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Efficient synthesis of differently protected methyl (ethyl 1-thio-β-D-glucopyranosid)uronates and their evaluation as glucuronic acid donors and acceptors

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Abstract

Methyl [ethyl 2-*O*-acetyl-3,4-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-1-thio-β-D-glucopyranosid]uronate (**7**), and its 2-*O*-benzoyl and -pivaloyl analogues, **13** and **14**, have been synthesised from methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranosyluronate bromide, via formation and rearrangement of a 1,2-thioorthoester, in a stereospecific and high-yielding manner. Dimethyl(methylthio)sulfonium trifluoromethanesulfonate (DMTST)-promoted glycosylations with these derivatives as donors gave high to excellent yields (59–95%) of exclusively β-linked disaccharides in coupling with monosaccharide acceptors. Removal of the tetraisopropyldisiloxyl acetal with tetrabutylammonium fluoride in tetrahydrofuran from one of the obtained disaccharides gave a 3′,4′-diol, which was used as acceptor in a DMTST-promoted coupling with ethyl 2,3,4-tri-*O*-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside as donor to give trisaccharides, albeit with low regioselectivity (3-O-linked 38%, 4-O-linked 57%). © 1998 Elsevier Science Ltd. All rights reserved

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1. Introduction

Uronic acids are abundant in Nature as residues in many polysaccharides and glycoconjugates, e.g., proteoglycans and bacterial capsular polysaccharides [1]. In a programme directed towards the synthesis of biologically relevant structures from a number of capsular polysaccharides (i.e., *Streptococcus pneumoniae*, *Cryptococcus neoformans* and *Haemophilus influenzae*), all containing terminal or internal β-linked glucuronic acid residues, development of new and more effective uronic acid donors became necessary. The known fully acylated bromide and thioglycoside glucuronate donors gave only low yields in the couplings and the use of the fully benzylated analogues gave low stereoselectivity. Therefore, a new thioglycoside donor, methyl (ethyl 2-*O*-benzoyl-3,4-di-*O*-benzyl-1-thio-β-D-glucopyranosid)uronate was constructed,

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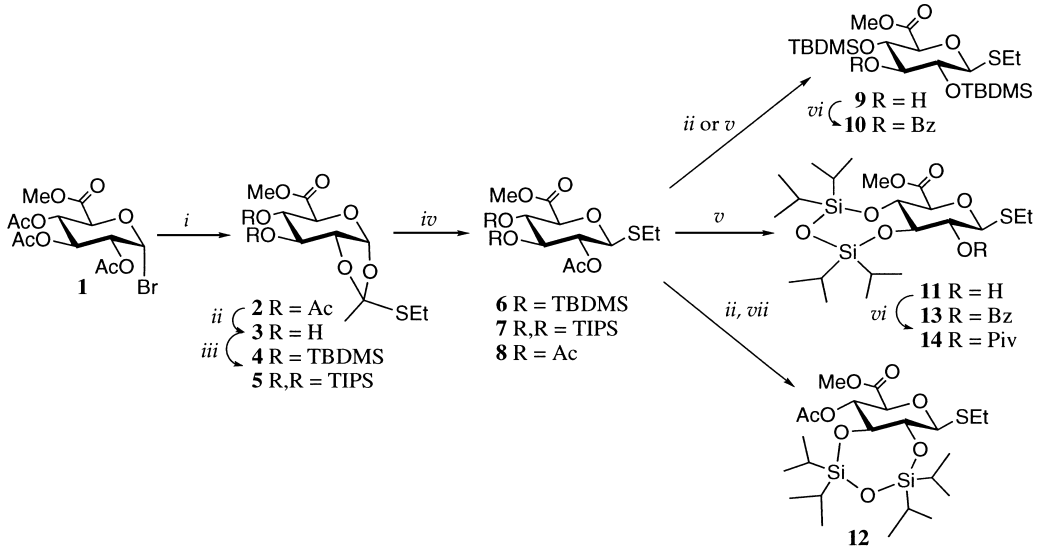
in which the use of a 2-*O*-acyl participating group ensured β-selectivity, whereas the alkyl group at O-3 and O-4 rendered activity to the donor, and high yields of β-linked disaccharides were obtained in couplings even with unreactive carbohydrate monosaccharide acceptors [2]. However, since benzylation of glucuronic acid esters is a problem and also the stereospecific formation of β-thioglycosides of glucuronic acid is not trivial, the synthesis of this donor was most efficient starting from a glucose derivative, ethyl 3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside, in a six-step protocol, in an overall yield of 26%. Although many intermediates are crystalline and all steps are easily performed in large scale, we felt that improvements in the synthesis of these types of donors would be of value. Accordingly, we now describe simple and high-yielding syntheses of similar glucuronic acid donors, with silyl protecting groups at O-3 and O-4, starting from glucuronic acid and the evaluation of these new donors in dimethyl(methylthio)sulfonium trifluoromethanesulfonate (DMTST)-promoted couplings with unreactive carbohydrate acceptors.

2. Results and discussion

Synthesis of 1,2-*trans*-thioglycosides are usually easily performed using the peracylated monosaccharide together with an alkyl thiol and a Lewis acid [3]. However, if these conditions are used on glucuronic acid, an α,β-mixture is obtained in a poor yield. Other methods to stereospecifically synthesise the β-linked thioglycoside are described in the literature, namely, displacement by a thioalkylate ion on an α-bromide [4] or rearrangement of a preformed β-xanthate [5]. We now describe another approach, namely, a Lewis acid rearrangement of a preformed thioorthoester, which stereospecifically and almost quantitatively yields the β-thioglycoside. The thioorthoester **2** was formed from the easily available glycosyl bromide **1** [6] by treatment with collidine and ethyl mercaptan (98% yield) [7] (Scheme 1). Treatment of **2** with a catalytic amount of trimethylsilyl triflate (TMSOTf) yielded the β-thioglycoside **8** in 95% yield. The orthoester intermediate also allows the easy introduction of the protection pattern desired for the more reactive type of donors. Compound **2** is deacetylated with methanolic sodium methoxide to give the 3,4-diol **3** (96%), which then can be protected with silyl ether groups. Treatment of **3** with either *tert*-butyldimethylsilyl (TBDMS) or tetraisopropyldisiloxyl (TIPS) chloride and imidazole in *N*,*N*-dimethylformamide gave the fully protected derivatives **4** (75%) and **5** (96%), respectively. Rearrangements of the thioorthoesters in **4** and **5** by treatment with TMSOTf, once more, gave almost quantitative yields of the β-thioglycosides **6** (95%) and **7** (99%) (Scheme 1).

Since different acyl groups as 2-*O*-participating groups in couplings with the 3,4-benzylated donors markedly affected the yields of coupling products

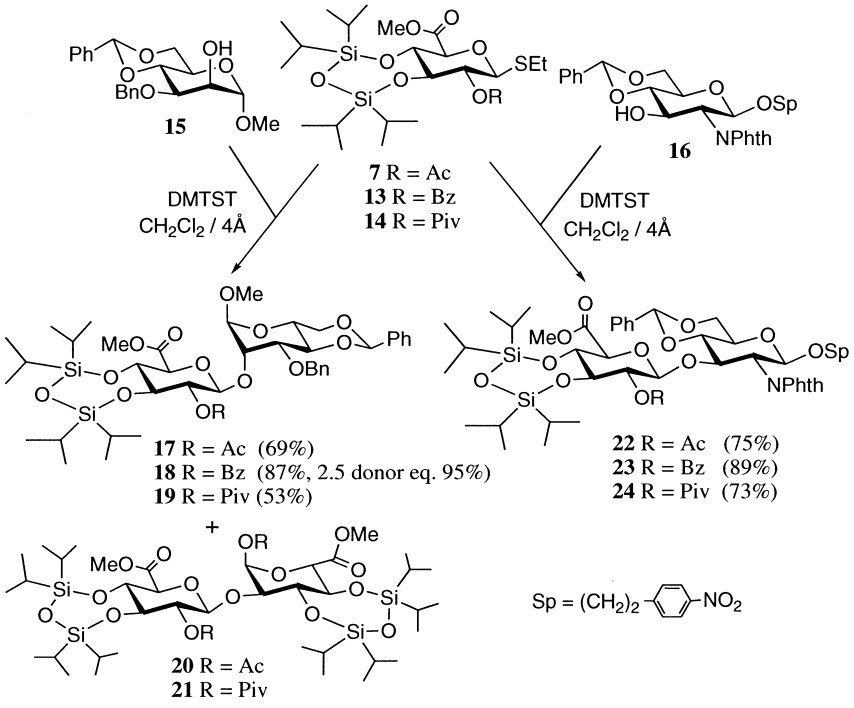


Scheme 1. (*i*) EtSH, collidine, CH_2Cl_2; (*ii*) MeO^-, MeOH; (*iii*) TIPS-Cl or TBDMS-Cl, imidazole, DMF; (*iv*) TMSOTf, EtSH, CH_2Cl_2; (*v*) K_2CO_3, MeOH; (*vi*) BzCl or PivCl, pyridine; (*vii*) Ac_2O, pyridine.

[2], the acetyl groups in compounds **6** and **7** were changed into a benzoyl or a pivaloyl group for evaluation. After deacetylation of **6** with methanolic sodium methoxide only one product was obtained (→**9**, 98%) which was benzoylated to give **10** (85%) (Scheme 1). However, as was evident from ^{1}H NMR analysis [δ 5.35 (t, 1 H, H-3)], **10** was not the expected 2-*O*-benzoyl derivative but instead the 3-*O*-benzoyl derivative, due to a complete 3-O→2-O-migration of the TBDMS group under the basic deprotection [8]. Several other conditions were tried but all gave **9** as the major product. Deacetylation of the TIPS-protected derivate **7** using sodium methoxide gave a mixture of the 2-OH compound **11** (71%) and the 4-OH analogue (24%) in which the TIPS-acetal had migrated to the 2,3-position (Scheme 1). The structure of the latter compound was confirmed by acetylation to give derivative **12** [^{1}H NMR, δ 5.13 (dd, 1 H, H-4)]. However, if potassium carbonate was used as base instead, the TIPS migration could be avoided, and compound **11** was obtained in 98% yield. Benzoylation or pivaloylation of **11**, with the corresponding acid chloride in pyridine gave compounds **13** (98%) and **14** (84%), which together with derivative **7** were evaluated as glycosyl donors.

Methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (**15**) [9], relevant for the synthesis of *Cryptococcus neoformans* capsular polysaccharide structures [10] and used in the evaluation of the corresponding 3,4-*O*-benzylated donors [2], and 2-(4-nitrophenyl)ethyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranoside (**16**), of interest as a model for proteoglycan synthesis, were chosen as acceptors with DMTST [11] as promoter.

With acceptor **15** all three donors (1.5 equiv), **7**, **13** and **14**, gave high yields of β-linked disaccharides, **17** (69%), **18** (87%), and **19** (53%) (Scheme 2) . These yields can be compared with the ones obtained with the 3,4-*O*-benzylated donors and the same acceptor, which were 25% (2-*O*-Ac), 68% (2-*O*-Bz) and 31% (2-*O*-Piv), respectively [2]. Here too, the 2-*O*-benzoylated donor was found to be best, but the acetylated and the pivaloylated donors also gave acceptable coupling yields. As was found earlier, an increase of the benzoylated donor from 1.5 to 2.5 equiv raised the coupling yield even further, and a 95% yield of disaccharide **18** was obtained. However, if this approach was tried with the acetylated and pivaloylated donors, **13** and **14**, the coupling yield actually decreased or only slightly improved (**17**, 45%; **19**, 59%) and a glucuronic acid dimer, which had also been isolated as a byproduct in the couplings using 1.5 equiv of donor, now became a major product. 50% of the acetylated donor and 45% of the pivaloylated donor was transformed into dimers. NMR



Scheme 2.

studies suggested the structures **20** and **21** for the dimers formed.

Couplings with acceptor **16**, using 1.5 equiv of the three donors, produced even higher yields of β-linked disaccharides, **22** (75%), **23** (89%) and **24** (73%) (Scheme 2). In none of these couplings any dimer formation was observed.

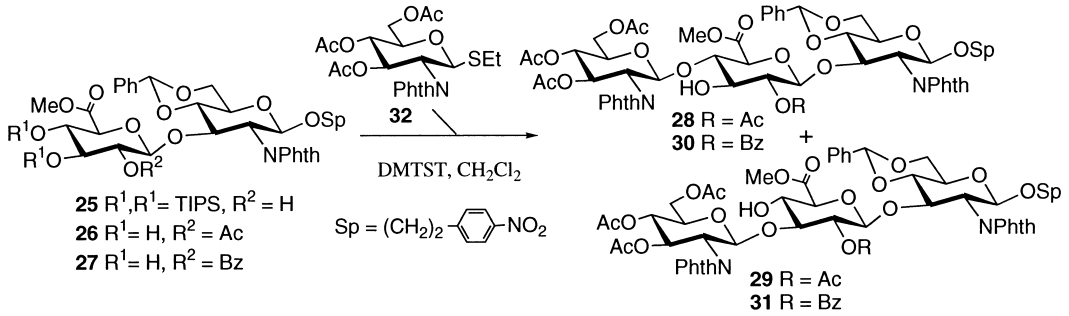
Thus, **13** seems to be a most attractive β-selective glucuronic acid donor, with compounds **7** and **14** as interesting alternatives. Their value as donors in more complex oligosaccharide synthesis, however, has to be tested. Apart from their easy accessibility and good donor properties these derivatives also contain another advantageous feature inherent in their protecting group pattern. The acyl and the silyl protecting group can be chemoselectively removed to produce partially protected derivatives, which then can be used as acceptors in continued oligosaccharide synthesis. To evaluate this prospect, selective deprotection of **22** and **23** was attempted. Debenzoylation of **23** with methanolic sodium methoxide gave a mixture of products, yet this time not a silyl migration had occurred but opening of the phthalimido moiety. This could be closed again by treatment with trifluoroacetic acid anhydride, and the resulting 2′-*O*-trifluoroacetylated derivative easily deacylated with potassium carbonate to give compound **25** (73%). The use of potassium carbonate from the onset, circumvented the problem and gave in a slow (4 days) but clean reaction **25** in 80% yield. Desilylation of **22** and **23** was performed with tetrabutylammonium fluoride in tetrahydrofuran to produce the 3,4-diols **26** (62%) and **27** (76%), respectively.

Investigating these 3,4-diols as acceptors, i.e., in terms of the regioselectivities attainable, glycosylation reactions were performed with ethyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**32**) [12] and DMTST as promoter (Scheme 3). Diol **26**, when coupled with 1.1 equiv of **32** gave an inseparable mixture of trisaccharides **28** and **29** (1:1, 69%). The benzoylated diol **27** was coupled with 2.2 equiv of donor to give 57% of the 4-O-linked trisaccharide **30** together with 38% of the 3-O-linked trisaccharide **31**, of which the linkages were established through benzoylation of **30** and identification of the downfield shifted H-3′. Thus, high yields of trisaccharides can be obtained but with low regioselectivity. To improve the regioselectivity, various tin activation procedures [13,14] of acceptor **27** were tried, but so far this has only resulted in low coupling yields and the formation of the 3,4-linked tetrasaccharide as major coupling product.

3. Experimental

General methods.—These were as described [15].

Methyl 3,4-di-O-*acetyl-1,2*-O-*(1-thioethyl)ethylidene*-α-D-*glucopyranuronate* (**2**).—Ethyl mercaptan (9.9 mL, 134 mmol) and dry *sym*-collidine (24.1 mL, 182 mmol) were added to a solution of methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranosyluronate bromide (**1**; 49 g, 122 mmol) [6] in distilled $MeNO_2$ (150 mL) containing 3 Å molecular sieves (3 g), and the mixture was stirred for 30 min under N_2. Tetrabutylammonium bromide (31.3 g, 97.1 mmol) was then added, and the mixture was stirred in the dark under N_2 for another 17 h at elevated temperature (50 °C). The reaction mixture was cooled to 0 °C and *sym*-collidine hydrobromide precipitated by addition of dry Et_2O (200 mL). Filtration through a bilayer plug of Celite and silica gel followed by concentration gave a residue, which was purified by silica gel chromatography (9:1 toluene–EtOAc + 0.5% pyridine) to



Scheme 3.

give **2** (47 g, 98%); $[\alpha]_D$ +6.1° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 15.0 (*Me*CH_2S), 20.7 (*Me*CO), 24.9 (Me*C*H_2S), 27.4 (Me orthoester), 52.8 (MeO), 68.2, 68.7, and 72.7 (C-2–5), 96.9 (C-1), 117.0 (C orthoester), 168.8, 168.9, and 169.3 (Me*C*O, *C*OOMe). Anal. Calcd for $C_{15}H_{22}O_9S$: C, 47.61; H, 5.86. Found: C, 47.56; H, 5.84.

Methyl 1,2-O-*(1-thioethyl)ethylidene*-α-D-*glucopyranuronate* (**3**).—Methanolic 1 M NaOMe (4.5 mL) was added to a solution of **2** (47 g, 120 mmol) in dry MeOH (200 mL). The reaction mixture was left for 10 h, then carefully neutralized by addition of Dowex H^+ ion-exchange resin, filtered, concentrated, and purified on a silica gel column (3:1 toluene–EtOAc + 1% pyridine). Crystallization from EtOAc–light petroleum bp 40–60 °C gave **3** (33.9 g, 96%); mp 80–83 °C; $[\alpha]_D$ +34° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$ + pyridine-d_6): δ 15.0 (*Me*CH_2S), 24.7 (Me*C*H_2S), 28.1 (Me orthoester), 52.7 (MeO), 70.4, 70.7, 72.8, and 76.6 (C-2–5), 96.9 (C-1), 116.9 (C orthoester), 170.9 (*C*OOMe). Anal. Calcd for $C_{11}H_{18}O_7S$: C, 44.89; H, 6.16. Found: C, 44.99; H, 6.11.

Methyl (ethyl 2-O-*acetyl-3,4-di*-O-tert-*butyldimethylsilyl-1-thio*-β-D-*glucopyranosid)uronate* (**6**).—*tert*–Butyldimethylsilyl chloride (1.1 g, 15 mmol) was added to a solution of **3** (1 g, 3.4 mmol) and imidazole (1.0 g, 7.5 mmol) in DMF (2 mL). The mixture was stirred overnight under N_2, then diluted by toluene and washed with $NaHCO_3$ (aq sat, 4 times) and water, dried (Na_2SO_4), filtered, concentrated and co-concentrated twice with toluene. The residue was purified on a silica gel column (9:1 light petroleum bp 60–70 °C–EtOAc + 1% pyridine) to yield methyl 3,4-di-*O*-*tert*–butyldimethylsilyl-1,2-*O*-(1-thioethyl)-ethylidene-α-D-glucopyranuronate (**4**; 1.33 g, 75%); $[\alpha]_D$ +7° (*c* 1.2, $CHCl_3$–pyridine-d_6); ^{13}C NMR ($CDCl_3$): δ −5.0, −4.7, and −4.5 (MeSi), 15.2 (*Me*CH_2S), 17.9 (Me_3*C*Si), 24.5 (Me*C*H_2S), 25.6 and 25.64 (Me_3CSi), 28.2 (Me orthoester), 52.1 (MeO), 70.2, 70.8, 74.1, and 75.7 (C-2–5), 96.2 (C-1), 117.5 (C orthoester), 170.4 (*C*OOMe). A mixture of **4** (18.8 g, 36 mmol) in freshly distilled CH_2Cl_2 (100 mL) containing 4Å molecular sieves (4 g) was stirred under N_2 for 30 min, whereafter ethyl mercaptan (3 mL, 36 mmol) and TMSOTf (652 μL, 3.6 mmol) were added. After 5 min, Et_3N (1.5 mL) was added and the resulting mixture filtered through Celite and concentrated. The residue was purified on a silica gel column (9:1 light petroleum bp 60–70 °C–EtOAc) to give **6** (17.8 g, 95%); $[\alpha]_D$ −19° (*c* 1.0, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ −4.8, −4.7, −4.6, and −4.4 (MeSi), 14.8 (*Me*CH_2S), 17.9 (Me_3*C*Si), 21.1 (*Me*CO), 23.8 (Me*C*H_2S), 25.6, 25.7, and 25.8 (Me_3CSi), 52.2 (MeO), 72.5, 73.4, 74.4, 79.9, and 80.0 (C-1–5), 169.6 and 169.7 (Me*C*O, *C*OOMe); ^1H, δ 4.30 (d, 1 H, *J* 2.8 Hz, H-1). Anal. Calcd for $C_{23}H_{46}O_7Si_2S$: C, 52.84; H, 8.87. Found: C, 52.70; H, 8.89.

Methyl [ethyl 2-O-*acetyl-3,4*-O-*(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-1-thio*-β-D-*glucopyranosid]uronate* (**7**).—Tetraisopropyldisiloxyl chloride (10 g, 31 mmol) was added to a cooled (0 °C) solution of **3** (7.8 g, 26 mmol) and imidazole (8.5 g, 125 mmol) in DMF (30 mL). The mixture was allowed to attain room temperature and stirred overnight under N_2, then diluted by toluene and washed with $NaHCO_3$ (aq sat, 3 times) and water, dried (Na_2SO_4), filtered, concentrated and co-concentrated twice with toluene. The residue was purified on a silica gel column (10:1 light petroleum bp 60–70 °C–EtOAc + 1% pyridine) to yield methyl 3,4-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-1,2-*O*-(1-thioethyl)ethylidene-α-D-glucopyranuronate (**5**; 13.6 g, 96%); $[\alpha]_D$ +80° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 12.0, 12.2, 12.7, and 12.9 CHSi), 15.1 (*Me*CH_2S), 17.1 and 17.2 (Me_2CHSi), 24.8 (Me*C*H_2S), 28.7 (Me orthoester), 52.2 (MeO), 72.8, 73.6, 78.8, and 79.2 (C-2–5), 98.6 (C-1), 115.2 orthoester), 169.3 (*C*OOMe). HRMS: 559.2196 $[M + Na]^+$. The thioorthoester **5** (13.4 g, 25 mmol) was rearranged as described for **4** (silica gel chromatography, 15:1 toluene–EtOAc) to give **7** (13.3 g, 99%); $[\alpha]_D$ −1° (*c* 1.0, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ 12.2, 12.8, and 12.9 (CHSi), 14.6 (*Me*CH_2S), 17.1 and 17.2 (Me_2CHSi), 20.8 (*Me*CO), 23.7 (Me*C*H_2S), 52.3 (MeO), 71.2, 74.4, 78.4, 79.5, and 83.6 (C-1–5), 168.4 and 169.2 (Me*C*O, *C*OOMe); ^1H, δ 4.43 (d, 1 H, *J* 9.8 Hz, H-1). Anal. Calcd for $C_{23}H_{44}O_8Si_2S$: C, 51.46; H, 8.26. Found: C, 51.57; H, 8.34.

Methyl (ethyl 2,3,4-tri-O-*acetyl-1-thio*-β-D-*glucopyranosid)uronate* (**8**).—The thioorthoester **2** (0.56 g, 1.6 mmol) was rearranged as described for **4** (silica gel chromatography, 6:1 toluene–EtOAc) to give crystalline **8** (532 mg, 95%); $[\alpha]_D$ −29° (*c* 1.0, $CHCl_3$); mp 108.5–109.5 °C (from Et_2O–light petroleum); NMR ($CDCl_3$): ^{13}C, δ 14.7 (*Me*CH_2S), 20.5, 20.6, and 20.7 (*Me*CO), 24.1 (Me*C*H_2S), 52.9 (MeO), 69.4, 69.5, 73.2, 76.4, and 83.7 (C-1–5), 167.0, 169.3, and 170.1 (Me*C*O, *C*OOMe); ^1H, δ 4.52 (d, 1 H, *J* 11.0 Hz, H-1). Anal. Calcd for $C_{15}H_{22}O_9S$: C, 47.61; H, 5.86. Found: C, 47.73; H, 5.79.

Methyl (ethyl 3-O-*benzoyl-2,4-di*-O-tert-*butyldimethylsilyl-1-thio*-β-D-*glucopyranosid)uronate* (**10**).—Methanolic 1 M NaOMe (1.5 mL) was added to a solution of **6** (18.8 g, 36 mmol) in MeOH (200 mL). The mixture was stirred for 5 h and then neutralized by addition of Dowex H^+ ion-exchange resin, filtered, concentrated, and the residue was purified on a silica gel column (10:1 toluene–EtOAc) to yield methyl (ethyl 2,4-di-*O*-*tert*-butyldimethylsilyl-1-thio-*β*-D-glucopyranosid)-uronate (**9**; 17.1 g, 98%); $[\alpha]_D$ −42° (*c* 1.0, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ −5.3, −4.1, −4.0, and −3.8 (MeSi), 14.8 (*Me*CH_2S), 18.0 and 18.3 (Me_3*C*Si), 24.7 (Me*C*H_2S), 25.7 and 26.1 (*Me*$_3$CSi), 52.2 (MeO), 72.5, 74.2, 79.5, 79.8, and 86.6 (C-1–5), 168.7 (*C*OOMe); ^1H, δ 4.34 (d, 1 H, *J* 9.2 Hz, H-1); HRMS: 503.2258 $[M+Na]^+$. Benzoyl chloride (2.1 mL, 26 mmol) was added to a solution of **9** (6.2 g, 12.9 mmol) in 4:1 CH_2Cl_2–pyridine (12.5 mL) and the mixture was stirred at 40 °C for 4 days, then diluted with toluene and washed with water, $NaHCO_3$ (aq, sat) and water, dried (Na_2SO_4), filtered, and concentrated. The residue was purified by silica gel chromatography (6:1 light petroleum bp 60–70 °C–EtOAc) to give **10** (6.4 g, 85%); $[\alpha]_D$ −24° (*c* 1.0, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ −4.9, −4.4, −3.7, and −3.6 (MeSi), 14.7 (*Me*CH_2S), 17.7 and 17.9 (Me_3*C*Si), 23.8 (Me*C*H_2S), 25.1, 25.4, 25.5, and 25.8 (*Me*$_3$CSi), 52.4 (MeO), 70.9, 72.4, 79.3, 80.0, and 87.0 (C-1–5), 128.2–133.0 (C aromatic), 165.2 (Ph*C*O), 168.7 (*C*OOMe); ^1H, δ 4.50 (d, 1 H, *J* 9.3 Hz, H-1), 5.35 (t, 1 H, *J* 8.8 Hz, H-3). Anal. Calcd for $C_{28}H_{48}O_7Si_2S$: C, 57.50; H, 8.27. Found: C, 57.77; H, 8.22.

Methyl [ethyl 3,4-O-*(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-1-thio*-β-D-*glucopyranosid]uronate* (**11**).—Method A: Compound **7** (8.5 g, 15.8 mmol) was deacetylated, as described for **6**, for 48 h. Silica gel chromatography (10:1 toluene–EtOAc) gave **11** (5.55 g, 71%) together with methyl [ethyl 2,3-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-1-thio-*β*-D-glucopyranosid]uronate (1.9 g, 24%); $[\alpha]_D$ −70° (*c* 1.0, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ 12.1, 12.2, 12.76, and 12.8 (CHSi), 15.0 (*Me*CH_2S), 17.18, 17.2, and 17.4 (*Me*$_2$CHSi), 24.9 (Me*C*H_2S), 52.6 (MeO), 71.9, 75.2, 77.8, 80.8, and 86.4 (C-1–5), 169.2 (*C*OOMe); ^1H, δ 4.45 (d, 1 H, *J* 9.2 Hz, H-1). Method B: Potassium carbonate (0.4 mL of a solution of 5 g K_2CO_3 in 100 mL MeOH) was added to a solution of **8** (50 mg, 93 μmol) in dry MeOH (3 mL), and the mixture was stirred for 48 h. Work-up as above and silica gel chromatography (10:1 toluene–EtOAc) gave **11** (45 mg, 98%); $[\alpha]_D$ −3° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 12.1, 12.2, 12.8, and 12.9 (CHSi), 15.0 (*Me*CH_2S), 17.1, 17.2, and 17.3 (*Me*$_2$CHSi), 24.3 (Me*C*H_2S), 52.2 (MeO), 72.5, 74.0, 79.5, 80.5, and 85.7 (C-1–5), 168.6 (*C*OOMe). HRMS: Calcd for $C_{21}H_{42}O_7Si_2S$ $[M+Na]^+$: 517.2088; found: 517.2081.

Methyl [ethyl 4-O-*acetyl-2,3*-O-*(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-1-thio*-β-D-*glucopyranosid]uronate* (**12**).—Acetylation of methyl [ethyl 2,3-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-1-thio-*β*-D-glucopyranosid]uronate (1.2 g, 2.4 mmol) with Ac_2O in pyridine gave, after conventional work-up and silica gel chromatography (10:1 toluene–EtOAc), **12** (1.25 g, 98%); $[\alpha]_D$ −55° (*c* 1.0, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ 12.1, 12.2, 12.7, and 12.8 (CHSi), 14.9 (*Me*CH_2S), 17.16, 17.2, 17.3, and 17.4 (*Me*$_2$CHSi), 20.5 (*Me*CO), 24.7 (Me*C*H_2S), 52.7 (MeO), 71.3, 75.5, 76.5, 78.4, and 85.9 (C-1–5), 167.8 and 169.3 (Me*C*O, *C*OOMe); ^1H, δ 4.42 (d, 1 H, *J* 9.3 Hz, H-1), 5.13 (dd, 1 H, $J_{3,4}$ 9, $J_{4,5}$ 10 Hz, H-4). HRMS: Calcd for $C_{23}H_{44}O_8Si_2S$ $[M+Na]^+$: 559.2193; found: 559.2195.

Methyl [ethyl 2-O-*benzoyl-3,4*-O-*(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-1-thio*-β-D-*glucopyranosid]uronate* (**13**).—Benzoyl chloride (86 μL, 0.75 mmol) was added to a solution of **11** (37 mg, 74.7 μmol) in pyridine (1.5 mL) and the mixture was stirred for 48 h. Conventional work-up and purification on a silica gel column (10:1 toluene–EtOAc) gave **13** (44 mg, 98%); $[\alpha]_D$ +23° (*c* 1.0, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ 12.1, 12.2, 12.76, and 12.8 (CHSi), 14.7 (*Me*CH_2S), 17.0, 17.1, and 17.2 (*Me*$_2$CHSi), 23.7 (Me*C*H_2S), 52.3 (MeO), 71.7, 74.5, 78.6, 79.5, and 83.7 (C-1–5), 128.3–133.0 (C aromatic), 165.0 (Ph*C*O), 168.4 (*C*OOMe); ^1H, δ 5.3 (t, 1 H, H-2). Anal. Calcd for $C_{28}H_{46}O_8Si_2S$: C, 56.15; H, 7.74. Found: C, 56.32; H, 7.86.

Methyl [ethyl 2-O-*pivaloyl-3,4*-O-*(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-1-thio*-β-D-*glucopyranosid]uronate* (**14**).—Trimethylacetyl chloride (0.63 mL, 5 mmol) was added to a solution of **11** (250 mg, 0.5 mmol) in pyridine (15 mL) and the mixture was stirred for 24 h, when 4-pyrrolidinopyridine (0.1 equiv) was added. After a further 24 h, conventional work-up and purification on a silica gel column (9:1 toluene–EtOAc) yielded **14** (244 mg, 84%); $[\alpha]_D$ −13° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$): δ 12.4, 12.7, and 13.1 (CHSi), 14.7 (*Me*CH_2S), 17.1, 17.2, 17.3, 17.5, and 17.7 (*Me*$_2$CHSi), 23.6 (Me*C*H_2S), 27.3 (*Me*$_3$CCO), 38.8

(Me_3CCO), 52.3 (MeO), 70.8, 74.5, 78.3, 79.4, and 83.8 (C-1–5), 168.5 (*C*OOMe), 176.7 (Me_3CCO). Anal. Calcd for $C_{26}H_{50}O_8Si_2S$: C, 53.94; H, 8.71. Found: C, 54.11; H, 8.67.

General glycosidation procedure.—The donor (1.5 equiv) and acceptor (1 equiv) were dissolved in CH_2Cl_2 (5 mL) and crushed 4 Å molecular sieves (0.3 g) was added and the mixture stirred under N_2 for 30 min, whereafter DMTST (4 equiv) was added. After an additional 12 h, Et_3N (1.5 mL) was added and the mixture was filtered through Celite and concentrated. The residue was purified directly by silica gel chromatography.

*Methyl {methyl [2-*O*-acetyl-3,4-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-*β*-*D*-glucopyranosyl]uronate}-(1→2)-3-*O*-benzyl-4,6-*O*-benzylidene-*α*-*D*-mannopyranoside* (**17**).—Donor **7** (50 mg, 93 μmol) and methyl 3-*O*-benzyl-4,6-*O*-benzylidene-*α*-D-mannopyranoside (**15**; 26 mg, 62 μmol) [9] were coupled using the procedure described above (silica gel chromatography 9:1 toluene–EtOAc) to give **17** (38 mg, 69%) together with 5 mg of the suggested dimer {methyl [2-*O*-acetyl-3,4-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-*β*-D-glucopyranosyl]uronate}-(1→2)-1-*O*-acetyl-3,4-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-*α*-D-glucopyranuronate (**20**).

If instead 2.5 equiv of **7** (50 mg, 93 μmol) was reacted with **15** (16 mg, 37 μmol), 45% of the disaccharide **17** (15 mg) was obtained together with the dimer **20** (25 mg); **17**: $[\alpha]_D$ +6° (*c* 0.9, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ 12.2, 12.8, and 12.9 (CHSi), 17.1 and 17.2 (Me_2CHSi), 20.6 (*Me*CO), 52.2 and 54.9 (MeO), 64.1, 68.8, 71.8, 72.5, 74.0, 74.3, 76.0, 76.1, and 78.1 (C-2–6,2′–5′, Ph*C*H_2), 99.6, 100.5, and 101.5 (C-1,1′, Ph*C*H), 126.1–138.7 (C aromatic), 168.0 and 168.8 (Me*C*O, *C*OOMe); ^1H, δ 4.52 (d, 1 H, *J* 8.0 Hz, H-1′), 4.65 (s, 1 H, H-1). Anal. Calcd for $C_{42}H_{62}O_{14}Si_2$: C, 59.55; H, 7.38. Found: C, 61.06; H, 7.80.

20: $[\alpha]_D$ +30° (*c* 1.0, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ 12.1, 12.4, and 12.8 (CHSi), 17.1 and 17.4 (Me_2CHSi), 20.9 (*Me*CO), 52.3 (MeO), 72.8, 73.0, 74.2, 74.5, 75.5, 76.2, and 77.4 (C-2–5), 90.9 (C-1α), 101.0 (C-1β), 168.0, 168.8, 169.0, and 169.2 (Me*C*O, *C*OOMe); ^1H, δ 4.72 (d, 1 H, *J* 7.9 Hz, H-1β), 6.23 (d, 1 H, *J* 3.8 Hz, H-1α); MS (FAB^+): *m*/*z* 989.6 $[M+Na]^+$.

*Methyl {methyl [2-*O*-benzoyl-3,4-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-β-D-glucopyranosyl]uronate}–(1→2)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside* (**18**).—Donor **13** (50 mg, 84 μmol) and **15** (23 mg, 56 μmol) were coupled using the general procedure (silica gel chromatography, 9:1 toluene–EtOAc) to give **18** (46 mg, 87%). If instead 2.5 equiv of **13** was reacted with **15** (23 mg, 56 μmol) the disaccharide **18** was obtained in 95% yield (51 mg); $[\alpha]_D$ +10° (*c* 1.1, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ 12.2, 12.8, and 12.9 (CHSi), 17.0, 17.1, 17.16, and 17.20 (Me_2CHSi), 52.2 and 54.8 (MeO), 63.9, 68.6, 71.9, 73.4, 74.3, 74.5, 76.2, 76.3, 77.2, and 78.2 (C-2–6,2′–5′, Ph*C*H_2), 99.3, 100.7, and 101.4 (C-1,1′, Ph*C*H), 125.3–138.8 (C aromatic), 164.7 (Ph*C*O), 168.2 (*C*OOMe); ^1H, δ 4.55 (d, 1 H, *J* 1.7 Hz, H-1), 4.75 (d, 1 H, *J* 8.0 Hz, H-1′).

*Methyl {methyl [2-*O*-pivaloyl-3,4-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-β-D-glucopyranosyl]uronate}-(1→2)-3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside* (**19**).—Donor **14** (50 mg, 86 μmol) and **15** (24 mg, 58 mmol) were coupled using the general procedure (silica gel chromatography, 9:1 toluene–EtOAc) to give **19** (29 mg, 53%) together with 30 mg of the suggested dimer {methyl [2-*O*-pivaloyl-3,4-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-β-D-glucopyranosyl]uronate}-(1→2)-1-*O*-pivaloyl-3,4-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-α-D-glucopyranuronate (**21**).

If instead 2.5 equiv of **14** (100 mg, 173 μmol) was reacted with **15** (29 mg, 69 μmol), 59% of the disaccharide **19** (38 mg) was obtained together with the dimer **21** (45 mg). **19**: $[\alpha]_D$ +11° (*c* 1.4, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ 12.3, 12.4, 12.7, and 13.1 (CHSi), 17.1, 17.2, 17.3, 17.5, and 17.7 (Me_2CHSi), 27.2 and 27.3 (Me_3CCO), 38.9 (Me_3CCO), 52.2 and 54.8 (MeO), 64.2, 68.8, 71.4, 72.6, 74.1, 74.3, 75.4, 75.9, 77.3, and 78.0 (C-2–6,2′–5′, Ph*C*H_2), 99.4, 100.4, and 101.4 (C-1,1′, PhCH), 126.1-138.8 (C aromatic), 168.1 (*C*OOMe), 176.3 (Me_3CCO); ^1H, δ 4.55 (d, 1 H, *J* 8.5 Hz, H-1′), 4.59 (d, 1 H, *J* 1.3 Hz, H-1). Anal. Calcd for $C_{45}H_{68}O_{14}Si_2$: C, 60.78; H, 7.71. Found: C, 60.50; H, 7.64.

21: $[\alpha]_D$ +67° (*c* 0.3, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ 12.3, 12.4, 12.5, 12.7, 12.72, 12.8, 13.0, and 13.2 (CHSi), 17.0, 17.1, 17.2, 17.3, 17.4, 17.6, and 17.7 (Me_2CHSi), 27.0, 27.2, and 27.3 (Me_3CCO), 38.7 and 39.0 (Me_3CCO), 52.4 (MeO), 73.0, 73.2, 73.8, 74.2, 74.4, 74.5, 75.7, and 79.4 (C-2–5), 90.7 (C-1α), 100.2 (C-1β), 168.3 and 169.1 (*C*OOMe), 176.0 (Me_3CCO); ^1H, δ 4.58 (d, 1 H, *J* 6 Hz, H-1β), 6.28 (d, 1 H, *J* 3.5 Hz, H-1α); MS (FAB^+): *m*/*z* 1051.4 $[M+H]^+$, 1073.6 $[M+Na]^+$.

*2-(4-Nitrophenyl)ethyl {methyl [2-*O*-acetyl-3,4-O-(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)-*

β-D-*glucopyranosyl]uronate}-(1→3)-4,6*-O-*benzylidene-2-deoxy-2-phthalimido*-β-D-*glucopyranoside* (**22**).—Donor **7** (259 mg, 550 μmol) and **16** (213 mg, 366 μmol) were coupled using the general procedure (silica gel chromatography, 6:1 toluene–EtOAc) to give **22** (290 mg, 75%); $[\alpha]_D$ −24° (*c* 1.0, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ 11.9, 12.1, 12.6, and 12.7 (CHSi), 16.9, 17.0, and 17.1 (Me_2CHSi), 20.0 (*Me*CO), 35.3 (Ph*C*H_2CH_2O), 52.0 (MeO), 55.0, 66.6, 68.6, 69.0, 72.8, 74.2, 75.2, 75.4, and 80.9 (C-2–6,2′–5′, $PhCH_2CH_2O$), 98.5, 100.2, and 101.3 (C-1,1′, Ph*C*H), 123.0–146.6 (C aromatic), 168.4 (Me*C*O, *C*OOMe); ^1H, δ 4.42 (d, 1 H, *J* 8.1 Hz, H-1′), 5.08 (d, 1 H, *J* 8.8 Hz, H-1). Anal. Calcd for $C_{50}H_{64}O_{17}Si_2N_2$: C, 58.81; H, 6.32. Found: C, 58.90; H, 6.20.

2-(4-Nitrophenyl)ethyl {methyl [2-O-*benzoyl-3,4*-O-*(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)*-β-D-*glucopyranosyl]uronate}-(1→3)-4,6*-O-*benzylidene-2-deoxy-2-phthalimido*-β-D-*glucopyranoside* (**23**).—Donor **13** (50 mg, 84 μmol) and acceptor **16** (32 mg, 55 μmol) were coupled using the general procedure (silica gel chromatography, 6:1 toluene–EtOAc) to give **23** (55 mg, 89%); $[\alpha]_D$ −8° (*c* 1.0, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ 11.8, 12.1, 12.4, and 12.7 (CHSi), 16.8, 16.9, 17.0, and 17.1 (Me_2CHSi), 35.2 (Ph*C*H_2CH_2O), 52.1 (MeO), 54.5, 66.3, 68.6, 69.0, 73.8, 74.3, 75.1, 76.0, 77.3, and 81.6 (C-2–6,2′–5′, $PhCH_2CH_2O$), 98.3, 100.2, and 101.6 (C-1,1′, Ph*C*H), 122.9–146.5 (C aromatic), 164.1 (Ph*C*O), 168.6 (*C*OOMe); ^1H, δ 4.74 (d, 1 H, *J* 8.4 Hz, H-1′), 4.99 (t, 1 H, H-2'), 5.03 (d, 1 H, *J* 8.8 Hz, H-1). Anal. Calcd for $C_{55}H_{66}O_{17}Si_2N_2$: C, 61.20; H, 6.16. Found: C, 60.94; H, 6.14.

2-(4-Nitrophenyl)ethyl {methyl [2-O-*pivaloyl-3,4*-O-*(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)*-β-D-*glucopyranosyl]uronate}-(1→3)-4,6*-O-*benzylidene-2-deoxy-2-phthalimido*-β-D-*glucopyranoside* (**24**).—Donor **14** (101 mg, 174 μmol) and acceptor **16** (67 mg, 116 μmol) were coupled using the general procedure (silica gel chromatography, 6:1 toluene–EtOAc) to give **24** (93 mg, 73%); $[\alpha]_D$ −20° (*c* 1.5, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ 12.3, 12.4, 12.6, and 12.9 (CHSi), 16.9, 17.0, 17.1, 17.3, 17.5, and 17.6 (Me_2CHSi), 26.8 (Me_3CCO), 35.3 (Ph*C*H_2CH_2O), 38.3 (Me_3CCO), 52.1 (MeO), 55.3, 66.5, 68.7, 68.9, 73.4, 74.1, 74.4, 74.9, 77.3, and 80.8 (C-2–6,2′–5′, $PhCH_2CH_2O$), 98.2, 98.9, and 101.7 (C-1,1′, Ph*C*H), 123.0–146.6 (C aromatic), 168.6 (*C*OOMe), 175.8 (Me_3CCO); ^1H, δ 4.62 (d, 1 H, *J* 8.1 Hz, H-1′), 5.13 (d, 1 H, *J* 8.6 Hz, H-1). Anal. Calcd for $C_{53}H_{70}O_{17}Si_2N_2$: C, 59.86; H, 6.64. Found: C, 58.87; H, 6.64.

2-(4-Nitrophenyl)ethyl {methyl [3,4-O-*(1,1,3,3-tetraisopropyl-1,3-disiloxane-1,3-diyl)*-β-D-*glucopyranosyl]uronate}-(1→3)-4,6*-O-*benzylidene-2-deoxy-2-phthalimido*-β-D-*glucopyranoside* (**25**).—Method A: Potassium carbonate (0.5 mL of a solution of 5 g K_2CO_3 in 100 mL MeOH) was added to a solution of **23** (40 mg, 36 μmol) in MeOH (5 mL), and the mixture was stirred for 4 days with an addition of the same amount of base each day. The reaction mixture was neutralized with Dowex H^+ ion-exchange resin, filtered, concentrated, and the residue was purified on a silica gel column (6:1 toluene–EtOAc) to yield **25** (28 mg, 80%).

Method B. NaOMe (1.5 mL, 1 M in MeOH) was added to a solution of **23** (41 mg, 35.8 μmol) in MeOH (5 mL). After 12 h the reaction mixture was neutralized with Dowex H^+ ion-exchange resin, filtered, and concentrated. The residue was dissolved in pyridine (15 mL) and trifluoroacetic anhydride (5 mL) was added at 0 °C. After 1 h, MeOH (1 mL) was added and the mixture was diluted with CH_2Cl_2 and washed with water, 1 M HCl and water, dried (Na_2SO_4), filtered, and concentrated. The residue was dissolved in MeOH (5 mL) and potassium carbonate was added (0.5 mL of a solution of 5 g K_2CO_3 in 100 mL MeOH). After 30 min, the reaction mixture was neutralized with Dowex H^+ ion-exchange resin, filtered, concentrated, and purified on a silica gel column (6:1 toluene–EtOAc) to yield **25** (27.3 mg, 73%); $[\alpha]_D$ −34° (*c* 1.0, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ 11.9, 12.1, 12.5, and 12.9 (CHSi), 16.8, 17.0, 17.1, and 17.2 (Me_2CHSi), 35.4 (Ph*C*H_2CH_2O), 51.9 (MeO), 55.5, 66.5, 68.6, 69.2, 72.2, 74.0, 75.6, 75.8, 78.6, and 80.3 (C-2–6,2′–5′, $PhCH_2CH_2O$), 98.8, 101.4, and 103.2 (C-1,1′, Ph*C*H), 123.0–149.8 (C aromatic), 168.4 (*C*OOMe); ^1H, δ 5.16 (d, 1 H, *J* 8.6 Hz, H-1). Anal. Calcd for $C_{48}H_{62}O_{16}Si_2N_2$: C, 58.88; H, 6.38. Found: C, 58.66; H, 6.22.

2-(4-Nitrophenyl)ethyl [methyl (2-O-*acetyl*-β-D-*glucopyranosyl)uronate]-(1→3)-4,6*-O-*benzylidene-2-deoxy-2-phthalimido*-β-D-*glucopyranoside* (**26**).—Tetrabutylammonium fluoride (260 μL from a stock solution of 8.3 g QF-$(H_2O)_3$ in 23 mL THF) was added to a solution of **22** (93 mg, 88 μmol) in THF (1.5 mL). After 45 min the mixture was carefully concentrated. The crude product was purified in two steps: (1) silica gel chromatography in acetonitrile; (2) the still not pure product was purified again on a silica gel column by gradient elution (9:1→6:1→3:1→1:1 toluene–EtOAc) to give **26** (44 mg, 62%); $[\alpha]_D$ −38° (*c* 1.4, $CHCl_3$); NMR

($CDCl_3$): ^{13}C, δ 20.0 (*Me*CO), 35.3 (Ph*C*H_2CH_2O), 52.6 (MeO), 54.9, 66.5, 68.7, 69.1, 71.7, 73.0, 73.4, 74.5, 75.5, and 81.0 (C-2–6,2′–5′, PhCH_2*C*H_2O), 98.4, 100.0, and 101.6 (C -1,1′, Ph*C*H), 123.0–146.5 (C aromatic), 169.4 and 169.7 (Me*C*O, *C*OOMe); ^1H, δ 4.45 (d, 1 H, *J* 8.1 Hz, H-1'), 5.1 (d, 1 H, *J* 8.8 Hz, H-1). HRMS: Calcd for $C_{38}H_{38}O_{16}N$ $[M+Na]^+$: 801.2119; found: 801.2127.

*2-(4-Nitrophenyl)ethyl [methyl (2-*O*-benzoyl-*β*-*D*-glucopyranosyl)uronate]-(1→3)-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-*β*-*D*-glucopyranoside* (**27**).—The TIPS-group was removed from disaccharide **23** (155 mg, 139 μmol) as described above for **26** to give **27** (93 mg, 76%); $[\alpha]_D$ −39° (*c* 1.2, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ 35.3 (Ph*C*H_2CH_2O), 52.6 (MeO), 54.6, 66.4, 68.8, 69.0, 71.8, 73.5, 73.8, 74.6, 76.1, and 81.5 (C-2–6,2′–5′, PhCH_2*C*H_2O), 98.3, 100.0, and 101.9 (C-1,1′, Ph*C*H), 122.9–146.5 (C aromatic), 165.0 (Ph*C*O), 169.4 (*C*OOMe); ^1H, δ 4.7 (d, 1 H, *J* 8.1 Hz, H-1′), 5.07 (d, 1 H, *J* 8.4 Hz, H-1). Anal. Calcd for $C_{43}H_{40}O_{16}N_2$: C, 61.43; H, 4.79. Found: C, 61.60; H, 4.89.

*2-(4-Nitrophenyl)ethyl (3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-*D*-glucopyranosyl)-(1→4)-[methyl (2-*O*-acetyl-*β*-*D*-glucopyranosyl)uronate]-(1→3)-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-*β*-*D*-glucopyranoside* (**28**) and *2-(4-nitrophenyl)ethyl (3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-*D*-glucopyranosyl)-(1→3)-[methyl (2-*O*-acetyl-*β*-*D*-glucopyranosyl)uronate]-(1→3)-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-*β*-*D*-glucopyranoside* (**29**).—Ethyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-1-thio-*β*-*D*-glucopyranoside [12] (**32**; 15 mg, 30 μmol) and **26** (23 mg, 28.3 μmol) were dissolved in CH_2Cl_2 (5 mL), 4Å molecular sieves (0.5 g) were added, and the mixture was stirred under N_2 for 1 h. The mixture was cooled to −40 °C and DMTST (29 mg, 113 μmol) was added. The reaction mixture was stirred at −20 °C for 12 h and then an additional 4 h at room temperature. Et_3N (0.5 mL) was added, and the mixture was filtered through Celite, concentrated, and purified by silica gel chromatography (1:1 toluene–EtOAc) to give **28** and **29** as an inseparable 1:1 mixture (24 mg, 68 %); NMR ($CDCl_3$): ^{13}C, δ 19.6, 20.2, 20.3, 20.4, and 20.6 (*Me*CO), 35.3 (Ph*C*H_2CH_2O), 51.7 and 52.6 (OMe), 54.2, 54.9, 55.1, 61.8, 62.1, 66.5, 68.5, 68.7, 69.0, 69.02, 70.0, 70.05, 71.6, 71.7, 71.8, 72.7, 72.8, 74.3, 74.8, 75.0, 77.2, 80.4, 80.7, 82.0, and 83.6 (C-2–6,2′–5′,2″-6″, PhCH_2*C*H_2O), 97.9, 98.3, 98.4, 98.7, 99.7, 100.1, 101.2, and 101.5 (C-1,1′,1″, Ph*C*H), 123.0–149.8 (C aromatic), 166.9, 167.9, 168.1, 169.0, 169.3, 169.5, 169.8, 170.5, and 170.53 (Me*C*O, *C*OOMe); ^1H, δ 5.23 (d, 0.5 H, *J* 8.6 Hz, H-1″), 5.3 (d, 0.5 H, *J* 8.6 Hz, H-1″). Anal. Calcd for $C_{58}H_{57}O_{25}N_3$: C, 58.24; H, 4.80. Found: C, 57.96; H, 4.87.

*2-(4-Nitrophenyl)ethyl (3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-*D*-glucopyranosyl)-(1→4)-[methyl (2-*O*-benzoyl-*β*-*D*-glucopyranosyl)uronate]-(1→3)-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-*β*-*D*-glucopyranoside* (**30**) and *2-(4-nitrophenyl)ethyl (3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-*D*-glucopyranosyl)-(1→3)-[methyl (2-*O*-benzoyl-*β*-*D*-glucopyranosyl)uronate]-(1→3)-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-*β*-*D*-glucopyranoside* (**31**).—Acceptor **27** (23 mg, 26.5 μmol) was coupled with donor **32** (26.5 mg, 53 μmol) as described for acceptor **26**, to give the 4-O-linked trisaccharide **30** (19 mg, 57%) and the 3-O-linked trisaccharide **31** (14 mg, 38%). **30**: $[\alpha]_D$ −14° (*c* 1.5, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ 20.2, 20.4, and 20.6 (*Me*CO), 35.3 (Ph*C*H_2CH_2O), 51.7 (MeO), 54.3, 54.7, 62.2, 66.4, 68.6, 69.0, 70.0, 71.6, 72.7, 72.8, 73.1, 75.8, 77.2, 81.1, and 82.0 (C-2–6,2′–5′,2″-6″, PhCH_2*C*H_2O), 98.4, 98.6, 99.5, and 101.1 (C-1,1′,1″, Ph*C*H), 123.0–146.4 (C aromatic), 164.5 and 166.9 (Ph*C*O), 169.5, 169.8, and 170.5 (Me*C*O, *C*OOMe); ^1H, δ 4.61 (d, 1 H, *J* 8.1 Hz, H-1′), 5.02 (d, 1 H, *J* 8.4 Hz, H-1), 5.35 (d, 1 H, *J* 8.7 Hz, H-1″). Anal. Calcd for $C_{63}H_{59}O_{25}N_3$: C, 60.14; H, 4.73. Found: C, 60.19; H, 5.12.

31: $[\alpha]_D$ −10° (*c* 1.2, $CHCl_3$); NMR ($CDCl_3$): ^{13}C, δ 20.2 and 20.4 (*Me*CO), 35.2 (Ph*C*H_2CH_2O), 52.5 (MeO), 54.4, 54.8, 62.1, 66.4, 68.7, 68.8, 70.2, 70.3, 71.7, 74.3, 75.3, 77.2, 81.0, and 84.6 (C-2–6,2′–5′,2″-6″, PhCH_2*C*H_2O), 98.0, 98.3, 99.5, and 101.7 (C-1,1′,1″, Ph*C*H), 122.9–146.5 (C aromatic), 163.5 (Ph*C*O), 168.3, 169.3, 169.6, and 170.4 (Me*C*O, *C*OOMe); ^1H, δ 4.6 (d, 1 H, *J* 8.1 Hz, H-1′), 4.93 (d, 1 H, *J* 8.8 Hz, H-1), 5.35 (d, 1 H, *J* 8.4 Hz, H-1″).

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