside **28** (see Scheme 3) in 55% yield by condensing the tetra-*O*-benzoyl-α-D-glucopyranosyl bromide (**27**) with the partially protected ethyl 1-thio-β-D-glucopyranoside **9** using silver triflate as the promoter. However, the latter glycosylation protocol proved to be not fully satisfactory in our hands. Despite many efforts the requisite dimer **28** could only be isolated in 38% yield. On the other hand, coupling of **9** with the imidate **17** in the presence of TMSOTf gave **28** in a nearly quantitative yield. The presence of the newly introduced β (1→3) union in **28** was unambiguously ascertained by NMR spectroscopy (see Figure 3) of its crystalline benzoylated derivative **29**.

Iodonium ion (NIS/TfOH) mediated extension of the terminal unit **5** with dimer **29** provided, after removal of the benzylidene group from the condensation product **30** with ethyleneglycol and catalytic *para*-toluenesulfonic acid, the crystalline diol **31**. Similarly, regioselective elongation of trimer **31** with the non-terminal synthon **7** led to the isolation of tetramer **32**. Acetylation and subsequent desilylation afforded the partially protected tetramer **33**. Furthermore, deacylation of **33** gave the fully deprotected tetramer **19**, which was in every aspect identical with the same branched-tetramer prepared earlier in Scheme 2. Glycosylation of **33** with the laminaribioside **29** proceeded smoothly to give the expected hexamer **34** in a good yield. Finally, regioselective coupling of diol **35**, obtained after transacetalation of **34**, with the terminal building block **8**, led to the isolation of the branched and partially protected heptamer **36**, which in turn was deacylated in one step with sodium methoxide in methanol, to give after purification (Sephadex LH-20) the target molecule **2**. Interestingly, FAB-MS analysis revealed that compound **2** was not completely homogeneous. The latter was also supported by HPLC analysis which showed (see Figure 4) the presence of one major (**I**) and two distinct minor products (**II** and **III**).

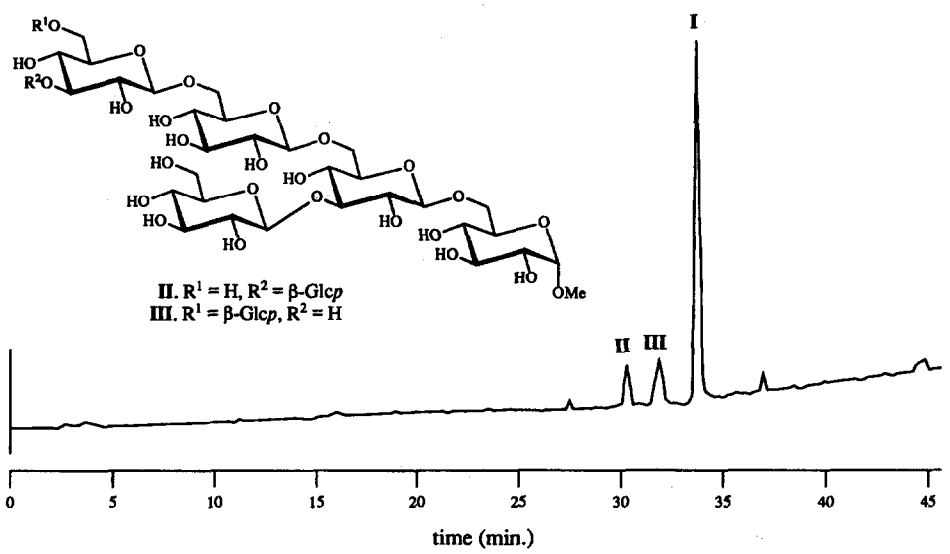
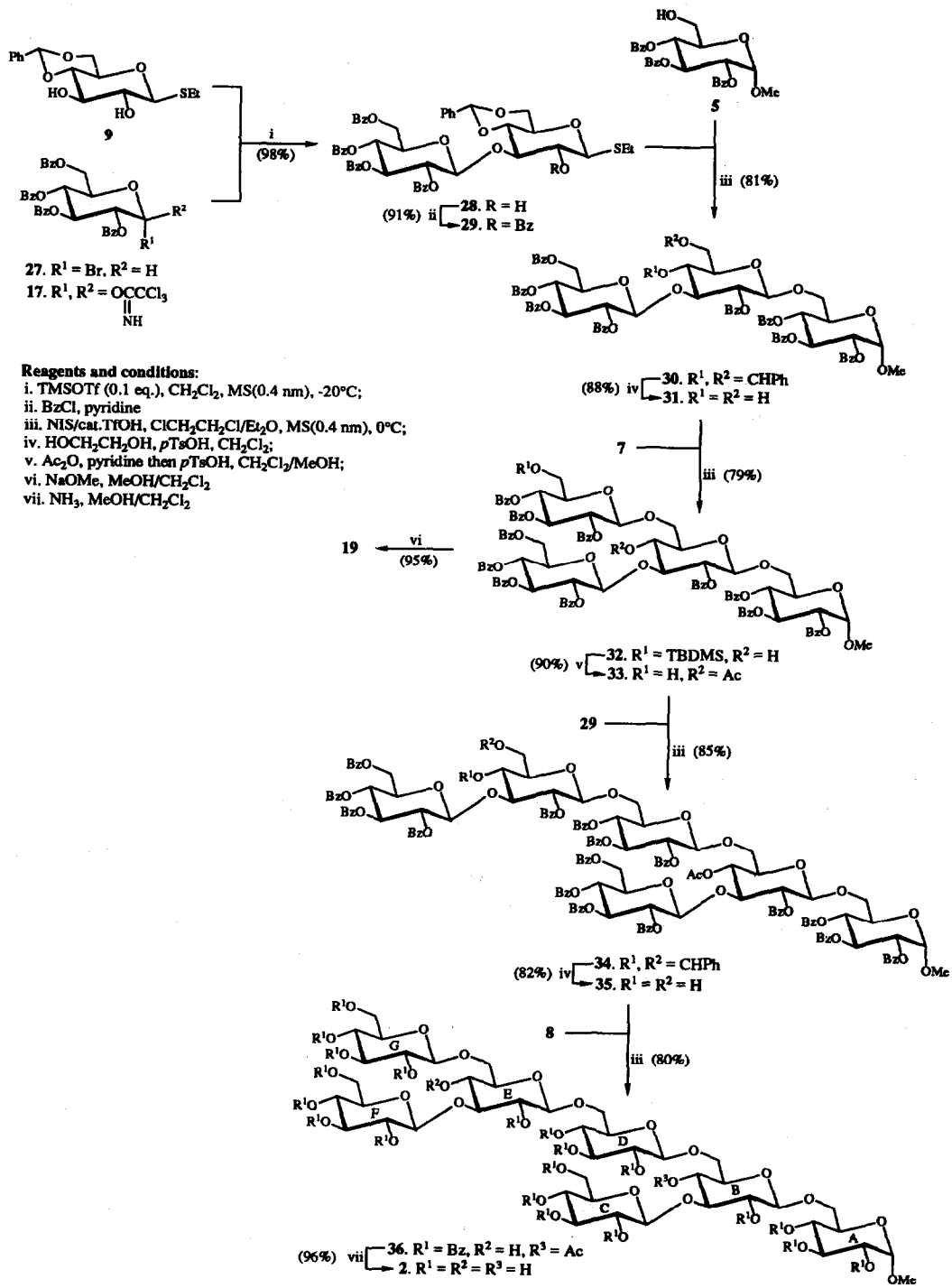


Figure 4. HPLC chromatogram of heptamer **2** obtained after deprotection of **36** with NaOMe in $MeOH/CH_2Cl_2$ followed by neutralization with excess Dowex (H^+-form).

Scheme 3



Reagents and conditions:
i. TMSOTf (0.1 eq.), CH_2Cl_2, MS(0.4 nm), -20°C;
ii. BzCl, pyridine
iii. NIS/cat.TfOH, $ClCH_2CH_2Cl/Et_2O$, MS(0.4 nm), 0°C;
iv. $HOCH_2CH_2OH$, *p*TsOH, CH_2Cl_2;
v. Ac_2O, pyridine then *p*TsOH, CH_2Cl_2/MeOH;
vi. NaOMe, $MeOH/CH_2Cl_2$
vii. NH_3, $MeOH/CH_2Cl_2$

Purification of crude **2** by HPLC and identification of the individual compounds by ^{1}H-NMR spectroscopy showed that the major product **I** was the desired heptaglucoside **2**. On the other hand, the ^{1}H-NMR data of the minor impurities were in good accord with the structures of the hexaglucosides **II** and **III**. The formation of the latter by-products may be ascribed to methanolysis of exposed glycosidic bonds in **2** by the strong cation-exchange resin Dowex (H^+-form) which was used in excess for the neutralization of the sodium methoxide in the final deacylation step of **36**. The latter assumption was endorsed by the finding that deacylation of **36** with sodium methoxide followed by neutralization with a slight excess of Dowex (H^+-form) or, more conveniently, with dry ammonia in methanol yielded homogeneous **2**, the FAB-MS and NMR data (see Figure 5) of which were in full agreement with those reported[3,6,16,18] for **1a,b**. In addition, the heptaglucoside **2** was found to be highly effective in eliciting phytoalexins in soybean cotyledons.

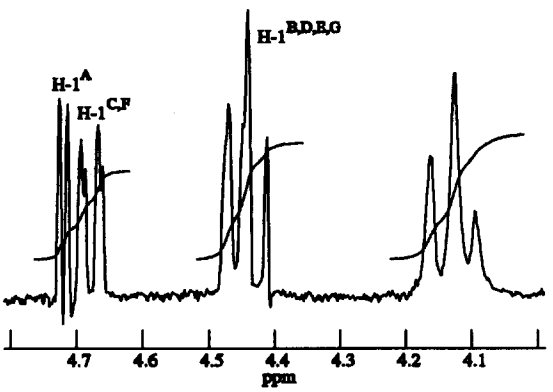


Figure 5. Anomeric region of the ^{1}H-NMR spectrum (D_2O, 285K) of heptamer **2**

In conclusion, the results presented in this paper show that the laminaribiosyl approach is efficient for the preparation of phythoalexin elicitor **2** and analogues thereof[19]. Further, preliminary experiments[20] showed that the approach could easily be adopted to a polymer-supported solution synthesis of **2**.

Experimental

General methods and materials - Pyridine was dried by refluxing with CaH_2 (5 g/L), methanol (MeOH) by refluxing with magnesium methoxide and toluene, 1,2-dichloroethane (DCE), diethylether (Et_2O) and dichloromethane (CH_2Cl_2) by refluxing with P_2O_5 (5 g/L) and then distilled. *N, N*-dimethylformamide (DMF) was dried by stirring with CaH_2 for 16 hr and then distilled under reduced pressure. Pyridine, DCE, CH_2Cl_2, DMF and acetonitrile (CH_3CN) were stored over molecular sieves 0.4 nm, MeOH over molecular sieves 0.3 nm, toluene and Et_2O over sodium wire. *N*-iodosuccinimide and trifluoromethanesulfonic acid were purchased from Aldrich and Fluka respectively. Column chromatography was performed on Merck Kieselgel 60 (230-400 mesh, ASTM) and TLC-analysis on DC Fertigfolien (Schleicher & Schüll F1500 LS254) with detection by UV where applicable and charring with 20% sulfuric acid in methanol. Optical rotations were determined at 20°C with a Perkin-Elmer 241 polarimeter. ^{13}C-NMR spectra were measured at 50.1 MHz, using a JEOL JNM-FX 200 spectrometer on line with a JEC 980 B computer. ^{1}H-NMR spectra were recorded at 300 MHz using a Bruker WM-300 spectrometer interfaced with an ASPECT-2000 computer operating in the Fourier transform mode. Chemical shifts are given in ppm (δ) relative to TMS as an internal standard. HPLC analysis was carried out on a BKK liquid chromatograph using a Dionex Carbopac PA1 (4 x 250 mm) column. Gradient elution was performed by building up a gradient starting with buffer A (100 mM NaOH) and applying buffer B (100 mM NaOH + 500 mM NaOAc) with a flow rate of 2.0 mL/min. Gradient: buffer A/buffer B, 100/0 → 80/20 (25 min) → 50/50 (40 min). The elution was monitored using a Dionex PAD-detector.

Methyl 2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (5) - A solution of α-methyl glucoside **3** (2.00 g, 10.3 mmol) and *tert*-butyldimethylsilyl chloride (1.80 g, 11.9 mmol) in pyridine (100 mL) was stirred at 20°C until TLC-analysis (toluene/MeOH, 4/1, v/v) showed complete conversion of **3**. Benzoyl chloride (3.90 mL, 33.6 mmol) was added and stirring was continued for 16 hr. Excess benzoyl chloride was destroyed with H_2O and the reaction mixture concentrated

in vacuo. The residue was taken up in EtOAc, washed with 0.1 M H_2SO_4, 10% $NaHCO_3$, H_2O and then concentrated. Crude **4** was redissolved in CH_3CN/H_2O (7/1, v/v, 80 mL) and the pH was adjusted to 3 with *para*-toluenesulfonic acid monohydrate. After 2 hr at 20°C, the reaction mixture was diluted with EtOAc, washed with 10% $NaHCO_3$ and H_2O, dried ($MgSO_4$) and concentrated. Silica gel column chromatography (light petroleum/EtOAc, 4/1 → 3/2, v/v) of the crude product afforded **5** (4.43 g, 85%) after crystallization from EtOAc/light petroleum. M.p. 140-141°C. R_f 0.30 (light petroleum/EtOAc, 3/2, v/v). $[\alpha]_D^{20}$ 53.3° (c 1, $CHCl_3$). $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 55.1 (OCH_3), 60.7 (C-6), 69.1, 69.6, 70.0, 71.7 (C-2,3,4,5), 96.7 (C-1), 127.9-133.2 ($CH_{arom.}$, $C_{quart.}$ benzoyl), 165.4, 165.6 (C=O benzoyl). ^1H-NMR ($CDCl_3$): δ 2.84 (dd, 1H, 6-OH, $J_{6,OH}$ = 5.7 Hz, $J_{6',OH}$ = 8.4 Hz), 3.47 (s, 3H, OCH_3), 3.75 (ddd, 1H, H-6, $J_{5,6}$ = 3.9 Hz, $J_{6,6'}$ = 12.9 Hz), 3.85 (ddd, 1H, H-6', $J_{5,6'}$ = 2.3 Hz), 4.06 (ddd, 1H, H-5), 5.28 (d, 1H, H-1, $J_{1,2}$ = 3.8 Hz), 5.31 (dd, 1H, H-2, $J_{2,3}$ = 9.6 Hz), 5.53 (dd, 1H, H-4, $J_{3,4}$ = $J_{4,5}$ = 9.8 Hz), 6.25 (dd, 1H, H-3), 7.2-7.6, 7.9-8.0 (m, 15H, $CH_{arom.}$ benzoyl).

Ethyl 2,3,4-tri-*O*-benzoyl-6-*O*-*tert*-butyldimethylsilyl-1-thio-β-D-glucopyranoside (7) - Prepared as described above for the conversion of **3** into **4**, starting from ethyl 1-thio-β-D-glucopyranoside **6** (2.20 g, 9.82 mmol). Purification of the crude product by silica gel column chromatography (light petroleum/EtOAc, 9/1 → 7/3, v/v) furnished **7** (5.68 g, 89%). R_f 0.48 (light petroleum/EtOAc, 4/1, v/v). $[\alpha]_D^{20}$ 3.4° (c 1, $CHCl_3$). $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ -5.6, -5.7 ($SiCH_3$ TBDMS), 14.6 (SCH_2CH_3), 18.0 ($SiC(CH_3)_3$ TBDMS), 23.4 (SCH_2CH_3), 25.5 ($SiC(CH_3)_3$ TBDMS), 62.5 (C-6), 69.2, 70.4, 74.4, 79.1 (C-2,3,4,5), 83.0 (C-1), 127.9-132.8 ($CH_{arom.}$, $C_{quart.}$ benzoyl), 164.7, 164.8, 165.4 (C=O benzoyl). ^1H-NMR ($CDCl_3$): δ 0.31, 0.38 (2xs, 6H, $SiCH_3$ TBDMS), 0.88 (s, 9H, $SiC(CH_3)_3$ TBDMS), 1.24 (t, 3H, SCH_2CH_3), 2.7-2.9 (m, 2H, SCH_2CH_3), 3.8-3.9 (m, 3H, H-5,6,6'), 4.81 (d, 1H, H-1, $J_{1,2}$ = 9.9 Hz), 5.54 (dd, 1H, H-2), 5.56 (dd, 1H, H-4, $J_{4,5}$ = 9.5 Hz), 5.89 (dd, 1H, H-3, $J_{2,3}$ = $J_{3,4}$ 9.5 Hz), 7.2-7.5, 7.8-8.0 (m, 15H, $CH_{arom.}$ benzoyl).

Ethyl 2,3,4,6-tetra-*O*-benzoyl-1-thio-β-D-glucopyranoside (8) - Benzoyl chloride (5.20 mL, 44.8 mmol) was added to a solution of **6** (2.31 g, 10.3 mmol) in pyridine (100 mL). After 16 hr at 20°C, excess benzoyl chloride was destroyed with H_2O and the reaction mixture was concentrated *in vacuo*. The residue was taken up in EtOAc, washed with 0.1 M H_2SO_4, 10% $NaHCO_3$, H_2O, dried ($MgSO_4$) and then concentrated. The crude product was purified by silica gel column chromatography (light petroleum/EtOAc, 4/1 → 3/2, v/v) to yield **8** (6.06 g, 92%). R_f 0.47 (toluene/acetone, 95/5, v/v). $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 14.9 (SCH_2CH_3), 24.3 (SCH_2CH_3), 63.2 (C-6), 69.6, 70.5, 74.1, 76.2 (C-2,3,4,5), 83.8 (C-1), 128.2-133.4 ($CH_{arom.}$, C_{quart} benzoyl), 165.1, 165.7, 166.0 (C=O benzoyl). ^1H-NMR ($CDCl_3$): δ 1.24 (t, 3H, SCH_2CH_3), 2.7-2.8 (m, 2H, SCH_2CH_3), 4.24 (ddd, 1H, H-5), 4.54 (dd, 1H, H-6', $J_{5,6'}$ = 5.3 Hz), 4.68 (dd, 1H, H-6, $J_{6,6'}$ = 12.2 Hz, $J_{5,6}$ = 3.1 Hz), 4.93 (d, 1H, H-1, $J_{1,2}$ = 10.0), 5.63 (dd, 1H, H-2), 5.74 (dd, 1H, H-4, $J_{4,5}$ = 9.8 Hz), 6.01 (dd, 1H, H-3, $J_{2,3}$ = $J_{3,4}$ = 9.6), 7.2-7.5, 7.8-8.0 (m, 20H, $CH_{arom.}$ benzoyl).

Ethyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (9) - *Para*-toluenesulfonic acid monohydrate (30 mg, 158 μmol) was added to a solution of **6** (3.00 g, 13.4 mmol) and benzaldehyde dimethylacetal (2.40 mL, 16.0 mmol) in CH_3CN (70 mL). After 30 min at 20°C, the reaction mixture was neutralized with Et_3N and then concentrated *in vacuo*. The residue was redissolved in EtOAc, washed with 10% $NaHCO_3$ and H_2O, dried ($MgSO_4$) and concentrated. Crystallization from EtOAc/light petroleum gave **9** (3.39 g, 81%). R_f 0.40 (toluene/MeOH, 85/15, v/v). $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 15.1 (SCH_2CH_3), 24.4 (SCH_2CH_3), 68.4 (C-6), 70.2, 73.1, 74.3, (C-2,3,5), 80.1 (C-4), 86.1 (C-1), 101.6 (CH benzylidene), 126.2, 128.2, 129.1 ($CH_{arom.}$ benzylidene), 136.9 ($C_{quart.}$ benzylidene). ^1H-NMR ($CDCl_3$): δ 1.27 (t, 3H, SCH_2CH_3), 2.6-2.8 (m, 2H, SCH_2CH_3), 3.32 (dd, 1H, H-2), 3.44 (dd, 1H, H-4), 3.49 (bd, 1H, H-6'), 3.64 (dd, 1H, H-3, $J_{2,3}$ = $J_{3,4}$ = 8.4 Hz), 3.69 (dd, 1H, H-6, $J_{5,6}$ = $J_{6,6'}$ = 10.0 Hz), 4.24 (bdd, 1H, H-5, $J_{4,5}$ = 4.4 Hz), 4.49 (d, 1H, H-1, $J_{1,2}$ = 9.8 Hz), 5.55 (s, 1H, CH benzylidene), 7.3-7.5 (m, 5H, $CH_{arom.}$ benzylidene).

Ethyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-*para*-methoxybenzyl-1-thio-β-D-glucopyranoside (11) - Di-*n*-butyltin oxide (1.10 g, 4.42 mmol) was added to a solution of **9** (1.20 g, 3.85 mmol) in MeOH (40 mL). After reflux for 1 hr, the reaction mixture was cooled (20°C) and concentrated *in vacuo*. The residue was coevaporated with toluene (3x) and then redissolved in toluene (15 mL). Molecular sieves (0.3 nm), *para*-methoxybenzyl chloride (680 μL, 5.02 mmol) and tetra-*n*-butylammonium bromide (1.30 g, 4.03 mmol) were added and the reaction mixture was heated under reflux for 24 hr. After cooling (20°C), the mixture was filtered over Hyflo and then concentrated *in vacuo*. Crude **10** thus obtained was dissolved in pyridine (20 mL) and benzoyl chloride (600 μL, 5.17 mmol) was added. After 3 hr at 20°C, excess benzoyl chloride was destroyed with H_2O and the reaction mixture was concentrated *in vacuo*. The residue was taken up in Et_2O, washed with 0.1 M H_2SO_4, 10% $NaHCO_3$ and H_2O, dried ($CaCl_2$) and concentrated. Purification by silica

gel column chromatography (light petroleum/EtOAc, 9/1 → 7/3, v/v) furnished **11** (1.49 g, 72%). R_f 0.43 (light petroleum/EtOAc, 3/1, v/v). $[\alpha]_D^{20}$ 28.2° (c 1, $CHCl_3$). $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 14.5 (SCH_2CH_3), 23.4 (SCH_2CH_3), 54.4 (OMe MeOBn), 68.1 (C-6), 70.2, 71.5, (C-2,5), 78.4 (C-4), 81.2 (C-3), 83.8 (C-1), 73.3 (CH_2 MeOBn), 100.7 (CH benzylidene), 113.4, 132.7 ($CH_{arom.}$ MeOBn), 124.9-129.7 ($CH_{arom.}$, $C_{quart.}$ benzylidene, benzoyl), 137.2, 137.3 ($C_{quart.}$ benzylidene, MeOBn), 158.7 ($OC_{quart.}$ MeOBn), 164.6 (C=O benzoyl). ^1H-NMR ($CDCl_3$): δ 1.24 (t, 3H, SCH_2CH_3), 2.7-2.8 (m, 2H, SCH_2CH_3), 3.5-3.6 (m, 1H, H-5), 3.71 (s, 3H, OMe MeOBn), 3.85 (dd, 1H, H-6), 3.85 (dd, 1H, H-4, $J_{4,5}$ = 11.3 Hz), 3.91 (dd, 1H, H-3, $J_{2,3} = J_{3,4}$ = 9.2 Hz), 4.43 (dd, 1H, H-6', $J_{5,6'}$ = 5.0, $J_{6,6'}$ = 10.6), 4.64 (d, 1H, H-1, $J_{1,2}$ = 10.1), 4.66, 4.78 (2xd, 2H, CH_2 MeOBn), 5.33 (dd, 1H, H-2), 5.64 (s, 1H, CH benzylidene), 6.62, 7.1-7.6, 8.02 (m, 14H, $CH_{arom.}$ benzylidene, benzoyl, MeOBn).

General procedure for iodonium ion mediated glycosylations

0.1 M stock-solution of NIS/cat.TfOH: trifluoromethanesulfonic acid (20 µL, 226 µmol) was added to a solution of *N*-iodosuccinimide (460 mg, 2.04 mmol) in DCE/Et_2O (1/1, v/v, 20 mL).

A 0.1 M solution of NIS/cat.TfOH (1 equiv. rel. to donor) in DCE/Et_2O was added to a mixture of acceptor, donor and powdered molecular sieves (0.4 nm) in DCE at 0°C under an atmosphere of N_2. After 10 min at 0°C, the reaction was stopped with Et_3N and the reaction mixture filtered, diluted with EtOAc and washed with 10% $Na_2S_2O_3$, 10% $NaHCO_3$ and H_2O, dried ($MgSO_4$) and concentrated.

Methyl6-*O*-(2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-*para*-methoxybenzyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (12) - Acceptor **5** (399 mg, 789 µmol) and donor **11** (402 mg, 750 µmol) in DCE (7.5 mL) were coupled as described in the general procedure. Purification by silica gel column chromatography (toluene/acetone, 98/2, v/v) afforded **12** (662 mg, 90%). R_f 0.41 (toluene/acetone, 95/5, v/v). $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 54.8 (2xOCH$_3$), 68.3 (C-6^{A,B}), 66.1, 69.7, 71.6, 72.8, 73.1, 73.4 (C-2^{A,B},3^A,4^A,5^{A,B}), 73.5 (CH_2 MeOBn), 77.1 (C-4^B), 81.4 (C-3^B), 96.4 (C-1^A), 101.1, 101.3 (C-1^B, CH benzylidene), 113.3, 133.0 ($CH_{arom.}$ MeOBn), 125.1-129.6 ($CH_{arom.}$, $C_{quart.}$ benzylidene, benzoyl), 137.1 ($C_{quart.}$ benzylidene, MeOBn), 158.7 ($OC_{quart.}$ MeOBn), 165.0, 165.3, 164.7 (C=O benzoyl).

Methyl 6-*O*-(2-*O*-benzoyl-3-*O*-*para*-methoxybenzyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (13) - Acetyl chloride in MeOH (0.25 M, 3.0 mL) was added to a solution of **12** (662 mg, 675 µmol) in CH_2Cl_2 (3.0 mL). After 2 hr at 20°C, the reaction mixture was neutralized with Et_3N and concentrated *in vacuo*. Purification by silica gel column chromatography (toluene/acetone, 4/1, v/v) gave **13** (482 mg, 80%). R_f 0.47 (toluene/MeOH, 85/15, v/v). $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 54.8 (2xOCH$_3$), 68.3 (C-6^{A,B}), 69.6, 69.9, 71.7, 72.7, 73.1, 74.1 (C-2^{A,B},3^A,4^A,5^{A,B}), 77.4 (C-4^B), 81.2 (C-3^B), 96.4 (C-1^A), 100.9 (C-1^B), 113.4, 133.0 ($CH_{arom.}$ MeOBn), 125.1-129.6 ($CH_{arom.}$, $C_{quart.}$ benzoyl), 158.6 ($OC_{quart.}$ MeOBn), 164.9, 165.0, 165.5 (C=O benzoyl).

Methyl 6-*O*-(6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-2-*O*-benzoyl-3-*O*-*para*-methoxybenzyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (14) - Donor **8** (155 mg, 242 µmol) and acceptor **13** (161 mg, 180 µmol) in DCE (2.5 mL) were coupled as described in the general procedure. Purification by silica gel column chromatography (toluene/acetone, 97/3, v/v) afforded **14** (209 mg, 79%). $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 54.8 (2xOCH$_3$), 63.0 (C-6^D), 72.6 (C-6^{A,B}), 73.8 (CH_2 MeOBn), 75.9 (C-4^B), 81.0 (C-3^B), 96.4 (C-1^A), 100.6, 100.7 (C-1^{B,D}), 113.7, 132.9 ($CH_{arom.}$ MeOBn), 129.2-133.4 ($CH_{arom.}$, $C_{quart.}$ benzoyl), 158.7 ($OC_{arom.}$ MeOBn), 164.1-165.2 (C=O benzoyl).

Methyl 6-*O*-(6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-2,4-di-*O*-benzoyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (16) - Benzoyl chloride (25 µL, 215 µmol) was added to a solution of **14** (209 mg, 142 µmol) in pyridine (3.0 mL). After 16 hr at 20°C, excess benzoyl chloride was destroyed with H_2O and the reaction mixture was concentrated *in vacuo*. The residue was taken up in EtOAc, washed with 0.1 M H_2SO_4, 10% $NaHCO_3$ and H_2O and concentrated. Crude **15** thus obtained was redissolved in CH_2Cl_2/H_2O (8/1, v/v, 1.8 mL) and 2,3-dichloro-5,6-dicyano-1,4-benzodiquinone (100 mg, 441 µmol) was added. After 1 hr at 20°C, the reaction mixture was filtered over Hyflo and then concentrated *in vacuo*. The residue was taken up in Et_2O, washed with H_2O, 10% $NaHCO_3$, H_2O, dried ($CaCl_2$) and concentrated. Purification by silica gel column chromatography (light petroleum/EtOAc, 3/2 → 2/3, v/v) yielded **16** (123 mg, 59%). $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 54.4 (OCH_3), 62.3 (C-6^D), 67.5 (C-6^{A,B}), 84.8 (C-3^B), 96.0 (C-1^A), 100.9, 101.1 (C-1^{B,D}), 127.5-132.1 ($CH_{arom.}$, $C_{quart.}$ benzoyl), 163.5-165.3 (C=O benzoyl).

Methyl 6-*O*-(3,6-di-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-2,4-di-*O*-benzoyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (18) - Trimethylsilyl trifluoromethanesulfonate in CH_2Cl_2 (0.1 M, 170 µL) was added to a mixture of **16** (123 mg, 83.9 µmol), **17** (125 mg, 169 µmol) and molecular sieves (0.4 nm) in dry CH_2Cl_2 (3.0 mL) at 0°C under an atmosphere of nitrogen. After 1 hr at 0°C, the reaction mixture was neutralized with Et_3N, filtered and then washed with 10% $NaHCO_3$ and H_2O. The organic layer was dried ($MgSO_4$), concentrated and then purified by silica gel column chromatography (light petroleum/EtOAc, 7/3 → 1/1, v/v) to afford **18** (95.5 mg, 56%). $^{13}C\{^1H\}$-NMR ($CDCl_3$) : δ 54.3 (OCH_3), 62.2, 62.3 (C-$6^{C,D}$), 67.7 (C-$6^{A,B}$), 85.0 (C-3^B), 96.0 (C-1^A), 100.8, 101.1, 101.2 (C-$1^{B,C,D}$), 128.2-133.3 ($CH_{arom.}$, $C_{quart.}$ benzoyl), 163.8-165.5 (C=O, benzoyl).

Methyl 6-*O*-(3,6-di-*O*-(β-D-glucopyranosyl)-β-D-glucopyranosyl)-α-D-glucopyranoside (19) - Sodium methoxide was added to a solution of **18** (95.5 mg, 47.0 µmol) in CH_2Cl_2/MeOH (1/2, v/v, 4.5 mL) until pH ≈ 12. After 24 hr, the reaction mixture was neutralized with Dowex 50 XW4 resin (H^+-form, 100-200 mesh), filtered and then concentrated *in vacuo*. The residue was purified by Sephadex LH-20 chromatography (MeOH) to afford **19** (30.4 mg, 95%). $^{13}C\{^1H\}$-NMR (D_2O): δ 56.02 (OCH_3), 61.47 (C-$6^{C,D}$), 69.30, 69.39 (C-$6^{A,B}$), 68.69, 70.04, 70.35, 71.29, 71.90, 73.60, 73.73, 73.86, 74.20, 75.41, 76.30, 76.41, 76.67, 76.75 (C-$2^{A,B,C,D}$, C-$3^{A,C,D}$, C-$4^{A,B,C,D}$, C-$5^{A,B,C,D}$), 84.86 (C-3^B), 100.10 (C-1^A), 103.32, 103.53, 103.66 (C-$1^{B,C,D}$). ^1H-NMR (D_2O, 285 K): δ 3.35 (s, OCH_3), 4.14 (bt, 2H), 4.46, 4.47 (2xd, 2H, H-$1^{B,D}$, $J_{1,2}$ = 8.0 Hz), 4.70 (d, 1H, H-1^C, $J_{1,2}$ = 7.9 Hz), 4.74 (d, 1H, H-1^A, $J_{1,2}$ = 3.7 Hz).

Methyl 6-*O*-(6-*O*-(2,3,4-tri-*O*-benzoyl-6-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyl)-2-*O*-benzoyl-3-*O*-*para*-methoxybenzyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (20) - Donor **7** (350 mg, 538 µmol) and acceptor **13** (321 mg, 360 µmol) in DCE (5.0 mL) were coupled as described in the general procedure. Purification by silica gel column chromatography (toluene/acetone, 97/3, v/v) afforded **20** (448 mg, 84%). R_f 0.31 (toluene/acetone, 95/5, v/v). $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ -5.6 ($SiCH_3$ TBDMS), 17.9 ($SiC(CH_3)_3$ TBDMS), 25.5 ($SiC(CH_3)_3$ TBDMS), 54.8 (2xOCH_3), 68.3 (C-6^D), 72.6 (C-$6^{A,B}$), 73.8 (CH_2 MeOBn), 77.9 (C-4^B), 81.2 (C-3^B), 96.4 (C-1^A), 100.7, 100.9 (C-$1^{B,D}$), 113.7, 133.0 ($CH_{arom.}$ MeOBn), 128.0-133.1 ($CH_{arom.}$, $C_{quart.}$ benzoyl), 158.8 ($OC_{arom.}$ MeOBn), 164.5-165.5 (C=O benzoyl).

Methyl 6-*O*-(6-*O*-(2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl)-2,4-di-*O*-benzoyl-3-*O*-*para*-methoxybenzyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (21) - Benzoyl chloride (50.0 µL, 431 µmol) was added to a solution of **20** (448 mg, 302 µmol) in pyridine (3.0 mL). After 16 hr at 20°C, excess benzoyl chloride was destroyed with H_2O and the reaction mixture was concentrated *in vacuo*. The residue was taken up in EtOAc, washed with 0.1 M H_2SO_4, 10% $NaHCO_3$ and H_2O and then concentrated. The residue was redissolved in CH_3CN/H_2O (7/1, v/v, 4.0 mL) and the pH was adjusted to 3 with *para*-toluenesulfonic acid monohydrate. After 2 hr at 20°C, the reaction mixture was diluted with EtOAc, washed with 10% $NaHCO_3$ and H_2O, dried ($MgSO_4$) and concentrated. Silica gel column chromatography (toluene/acetone, 95/5, v/v) of the crude product yielded **21** (408 mg, 92%). R_f 0.25 (toluene/acetone, 95/5, v/v). $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 54.8 (2xOCH_3), 68.2 (C-6^D), 72.6 (C-$6^{A,B}$), 81.1 (C-3^B), 96.4 (C-1^A), 100.4, 100.8 (C-$1^{B,D}$), 113.3, 133.0 ($CH_{arom.}$ MeOBn), 127.9-133.2 ($CH_{arom.}$, $C_{quart.}$ benzoyl), 158.8 ($OC_{quart.}$ MeOBn), 164.5-165.4 (C=O benzoyl).

Methyl 6-*O*-(6-*O*-(6-*O*-(2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-*para*-methoxybenzyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl)-2,4-di-*O*-benzoyl-3-*O*-*para*-methoxybenzyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (22) - Donor **11** (225 mg, 420 µmol) and acceptor **21** (408 mg, 278 µmol) in DCE (4.0 mL) were coupled as described in the general procedure. Purification by silica gel column chromatography (toluene/acetone, 97/3, v/v) afforded **22** (449 mg, 83%). R_f 0.29 (toluene/acetone, 95/5, v/v). $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 54.7, 54.8 (3xOCH_3), 68.0, 68.5 (C-$6^{A,B,D,E}$), 73.4, 73.6 (CH_2 MeOBn), 77.2 (C-4^E), 81.1, 81.5 (C-$3^{B,E}$), 96.4 (C-1^A), 100.7, 100.8, 101.0, 101.9 (C-$1^{B,D,E}$, CH benzylidene), 113.3, 113.4, 133.0 ($CH_{arom.}$ MeOBn), 125.1-129.6 ($CH_{arom.}$, $C_{quart.}$ benzylidene, benzoyl), 137.2 ($C_{quart.}$ benzylidene), 158.9 ($OC_{quart.}$ MeOBn), 164.6-166.8 (C=O benzoyl).

Methyl 6-*O*-(6-*O*-(6-*O*-(2-*O*-benzoyl-3-*O*-*para*-methoxybenzyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl)-2,4-di-*O*-benzoyl-3-*O*-*para*-methoxybenzyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (23) - Acetyl chloride in MeOH (0.25 M, 1.0 mL) was added to a solution of **22** (449 mg, 231 µmol) in CH_2Cl_2 (1.0 mL). After 2 hr at 20°C, the reaction mixture was neutralized with Et_3N and concentrated *in vacuo*. Purification by silica gel column chromatography (toluene/acetone, 4/1, v/v) gave **23** (292 mg, 68%). R_f 0.49

(toluene/MeOH, 85/15, v/v). $^{13}C\{^1H\}$-NMR ($CDCl_3$) : δ 54.8, 55.0 (3xOCH_3), 67.7, 68.1, 68.4 (C-$6^{A,B,D,E}$), 74.0 (2xCH_2 MeOBn), 78.8 (C-4^E), 81.9 (C-$3^{B,E}$), 96.3 (C-1^A), 100.5, 100.7, 101.0 (C-$1^{B,D,E}$), 113.4, 113.7, 133.0, 133.4 ($CH_{arom.}$ MeOBn), 125.2-130.0 ($CH_{arom.}$, $C_{quart.}$ benzoyl), 158.9, 159.1 ($OC_{arom.}$ MeOBn), 164.7-165.6 (C=O benzoyl).

Methyl 6-*O*-(6-*O*-(6-*O*-(6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-2-*O*-benzoyl-3-*O*-*para*-methoxybenzyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl)-2,4-di-*O*-benzoyl-3-*O*-*para*-methoxybenzyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (24) - Donor **8** (150 mg, 234 µmol) and acceptor **23** (292 mg, 157 µmol) in DCE (2.5 mL) were coupled as described in the general procedure. Purification by silica gel column chromatography (toluene/acetone, 97/3, v/v) afforded **24** (340 mg, 89%). R_f 0.21 (light petroleum/EtOAc, 2/3, v/v). $^{13}C\{^1H\}$-NMR ($CDCl_3$) : δ 54.7, 54.9 (3xOCH_3), 62.5 (C-6^O), 67.9, 68.1, 68.5 (C-$6^{A,B,D,E}$), 73.9 (2xCH_2 MeOBn), 78.5 (C-4^E), 81.7 (C-$3^{B,E}$), 96.4 (C-1^A), 100.5, 100.8, 101.1 (C-$1^{B,D,E,O}$), 113.4, 113.6, 133.0, 133.5 ($CH_{arom.}$ MeOBn), 125.0-129.8 ($CH_{arom.}$, $C_{quart.}$ benzoyl), 159.0 ($OC_{arom.}$ MeOBn), 164.7-165.9 (C=O benzoyl).

Methyl 6-*O*-(6-*O*-(6-*O*-(6-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-2,4-di-*O*-benzoyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl)-2,4-di-*O*-benzoyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (26) - Benzoyl chloride (25 µL, 215 µmol) was added to a solution of **24** (340 mg, 140 µmol) in pyridine (3.0 mL). After 16 hr at 20°C, excess benzoyl chloride was destroyed with H_2O and the reaction mixture was concentrated *in vacuo*. The residue was taken up in EtOAc, washed with 0.1 M H_2SO_4, 10% $NaHCO_3$ and H_2O and concentrated. Crude **25** thus obtained was redissolved in CH_2Cl_2/H_2O (8/1, v/v, 1.8 mL) and 2,3-dichloro-5,6-dicyano-1,4-benzodiquinone (100 mg, 441 µmol) was added. After 1 hr at 20°C, the reaction mixture was filtered over Hyflo and then concentrated *in vacuo*. The residue was taken up in Et_2O, washed with H_2O, 10% $NaHCO_3$, H_2O, dried ($CaCl_2$) and concentrated. Purification by silica gel column chromatography (light petroleum/EtOAc, 1/1 → 3/7, v/v) yielded **26** (212 mg, 66%). $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 54.9 (OCH_3), 62.6 (C-6^O), 67.9, 68.2, 68.6 (C-$6^{A,B,D,E}$), 82.6 (C-$3^{B,E}$), 96.4 (C-1^A), 100.6, 100.8, 101.0 (C-$1^{B,D,E,O}$), 125.3-130.1 ($CH_{arom.}$, $C_{quart.}$ benzoyl), 164.5-165.8 (C=O benzoyl).

Ethyl 3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (28) - Trimethylsilyl trifluoromethanesulfonate (150 µL, 0.83 mmol) was added to a mixture of **9** (2.20 g, 7.05 mmol), **17** (6.00 g, 8.10 mmol) and molecular sieves (0.4 nm) in dry CH_2Cl_2 (150 mL) at -20°C under an atmosphere of nitrogen. After 1 hr at -20°C, the reaction mixture was neutralized with Et_3N, filtered and then washed with 10% $NaHCO_3$ and H_2O. The organic layer was dried ($MgSO_4$), concentrated and then purified by silica gel column chromatography (light petroleum/EtOAc, 9/1 → 3/2, v/v) to afford **28** (6.15 g, 98%). R_f 0.21 (light petroleum/EtOAc = 3/2). $[\alpha]_D^{20}$ 5.3° (c 1, $CHCl_3$), lit.[8] $[\alpha]_D^{20}$ 6° (c 1.1, $CHCl_3$). $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 15.0 (SCH_2CH_3), 24.0 (SCH_2CH_3), 62.7 (C-6'), 68.4 (C-6), 69.4, 70.7, 71.9, 72.4, 72.6 (C-2,5,2',3',4',5'), 78.9 (C-4), 82.5 (C-3), 86.0 (C-1), 101.1, 101.4 (C-1', CH benzylidene), 125.8-133.2 ($CH_{arom.}$, $C_{quart.}$ benzylidene, benzoyl), 136.9 ($C_{quart.}$, benzylidene), 164.9, 165.5, 165.6 (C=O benzoyl). ^1H-NMR ($CDCl_3$): δ 1.21 (t, 3H, SCH_2CH_3), 2.53-2.68 (m, 2H, SCH_2CH_3), 3.40-3.53 (m, 2H, H-2,6a), 3.70 (dd, 1H, H-4), 3.67-3.82 (m, 1H, H-5), 3.89 (dd, 1H, H-3), 3.91-3.97 (m, 1H, H-5'), 4.28-4.33 (m, 2H, H-6b,6'a), 4.36 (d, 1H, H-1, $J_{1,2}$ = 9.9 Hz), 4.49 (dd, 1-H, H-6'b), 5.22 (d, 1H, H-1', $J_{1',2'}$ = 7.8 Hz), 5.55 (dd, 1H, H-2'), 5.56 (s, 1H, CH benzylidene), 5.71 (dd, 1H, H-4'), 5.93 (dd, 1H, H-3'), 7.2-8.1 (m, 25H, $CH_{arom.}$, benzoyl benzylidene).

Ethyl3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-2-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (29) - Benzoyl chloride (1.10 mL, 9.48 mmol) was added to a solution of **28** (6.15 g, 6.91 mmol) in pyridine (50 mL). After 16 hr at 20°C, excess benzoyl chloride was destroyed with H_2O and the reaction mixture was concentrated *in vacuo*. The residue was taken up in EtOAc, washed with 0.1 M H_2SO_4, 10% $NaHCO_3$ and H_2O, dried ($MgSO_4$) and concentrated. Crystallization from CH_2Cl_2/light petroleum gave **29** (6.25 g, 91%). M.p. 227-228°C, lit.[8] m.p. 228-229°C. R_f 0.37 (light petroleum/EtOAc, 7/3, v/v). $[\alpha]_D^{20}$ 15.7° (c 1, $CHCl_3$), lit.[8] $[\alpha]_D^{20}$ 16° (c 2.1, $CHCl_3$). $^{13}C\{^1H\}$-NMR ($CDCl_3$) : δ 14.3 (SCH_2CH_3), 23.4 (SCH_2CH_3), 62.6 (C-6'), 68.2 (C-6), 69.3, 70.5, 71.1, 71.4, 71.8, 72.7 (C-2,5,2',3',4',5'), 79.0 (C-4), 79.7 (C-3), 83.7 (C-1), 100.4, 101.1 (C-1', CH benzylidene), 125.7-133.0 ($CH_{arom.}$, $C_{quart.}$ benzylidene, benzoyl), 136.7 ($C_{quart.}$, benzylidene), 164.3, 164.5, 164.7, 165.3, 165.7 (C=O benzoyl). ^1H-NMR ($CDCl_3$): δ 1.15 (t, 3H, SCH_2CH_3), 2.55-2.70 (m, 2H, SCH_2CH_3), 3.57 (dd, 1H, H-6a), 3.83 (ddd, 1H, H-5), 3.91 (dd, 1H, H-4), 4.23 (dd, 1H, H-3), 4.27 (dd, 1H, H-6'a), 4.38 (dd, 1H, H-6b), 4.48 (dd, 1H, H-6'b), 4.57 (d, 1H, H-1, $J_{1',2'}$ = 7.8 Hz), 5.35 (dd, 1H, H-2), 5.47 (dd, 1H, H-2'), 5.60 (dd, 1H, H-4'), 5.64 (s, 1H, CH benzylidene), 5.71 (dd, 1H, H-3'), 7.1-8.1 (m, 30H, $CH_{arom.}$ benzoyl, benzylidene).

Methyl 6-*O*-(3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (30) - Acceptor **5** (478 mg, 945 µmol) and donor **29** (1.05 g, 1.06 mmol) in DCE (10.0 mL) were coupled as described in the general procedure. Purification by silica gel column chromatography (light petroleum/EtOAc, 4/1 → 3/2, v/v) afforded **30** (1.10 g, 81%). R_f 0.34 (light petroleum/EtOAc, 3/2, v/v). $[\alpha]_D^{20}$ 34.7° (c 1, $CHCl_3$). $^{13}C\{^1H\}$-NMR ($CDCl_3$) : δ 54.5 (OCH_3), 62.8 (C-6^C), 68.5 (C-$6^{A,B}$), 78.6, 79.2 (C-3^B,4^B), 96.0 (C-1^A), 100.5, 101.2, 101.6 (C-$1^{B,C}$, CH benzylidene), 125.8-133.3 ($CH_{arom.}$, $C_{quart.}$ benzylidene, benzoyl), 136.8 ($C_{quart.}$ benzylidene), 164.2-165.7 (C=O, benzoyl).

Methyl 6-*O*-(3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-2-*O*-benzoyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (31) - Ethylene glycol (190 µL, 3.40 mmol) and a catalytic amount of *para*-toluenesulfonic acid were added to a solution of **30** (1.10 g, 765 µmol) in CH_2Cl_2 (8.0 mL). After 16 hr at 20°C, the reaction mixture was neutralized with Et_3N and then concentrated *in vacuo*. Crystallization from CH_2Cl_2/light petroleum gave **31** (909 mg, 88%). M.p. 217-218°C. R_f 0.25 (toluene/MeOH, 95/5, v/v). $[\alpha]_D^{20}$ 12.7° (c 1, $CHCl_3$). $^{13}C\{^1H\}$-NMR ($CDCl_3$) : δ 54.4 (OCH_3), 61.2 (C-6^C), 62.3 (C-6^B), 67.5 (C-6^A), 75.7 (C-4^B), 84.3 (C-3^B), 96.0 (C-1^A), 100.8, 101.2 (C-$1^{B,C}$), 127.7-132.9 ($CH_{arom.}$, $C_{quart.}$ benzoyl), 164.3-165.9 (C=O, benzoyl).

Methyl 6-*O*-(3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-6-*O*-(2,3,4-tri-*O*-benzoyl-6-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyl)-2-*O*-benzoyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (32) - Donor **7** (650 mg, 1.00 mmol) and acceptor **31** (909 mg, 673 µmol) in DCE (10.0 mL) were coupled as described in the general procedure. Purification by silica gel column chromatography (light petroleum/EtOAc, 4/1 → 3/2, v/v) afforded **32** (1.03 g, 79%). R_f 0.32 (light petroleum/EtOAc, 3/2, v/v). $[\alpha]_D^{20}$ 5.9° (c 1, $CHCl_3$). $^{13}C\{^1H\}$-NMR ($CDCl_3$) : δ -5.7 ($SiCH_3$ TBDMS), 17.8 ($SiC(CH_3)_3$ TBDMS), 25.4 ($SiC(CH_3)_3$ TBDMS), 54.3 (OCH_3), 62.3 (C-$6^{C,D}$), 67.5 (C-$6^{A,B}$), 76.1 (C-4^B), 85.2 (C-3^B), 96.0 (C-1^A), 100.9, 101.1, 101.3 (C-$1^{B,C,D}$), 127.7-132.8 ($CH_{arom.}$, $C_{quart.}$ benzoyl), 163.7-165.5 (C=O, benzoyl).

Methyl 6-*O*-(3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-6-*O*-(2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl)-2-*O*-acetyl-4-*O*-benzoyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (33) - Acetic anhydride (2.0 mL, 21.2 mmol) was added to a solution of **32** (1.03 g, 532 µmol) in pyridine (5.0 mL). After 16 hr at 20°C, excess acetic anhydride was destroyed with H_2O and the reaction mixture was concentrated *in vacuo*. The residue was taken up in EtOAc, washed with 0.1 M H_2SO_4, 10% $NaHCO_3$ and H_2O and then concentrated. The residue was redissolved in CH_2Cl_2/MeOH (1/2, v/v, 6.0 mL) and the pH was adjusted to 3 with *para*-toluenesulfonic acid monohydrate. After 3 hr at 20°C, the reaction mixture was neutralized with Et_3N and then concentrated *in vacuo*. Crystallization from CH_2Cl_2/light petroleum afforded **33** (893 mg, 90%). M.p. 163-164°C. R_f 0.24 (light petroleum/EtOAc, 1/1, v/v). $[\alpha]_D^{20}$ 1.2° (c 1, $CHCl_3$). $^{13}C\{^1H\}$-NMR ($CDCl_3$) : δ 54.4 (OCH_3), 62.3, 62.4 (C-$6^{C,D}$), 67.5 (C-$6^{A,B}$), 85.1 (C-3^B), 96.0 (C-1^A), 100.9, 101.1, 101.2 (C-$1^{B,C,D}$), 127.9-132.9 ($CH_{arom.}$, $C_{quart.}$ benzoyl), 164.0-165.8 (C=O, benzoyl).

Methyl 6-*O*-(3,6-di-*O*-(β-D-glucopyranosyl)-β-D-glucopyranosyl)-α-D-glucopyranoside (20) - Compound **33** (290 mg, 156 µmol) was converted, as already described for compound **19**, into **20** (101 mg, 95%). All analytical data were identical to **20** obtained earlier (*vide supra*).

Methyl 6-*O*-(6-*O*-(6-*O*-(3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-2-*O*-benzoyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl)-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-2-*O*-acetyl-4-*O*-benzoyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (34) - Donor **29** (480 mg, 483 µmol) and acceptor **33** (603 mg, 323 µmol) in DCE (5.0 mL) were coupled as described in the general procedure. Purification by silica gel column chromatography (light petroleum/EtOAc, 7/3 → 1/1, v/v) gave **34** (768 mg, 85%). R_f 0.50 (light petroleum/EtOAc, 1/1, v/v). $[\alpha]_D^{20}$ 4.4° (c 2, $CHCl_3$). $^{13}C\{^1H\}$-NMR ($CDCl_3$) : δ 54.3 (OCH_3), 62.8 (C-$6^{C,F}$), 78.6 (C-4^E), 85.5 (C-$3^{B,E}$), 96.1 (C-1^A), 100.5, 100.6, 100.9, 101.1, 101.3 (C-$1^{B,C,D,E,F}$, CH benzylidene), 125.7-132.9 ($CH_{arom.}$, $C_{quart.}$ benzylidene, benzoyl), 136.7 ($C_{quart.}$ benzylidene), 163.8-165.6 (C=O benzoyl).

Methyl 6-*O*-(6-*O*-(6-*O*-(3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-2-*O*-benzoyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl)-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-2-*O*-acetyl-4-*O*-benzoyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (35) - Ethylene glycol (80 µL, 1.43 mmol) and a catalytic amount of *para*-toluenesulfonic acid were added to a solution of **34** (768 mg, 275 µmol) in CH_2Cl_2 (3.0 mL). After 16

hr at 20°C, the reaction mixture was neutralized with Et_3N and then concentrated *in vacuo*. The residue was redissolved in EtOAc, washed with 10% $NaHCO_3$ and H_2O, dried ($MgSO_4$) and then concentrated. Purification by silica gel column chromatography (light petroleum/EtOAc, 3/2 → 2/3, v/v) yielded **35** (611 mg, 82%). R_f 0.26 (toluene/MeOH, 95/5, v/v). $[\alpha]_D^{20}$ -5.2° (c 2, $CHCl_3$). $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 54.4 (OCH_3), 61.7 ($C\text{-}6^{C,E,F}$), 77.2 ($C\text{-}4^{E}$), 85.4 ($C\text{-}3^{B,E}$), 96.0 ($C\text{-}1^{A}$), 100.6, 100.9, 101.3, 101.4, 101.5 ($C\text{-}1^{B,C,D,E,F}$), 128.0-133.0 ($CH_{arom.}$, $C_{quart.}$ benzoyl), 164.0-166.7 (C=O benzoyl).

Methyl 6-*O*-(6-*O*-(6-*O*-(3,6-di-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-2-*O*-benzoyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl)-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-2-*O*-acetyl-4-*O*-benzoyl-β-D-glucopyranosyl)-2,3,4-tri-*O*-benzoyl-α-D-glucopyranoside (36) - Donor **8** (190 mg, 297 µmol) and acceptor **35** (547 mg, 197 µmol) in DCE (3.0 mL) were coupled as described in the general procedure. Purification by silica gel column chromatography (light petroleum/EtOAc, 3/2 → 1/1, v/v) gave **36** (528 mg, 80%). R_f 0.34 (light petroleum/EtOAc, 1/1, v/v). $[\alpha]_D^{20}$ 18.8° (c 2, $CHCl_3$). $^{13}C\{^1H\}$-NMR ($CDCl_3$): δ 54.4 (OCH_3), 61.7, 61.8 ($C\text{-}6^{C,E,F,G}$), 76.7 ($C\text{-}4^{E}$), 85.3 ($C\text{-}3^{B,E}$), 96.0 ($C\text{-}1^{A}$), 100.8, 100.9, 101.2, 101.5, 101.6 ($C\text{-}1^{B,C,D,E,F,G}$), 127.8-133.2 ($CH_{arom.}$, $C_{quart.}$ benzoyl), 163.9-167.1 (C=O benzoyl).

Methyl 6-*O*-(6-*O*-(6-*O*-(3,6-di-*O*-(β-D-glucopyranosyl)-β-D-glucopyranosyl)-β-D-glucopyranosyl)-3-*O*-(β-D-glucopyranosyl)-β-D-glucopyranosyl)-α-D-glucopyranoside (2) - Method A. Sodium methoxide was added to a solution of **36** (205 mg, 60.2 µmol) in CH_2Cl_2/MeOH (1/2, v/v, 1.2 mL) until pH ≈ 12. After 24 hr, the reaction mixture was neutralized with excess Dowex 50 XW4 resin (H^+-form, 100-200 mesh), filtered and then concentrated *in vacuo*. The residue was purified by Sephadex LH-20 chromatography (MeOH) followed by preparative HPLC (see General methods and materials) to give **2** (10.1 mg, 14%), **II** (0.5 mg) and **III** (0.5 mg).

Method B. A saturated solution of ammonia in MeOH (5.0 mL) was added to **36** (323 mg, 94.9 µmol) in CH_2Cl_2/MeOH (1/2, v/v, 4.5 mL). After 24 hr at 20°C, the reaction mixture was concentrated *in vacuo* and the residue was purified by Sephadex LH-20 chromatography (MeOH) to afford **2** (105 mg, 96%). $[\alpha]_D^{20}$ = 2.2° (c 1, H_2O). FAB-MS: $[M+Na]^+$ 1189. $^{13}C\{^1H\}$-NMR (D_2O): δ 55.8 (OCH_3), 61.3 ($C\text{-}6^{C,F,G}$), 69.2, 69.4 ($C\text{-}6^{A,B,D,E}$), 84.7 ($C\text{-}3^{B,D}$), 99.9 ($C\text{-}1^{A}$), 103.3, 103.5 ($C\text{-}1^{B,C,D,E,F,G}$). ^1H-NMR (D_2O, 285K): δ 4.21 (bt, 4H), 4.44 (bt, 4H, $H\text{-}1^{B,D,E,G}$, $J_{1,2}$ = 8.7 Hz), 4.67, 4.68 (2xd, 2H, $H\text{-}1^{C,F}$, $J_{1,2}$ = 7.8 Hz), 4.72 (d, 1H, $H\text{-}1^{A}$, $J_{1,2}$ = 3.7 Hz). Product **II**. ^1H-NMR (D_2O, 285K): δ 4.09 (bt, 3H), 4.41 (bt, 3H, $H\text{-}1^{B,D,E}$, $J_{1,2}$ = 8.1 Hz), 4.65 (2xd, 2H, $H\text{-}1^{C,F}$, $J_{1,2}$ = 7.7 Hz), 4.69 (d, 1H, $H\text{-}1^{A}$, $J_{1,2}$ = 3.2 Hz). Product **III**. ^1H-NMR (D_2O, 285K): δ 4.09 (bdd, 4H), 4.42, 4.50 (4xd, 4H, $H\text{-}1^{B,D,E,G}$, $J_{1,2}$ = 7.8 Hz), 4.66 (d, 1H, $H\text{-}1^{C}$, $J_{1,2}$ = 8.0 Hz), 4.69 (d, 1H, $H\text{-}1^{A}$, $J_{1,2}$ = 3.5 Hz).

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19. For instance, an analogue of methyl heptaglucoside **2** in which the terminal glucosyl unit G was replaced by a β-galactose moiety was readily accessible.

20. Verduyn, R. *et al.*, to be published.

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