Synthesis of Oligosaccharide Structures from the Lipopolysaccharide of *Moraxella catarrhalis*

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The synthesis of the octasaccharide [*p*-(trifluoroacetamido)phenyl]ethyl 4-*O*-[2-*O*-(2-acetamido-2-deoxy-α-D-glucopyranosyl)-*β*-D-glucopyranosyl]-6-*O*-[2-*O*-[4-*O*-(4-*O*-α-D-galactopyranosyl-*β*-D-galactopyranosyl)-α-D-glucopyranosyl]-*β*-D-glucopyranosyl]-3-*O*-*β*-D-glucopyranosyl-α-D-glucopyranoside, representing the outer part of the lipooligosaccharide from *Moraxella catarrhalis* serotype A, is described, together with a hepta-, a hexa-, and a pentasaccaride, composing parts thereof with shorter oligosaccharide chains substituted in the 6-position of the central 3,4,6-branched glucose moiety. The versatility of the use of thioglycosides in oligosaccharide synthesis is shown, since throughout the synthesis thioglycosides are used as glycosyl donor precursors, either directly in dimethyl(methylthio)sulfonium triflate (DMTST)-promoted coupling reactions or after conversion to the corresponding glycosyl bromide in silver triflate-promoted couplings. The effects of different protecting groups, anomeric leaving groups, and solvents used in the various coupling reactions are often substantial, which necessitates the use of easily convertible intermediates.

Introduction

Moraxella catarrhalis has been increasingly recognized as a major pathogen in a number of respiratory diseases, especially in children.[1] The bacterium is divided into three serogroups, A, B, and C. The structures of the cell-surface lipopolysaccharide (LPS) from *Moraxella catarrhalis* strains of serotype A and C have recently been determined.[2−4] They lack the extended polymeric O-antigenic side chains, and the structure without the lipid A part of one of the strains of serotype A is shown in Chart 1.

Some heterogeneity in the LPS within the serogroups is known, e.g., different lengths of the oligosaccharide chain in the primary position of the central glucose moiety. In serogroup C elongation of the 4-*O*-substituent is often found. To investigate the antigenicity of different parts of the LPS structure synthesis was necessary. As a first approach the tetrasaccharide and the pentasaccharide shown in Chart 2 were synthesized,[5] both containing the central branched structure common for all three serotypes of *M. catarrhalis*.

In the structural elucidation, NMR experiments showed anomalities in some of the NOE values, indicating a conformational change in the oligosaccharide as the substituents on the central glucose moiety grew longer. To investigate when this change takes place and to further evaluate the antigenicity of various structures of the LPS, syntheses of larger structures have been performed, including the complete hexose-containing octasaccharide of serotype A and derivatives thereof with shorter 6-*O*-substituents.

Results and Discussion

In the retrosynthetic analysis of the target compounds, care has to be taken of the order of introduction of the different substituents on the branched central glucose moiety, since in the synthesis of oligosaccharides there is always the possibility to encounter problems with unreactive glycosyl acceptors, especially when the structure is large and/or highly branched. The knowledge about the conformational changes in the native structures further emphasized this possibility. The decision was therefore taken to introduce the 3- and 4-substituent first and then lastly the primary, hopefully more accessible, 6-*O*-substituent. This scheme would also imply the shortest way to derivatives with different length of the 6-*O*-chain by the introduction of various substituent donors to a common intermediate. Benzyl groups were chosen as permanent protection groups, whereas silyl groups and, from the start, benzoyl groups were chosen as temporary protecting groups. The known disaccharide derivative **1**,[5] used in the earlier synthesis of the central branched tetrasaccharide and already containing the 3-*O*-substituent, was chosen as precursor.

The benzoyl groups in the starting disaccharide derivative **1** were changed to permanent benzyl groups (→**2**, 78%), whereafter the spacer arm, necessary for the formation of glycoconjugates, was introduced via a dimethyl(methylthio)sulfonium triflate[6] (DMTST)-promoted coupling in diethyl ether between the thioglycoside **2** and [*p*-(trifluoroacetamido)phenyl]ethanol to give the α-linked *O*-glycoside **3** (61%) (Scheme 1). To allow introduction of the 4-*O*-substituents and later the 6-*O*-substituents, the benzylidene acetal was removed (87%) and the resulting diol **4** was regioselectively silylated at the primary hydroxyl group to give compound **5** (93%). Two ways were considered for the entry of the 4-*O*-linked disaccharide α-D-GlcNAc-(1→2)-*β*-D-Glc: a block synthesis, in which a disaccharide donor is constructed first and then coupled to acceptor **5**, or a consecutive stepwise synthesis. Although the α-coupling of the glucos-

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(3) Edebrink, P.; Jansson, P.-E.; Rahman, M. M.; Widmalm, G.; Holme, T.; Rahman, M.; Weintraub, A. *Carbohydr. Res.* **1994**, *257*, 269.

(4) Edebrink, P.; Jansson, P.-E.; Mahbur, R.; Widmalm, G.; Holme, T.; Rahman, M *Carbohydr. Res.* **1995**, *266*, 237.

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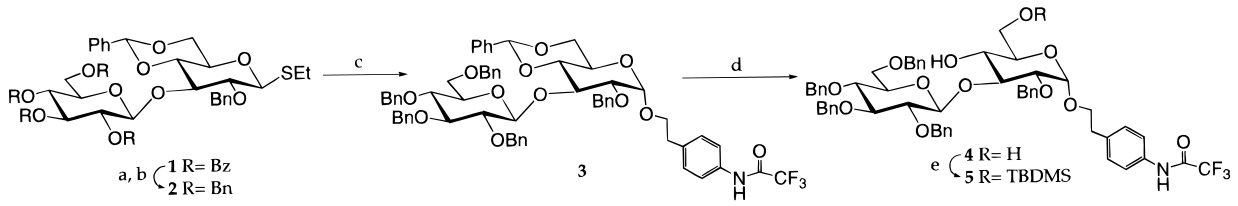
Chart 1

α-D-Glc*p*NAc-(1→2)-β-D-Glc*p*
1
↓
4
α-D-Gal*p*-(1→4)-β-D-Gal*p*-(1→4)-α-D-Glc*p*-(1→2)-β-D-Glc*p*-(1→6)-α-D-Glc*p*-(1→5)-α-D-Kdo*p*
3 4
↑ ↑
1 2
β-D-Glc*p* α-D-Kdo*p*

Chart 2

β-D-Glc*p* β-D-Glc*p*
1 1
↓ ↓
4 4
β-D-Glc*p*-(1→6)-α-D-Glc*p*-(1→O-spacer β-D-Glc*p*-(1→6)-α-D-Glc*p*-(1→5)-α-D-Kdo*p*-(2→O-spacer
3 3
↑ ↑
1 1
β-D-Glc*p* β-D-Glc*p*

Scheme 1[a]



[a] Key: (a) NaOMe, MeOH (89%); (b) BnBr, NaH, DMF (88%); (c) *p*-$CF_3CONHPhCH_2CH_2OH$, DMTST, diethyl ether (61%); (d) HOAc (aqueous), CH_3CN (87%); (e) TBDMSCl, imidazole, DMF (93%).

acetamide moiety was expected to be the most difficult and, thus, should be performed as early as possible in the synthesis, the latter strategy was chosen, since this would allow the use of a 2-*O*-participating group and accordingly stereoselective *β*-coupling of the glucose donor. As donor, the 2-*O*-benzoylated derivative **7**, obtained from the known derivative ethyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-1-thio-*β*-D-glucopyranoside[7] through deacetylation (→ **6**, 96%) and benzoylation (93%), was chosen since benzoates are known to give less side products in the coupling reaction.[8] Using, once more, DMTST as promoter, the trisaccharide **9** was cleanly produced in 93% yield (Scheme 2). The debenzoylation to the 2″-OH derivative proved to be time-consuming, due to the often noticed unreactivity of the 2-position of glucose in oligosaccharides. Thus, treatment of derivative **9** with methanolic sodium methoxide required 14 days for complete deacylation, and during that time the trifluoroacetamide group was also cleaved. Therefore, subsequent *N*-trifluoroacetylation had to be performed in two steps to finally give compound **10** (89%). As a way to circumvent this delay the 2-*O*-chloroacetyl donor **8** was synthesized and converted to the glycosyl bromide by treatment with bromine and then coupled to acceptor **5** using silver triflate as promotor to give trisaccharide **11** (86%), which was found to rapidly (1 h) form **10** after treatment with sodium methoxide. If the thioglycoside **8** was used directly as donor in a DMTST-promoted coupling, only moderate yields of tetrasaccharide **11** were obtained.

The introduction of the glucosamine motif caused, as expected, problems to start with. Since an α-linkage was to be constructed, ethyl 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-1-thio-*β*-D-glucopyranoside, with the nonparticipating azido group as amino precursor in the 2-position, was selected as donor. Different promoters (DMTST, NIS/silver triflate) and different solvents (CH_2Cl_2, diethyl ether) were tested, and when all these couplings failed, different anomeric leaving group in the donor (bromide, trichloroacetimidate) were also tested without success. In all these experiments the reactivity of the donor was shown to be poorly matched to that of the aglycon.[9] The high reactivity of the donor caused decomposition before coupling could occur to the unreactive acceptor. Therefore, the protection groups were changed from benzyl groups to acetyl groups to decrease the reactivity of the donor.[10] This time, the bromo sugar donor (obtained from the thioglycoside **12**) promoted by silver triflate stereoselectively gave a tetrasaccharide product (Scheme 2), which was shown to be the desired α-glycoside **13** by NMR [δ 5.53 (d, $J_{1''',2'''} = 3.3$ Hz, H-1‴)]. The yield, 54%, was acceptable, especially when taking into consideration the stereoselectivity and the fact that 27% of the acceptor could be recovered (74% coupling yield calculated on consumed acceptor). In this coupling donor **12** could also be used in a DMTST-promoted coupling with similar results (see Experimental Section).

The silyl group was removed from compound **13** by acid treatment to give derivative **14** (85%), with a free 6-OH group. In the elongation at 6-OH it was again decided to proceed via a stepwise procedure to be able to use a stereoauxiliary group in position 2 of the donor to create the *β*-linkage to the primary hydroxyl group in the acceptor. The necessity of using acetyl groups as protect-

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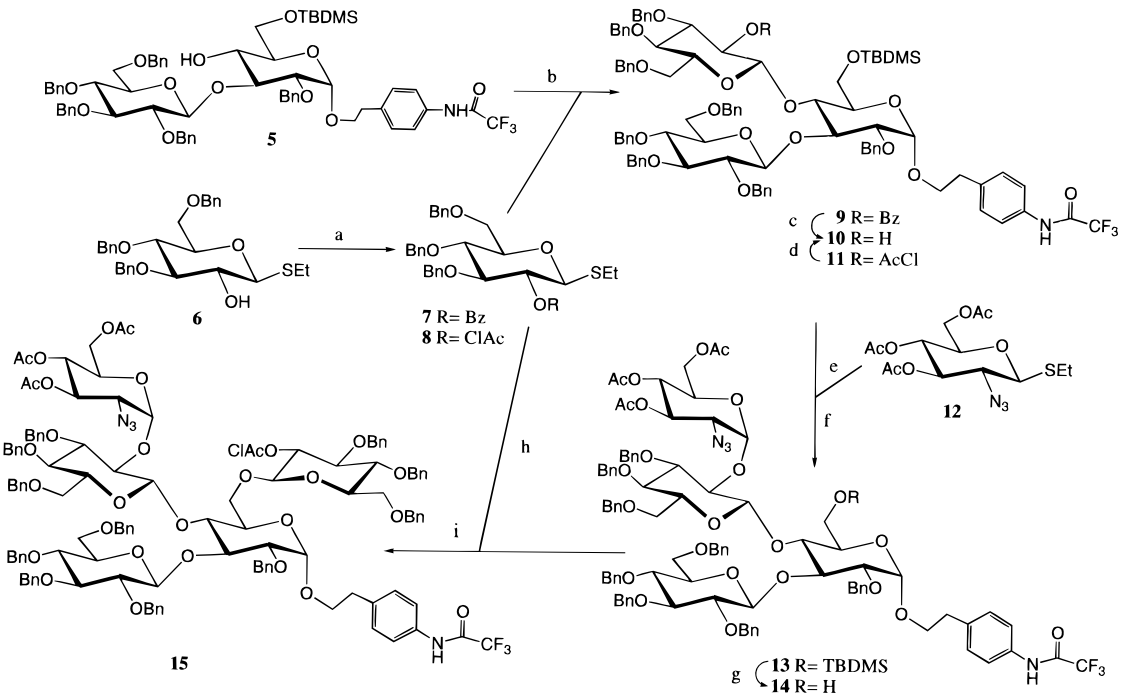
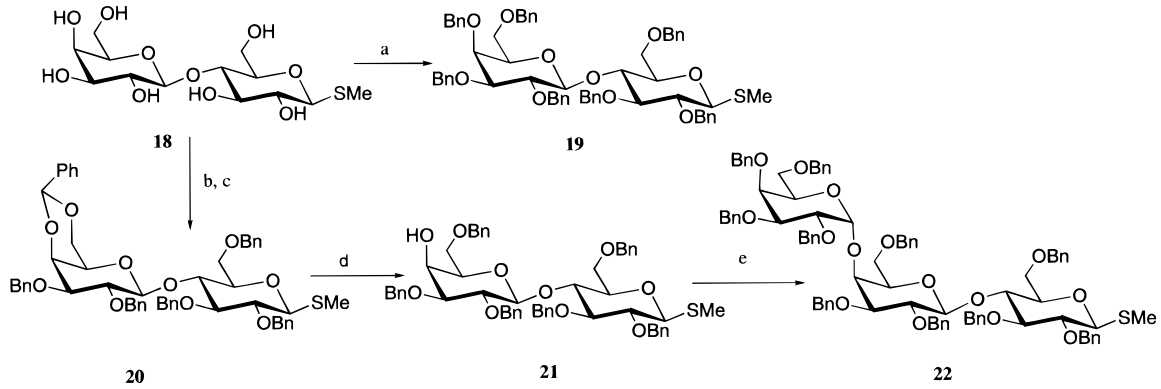
Scheme 2[a]



[a] Key: (a) RCl, pyridine, CH_2Cl_2 (93 or 81%); (b) **7**, DMTST, CH_2Cl_2 (94%) or **8**, Br_2, CH_2Cl_2 and then AgTf (86%); (c) (i) NaOMe, MeOH, (ii) TFAA, pyridine, CH_2Cl_2, (iii) NaOMe, MeOH (89%); (d) NaOMe, MeOH; (e) Br_2, CH_2Cl_2; (f) AgTf, CH_2Cl_2 (54%); (g) HOAc (aqueous) (85%); (h) Br_2, CH_2Cl_2; (i) AgTf, CH_2Cl_2 (79%).

Scheme 3[a]



[a] Key: (a) BnBr, NaH, DMF (90%); (b) $PhCH(OMe)_2$, *p*-TsOH; (c) BnBr, NaH, DMF (78%); (d) $NaCNBH_3$, HCl, THF (56%); (e) 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl chloride, AgTf, diethyl ether (62%).

ing groups in the azido donor precluded the use of benzoates as temporary protecting groups, and therefore, the monochloroacylated compound **8** was selected as donor. In a DMTST-promoted coupling this donor once more gave only moderate yields of coupling product, this time together with the orthoester product (total 83% yield). Various ways to avoid orthoester formation in glycosidations with participating acetyl groups have been described.[11] Here, once more the thioglycoside was transformed into the bromo sugar before coupling. Silver triflate was used as promoter, and the *β*-linked pentasaccharide product **15** was obtained in 79% yield (Scheme 2). Selective removal of the monochloroacetyl group in the presence of the acetyl groups was accomplished with hydrazine dithiocarbonate[12] to give a key intermediate **16** (79%), with a free 2-hydroxyl group ready for elongation with various glycosyl donors. Pentasaccharide **15** was also completely deprotected through Zemplén deacylation and catalytic hydrogenolysis to remove benzyl groups and reduce the azido function. Selective *N*-acetylation of the obtained amino group then afforded the first target product **17** (Scheme 4).

The donors to be used in the subsequent couplings were synthesized from the known methyl 1-thio-*β*-D-lactopyranoside (**18**)[13] through benzylation to give the lactose donor **19** and via benzylidenation, benzylation, reductive benzylidene opening, and a silver triflate-promoted coupling with 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl chloride[14] to yield the globotriose donor **22** (Scheme 3). The α-configuration in the latter coupling was evident from NMR [δ 5.19 (1H, d, $J_{1'',2''} = 2.9$ Hz, H-1″)].

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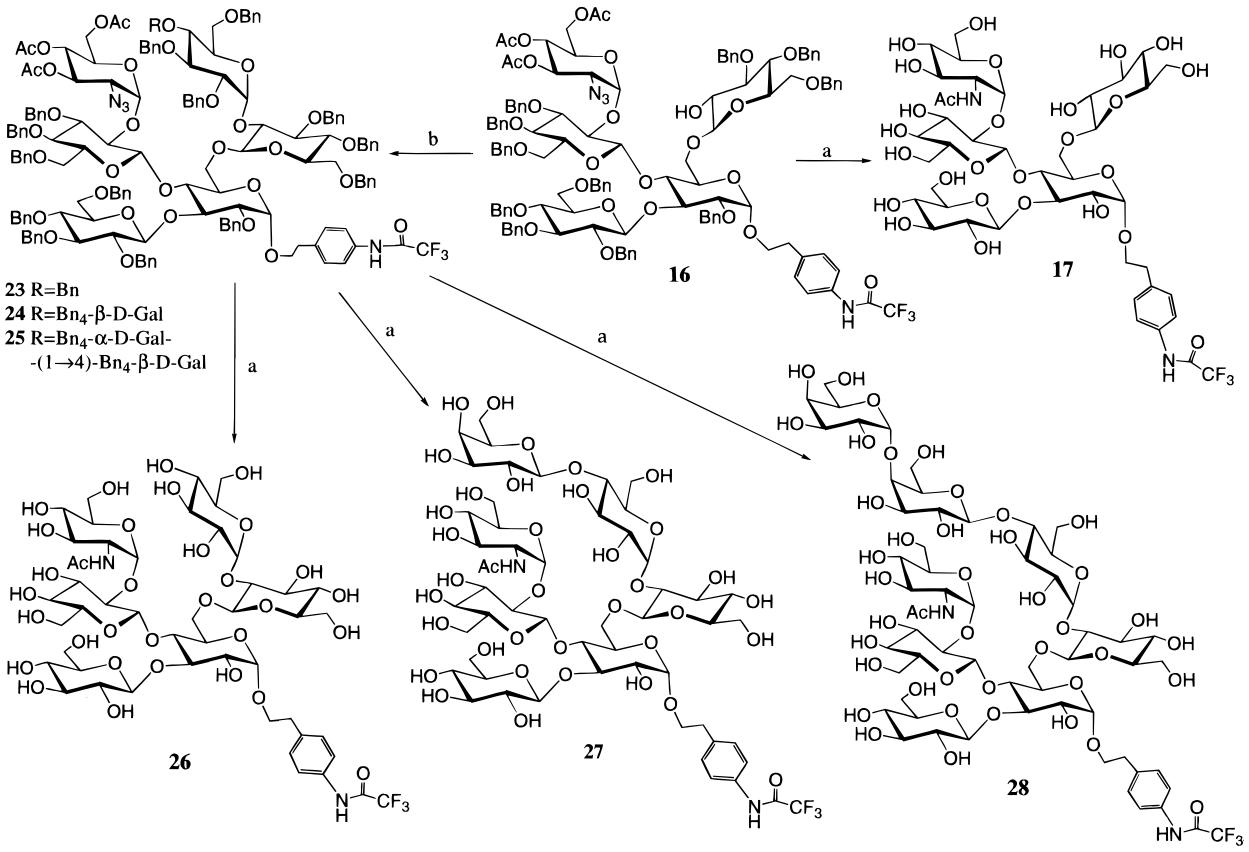
Scheme 4[a]



[a] Key: (a) (i) NaOMe, MeOH, (ii) H_2, Pd−C, (iii) Ac_2O; (b) (i) 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl bromide or **19**, Br_2 or **22**, Br_2, (ii) AgTf, diethyl ether.

As a model donor, which also would yield the hexasaccharide target compound, a 2,3,4,6-tetra-*O*-benzylated glucose derivate was chosen. Once again, problems were encountered with the low reactivity of the 2-position of glucose, here in acceptor **16**, and this time the stereoselectivity in the coupling was found to be a further complication. Initially, the glucopyranosyl bromide[15] was tried as donor in a silver triflate-promoted coupling in CH_2Cl_2, which gave a hexasaccharide product, but only in 47% yield and and as an α/*β*-mixture (ratio 1/1). Halide-assisted conditions were tried in an attempt to improve the α/*β*-ratio but were found to be too mild to yield any coupling product. The *β*-anomeric trichloroacetimidate donor[16] and the ethyl thioglycoside donor[15] analogs were also tested with various promoters, but with even worse results than in the initial coupling using the bromide as donor. A nonparticipating group is required at the 2-position of the donor to enable the formation of the desired α-linkage. Perhaps a modulation of the reactivity of the donor by the introduction of acyl groups at other positions would have improved the yields of coupling product, but this would at the same time considerably complicate the synthesis of the donors. Fortunately, a simple solution to the problem was found, as diethyl ether was tried as solvent in the initial silver triflate-promoted coupling with the bromide as donors. This solvent has previously been used to improve the amount of α-glycosidically linked product formed, inter alia, by us in DMTST-promoted couplings with thioglycoside donor.[17] Here, it also seemed to have a stabilizing effect on the activated donor, and a high yield (75%) of the pure α-linked hexasaccharide **23** was obtained. These coupling conditions were found to function as well with the lactose and the globotriose donors. Couplings with the bromo sugar obtained from **19** or **22** with acceptor **16** gave stereoselectively the heptasaccaride **24** (69%) and the octasaccharide **25** (63%), respectively (Scheme 4).

Deprotection of the coupling products **23**, **24**, and **25**, using the same protocol as for compound **15** above, gave the final target compounds **26**, **27**, and **28**, respectively (Scheme 4).

This synthesis shows the versatility of thioglycoside donors. They are easy to synthesize, are stable under almost any protecting group manipulations, often function well as glycosyl donors using thiophilic promotors, and if these couplings fail are easy to transform into most other types of donors commonly used, even unstable benzylated oligosaccharide glycosyl bromides as described here.

Experimental Section

General Remarks. Melting points are corrected. Organic solutions were dried over $MgSO_4$ before concentrating, which was performed under reduced pressure at <40 °C (bath temperature). NMR spectra were recorded at 25 °C at 270 MHz (^1H) or 67.5 MHz (^{13}C) in $CDCl_3$ with Me_4Si as internal standard ($\delta = 0$ ppm) or in D_2O with acetone as internal standard (^{13}C: $\delta = 31.0$ ppm; ^1H: $\delta = 2.225$ ppm), unless

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otherwise stated. TLC was performed on Silica Gel F_{254} (E. Merck) with detection by UV light and/or by charring with 8% sulfuric acid. Silica gel (0.040−0.063 mm, Amicon) was used for column chromatography.

Ethyl 2-*O*-Benzyl-4,6-*O*-benzylidene-3-*O*-(2,3,4,6-tetra-*O*-benzoyl-*β*-D-glucopyranosyl)-1-thio-*β*-D-glucopyranoside (1). Silver triflate was added at −30 °C to a stirred mixture of ethyl 2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-*β*-D-glucopyranoside[5] (200 mg, 0.50 mmol) and 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl bromide[18] (500 mg, 0.76 mmol) in CH_2Cl_2 (5 mL) containing molecular sieves (4 Å). The temperature was allowed to rise to −5 °C during 1.5 h. Triethylamine (1 mL) was added, and stirring was continued for 20 min. The mixture was diluted with CH_2Cl_2, filtered through Celite, concentrated, and purified by silica gel chromatography (toluene−EtOAc 30:1) to give **1** (420 mg, 86%): $[\alpha]_D$ +2.5° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 14.9, 24.9, 63.0, 68.6, 69.7, 70.3, 71.9, 72.3, 73.2, 75.4, 79.2, 80.9, 81.8, 85.5, 100.4, 101.3, 125.2−137.7, 165.0, 165.1, 165.7, 165.9. Anal. Calcd for $C_{56}H_{52}O_{14}S$: C, 68.56; H, 5.34. Found: C,68.49; H, 5.45.

Ethyl 2-*O*-Benzyl-4,6-*O*-benzylidene-3-*O*-(2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl)-1-thio-*β*-D-glucopyranoside (2). A solution of **1** (3.5 g, 3.6 mmol) in methanol (200 mL) was treated with a catalytic amount of 1 M sodium methoxide. The solution was stirred overnight and then neutralized with Dowex-50 (H^+) resin, filtered, and concentrated. The residue was crystallized from MeOH, and the mother liquor was purified by silica gel chromatography ($CHCl_3$−MeOH 30:1) to give more ethyl 2-*O*-benzyl-4,6-*O*-benzylidene-3-*O*-(*β*-D-glucopyranosyl)-1-thio-*β*-D-glucopyranoside (total 1.8 g, 89%). To a suspension of sodium hydride (60%, 411 mg, 10.3 mmol) in DMF (2 mL) was added a solution of the above compound (966 mg, 1.71 mmol) in DMF (7 mL) at rt, followed by a solution of benzyl bromide (1.1 mL, 9.58 mmol) in DMF (5 mL). After 3 h, MeOH (5 mL) was added, and stirring was continued for 30 min. The mixture was diluted with toluene, washed with water, dried (Na_2SO_4), and concentrated. The residue was purified by silica gel chromatography (light petroleum bp 40−60 °C−EtOAc 6:1) to give **2** (1.4 g, 88%): mp 155−156 °C (diethyl ether−*n*-hexane); $[\alpha]_D$ −1.9° (*c* 1.1, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 15.1, 25.1, 68.6, 68.9, 70.5, 73.5, 74.8, 74.9 75.0, 75.2, 75.5, 78.0, 79.2, 79.9, 81.8, 82.9, 84.8, 85.7, 101.1, 102.1, 126.1−138.5. Anal. Calcd for $C_{56}H_{60}O_{10}S$: C, 72.71; H, 6.54. Found: C, 72.93; H, 6.58.

[*p*-(Trifluoroacetamido)phenyl]ethyl 2-*O*-Benzyl-4,6-*O*-benzylidene-3-*O*-(2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl)-α-D-glucopyranoside (3). DMTST (2.18 g, 8.44 mmol) was added at rt to a stirred mixture of **2** (1.98 g, 2.14 mmol) and 2-[4-(trifluoroacetamido)phenyl]ethanol (0.59 g, 2.55 mmol) in dry diethyl ether (25 mL) containing molecular sieves (4 Å). After 44 h triethylamine (2 mL) was added, and stirring was continued for 20 min. The mixture was diluted with CH_2Cl_2, filtered through Celite, concentrated, and purified by silica gel chromatoraphy (toluene−EtOAc 10:1) to give **3** (1.44 g, 61%): ^{13}C NMR ($CDCl_3$) δ 35.4, 62.2, 68.7, 68.8, 69.0, 73.4, 74.7, 74.8, 75.5, 76.1 77.9, 80.2, 80.4, 82.8, 84.8, 97.3, 101.3, 102.5, 121.0−138.8.

[*p*-(Trifluoroacetamido)phenyl]ethyl 2-*O*-Benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl)-α-D-glucopyranoside (4). Aqueous acetic acid (70%, 3 mL) was added to a solution of **3** (485 mg, 0.44 mmol) in CH_3CN (1 mL). The solution was stirred at 70 °C for 4 h and then concentrated and purified by silica gel chromatography (toluene−EtOAc 2:1) to give **4** (390 mg, 87%): mp 145−146 °C (EtOAc−*n*-hexane); $[\alpha]_D$ +51° (*c* 0.9, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 35.3, 63.0, 68.5, 68.9, 70.2, 70.9, 73.0, 73.5, 74.3, 74.5, 75.0, 75.7, 77.7, 78.9, 82.0, 82.8, 84.6, 96.7, 103.5, 120.6−138.5, 154.3, 154.9. Anal. Calcd for $C_{57}H_{60}O_{12}F_3N$: C, 67.91; H, 6.00; N 1.39. Found: C, 67.86; H, 5.99; N, 1.41.

[*p*-(Trifluoroacetamido)phenyl]ethyl 2-*O*-Benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl)-6-*O*-(*t*-butyldimethylsilyl)-α-D-glucopyranoside (5). *tert*-Butyldimethylsilyl chloride (237 mg, 1.6 mmol) and imidazole (132 mg, 1.9 mmol) were added to a solution of **4** (1.22 g, 1.2 mmol) in DMF (10 mL). The solution was stirred for 1.5 h and then diluted with toluene, washed with water, dried, and concentrated. Purification by silica gel chromatography (toluene−EtOAc 15:1) gave **5** (1.26 g, 93%): $[\alpha]_D$ +49° (*c* 1.1, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ −5.2, 18.5, 26.0, 35.3, 62.9, 68.1, 68.6, 68.9, 72.3, 72.9, 73.5, 74.3, 74.5, 75.0, 75.7, 77.6, 79.1, 82.0, 82.9, 84.6, 96.4, 103.5, 120.6−138.6. Anal. Calcd for $C_{63}H_{74}O_{12}F_3NSi$: C, 67.42; H, 6.65; N, 1.25. Found: C, 67.18; H, 6.50; N, 1.39.

Ethyl 3,4,6-Tri-*O*-benzyl-1-thio-*β*-D-glucopyranoside (6). A solution of ethyl 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-1-thio-*β*-D-glucopyranoside[7] (0.80 g, 1.5 mmol) in MeOH (25 mL) was treated with a catalytic amount of 1 M sodium methoxide. The solution was stirred at rt for 5 days and then neutralized with Dowex-50 (H^+) resin, filtered, concentrated, and purified by silica gel chromatography (toluene−EtOAc 20:1) to give **6** (0.71 g, 96%): mp 78−79 °C (EtOAc−*n*-hexane); $[\alpha]_D$ −12° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 15.4, 24.2, 69.0, 73.3, 73.4, 75.0, 75.2, 77.5, 86.0, 127.5−128.5. Anal. Calcd for $C_{29}H_{34}O_5S$: C, 70.41; H, 6.93. Found: C, 70.39; H, 7.01.

Ethyl 2-*O*-Benzoyl-3,4,6-tri-*O*-benzyl-1-thio-*β*-D-glucopyranoside (7). Benzoyl chloride (1.9 mL, 17 mmol) was added to a solution of **6** (4.11 g, 8.31 mmol) in pyridine (50 mL). The mixture was stirred at rt for 19 h and then concentrated. Purification of the residue by silica gel chromatography (toluene−EtOAc 20:1) gave **7** (4.65 g, 93%): mp 107−109 °C (EtOAc−*n*-hexane); $[\alpha]_D$ +33° (*c* 0.9, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 14.9, 23.8, 68.9, 72.4, 73.5, 75.1, 75.2, 77.9, 79.6, 83.5, 84.3, 127.6−138.2, 165.3. Anal. Calcd for $C_{36}H_{39}O_6S$: C, 72.20; H, 6.40. Found: C, 72.01; H, 6.50.

Ethyl 3,4,6-Tri-*O*-benzyl-2-*O*-chloroacetyl-1-thio-*β*-D-glucopyranoside (8). Chloroacetyl chloride (0.74 mL, 9.30 mmol) was added to a solution of **6** (2.31 g, 4.67 mmol) in CH_2Cl_2 (60 mL) and pyridine (4 mL). The mixture was stirred for 1 h and then diluted with CH_2Cl_2 and washed with water. The organic phase was dried and concentrated, and the residue was purified by silica gel chromatography (toluene:EtOAc 20:1) to give **8** (2.15 g, 81%): mp 72−73 °C (diethyl ether−light petroleum bp 40−60 °C); $[\alpha]_D$ +8.1° (*c* 1.2, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 14.9, 23.7, 40.7, 68.7, 73.2, 73.5, 75.1, 75.3, 77.9, 79.5, 83.0, 84.0, 127.6−138.1, 166.1. Anal. Calcd for $C_{31}H_{35}O_6SCl$: C, 65.19; H, 6.18. Found: C, 65.24; H, 6.08.

[*p*-(Trifluoroacetamido)phenyl]ethyl 2-*O*-Benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl)-4-*O*-(3,4,6-tri-*O*-benzyl-2-*O*-benzoyl-*β*-D-glucopyranosyl)-6-O-(*tert*-butyldimethylsilyl)-α-D-glucopyranoside (9). DMTST (0.97 g, 3.74 mmol) was added to a mixture of **5** (1.05 g, 0.94 mmol) and **7** (0.67 g, 1.12 mmol) in CH_2Cl_2 (7 mL) containing molecular sieves (4 Å). After 18 h, triethylamine (1 mL) was added, and the stirring was continued for 20 min. The mixture was diluted with CH_2Cl_2, filtered through Celite, concentrated, and purified by silica gel chromatography (toluene−EtOAc 15:1) to give **9** (1.46 g, 94%): $[\alpha]_D$ +36° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ −5.2, −5.0, 18.4, 26.0, 35.2, 62.1, 67.9, 69.2 (2 C), 71.3, 72.4, 73.1, 73.3, 73.5, 74.4 (2 C), 74.6 (3 C), 74.7 (2 C), 75.0, 75.5, 78.1, 78.5, 82.3, 82.7, 82.8, 84.9, 95.9, 97.2, 102.2, 120.7−138.9, 154.4, 165.3. Anal. Calcd for $C_{97}H_{106}O_{18}NF_3Si$: C, 70.22; H, 6.44; N, 0.84. Found: C, 69.67; H, 6.43; N,0.91.

[*p*-(Trifluoroacetamido)phenyl]ethyl 2-*O*-Benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl)-4-*O*-(3,4,6-tri-*O*-benzyl-*β*-D-glucopyranosyl)-6-*O*-(*tert*-butyldimethylsilyl)-α-D-glucopyranoside (10). A solution of **9** (100 mg, 0.06 mmol) in MeOH (5 mL) was treated with a catalytic amount of 1 M sodium methoxide. The solution was stirred for 14 days, neutralized with TFA, and concentrated. The residue was dissolved in pyridine/CH_2Cl_2 (6:1, 21 mL), and trifluoroacetic anhydride (24 μL, 0.17 mmol) was added. After 20 h, methanolic sodium methoxide was added until pH 9. The solution was stirred for 10 min and then neutralized with Dowex-50 (H^+) resin, filtered, concentrated, and purified by silica gel chromatography (toluene−EtOAc 20:1) to yield **10** (84 mg, 89%): $[\alpha]_D$ +40° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ −5.1, 18.4, 26.0, 35.2 , 63.8, 67.8, 68.6, 69.2, 70.3, 72.0, 73.2, 73.3 (2 C), 73.6, 74.9, 75.0, 75.1, 75.2, 75.3, 75.4, 75.5, 75.7, 76.7, 77.9, 81.7, 82.8, 84.8, 84.9, 95.4, 101.1, 102.1, 120.6−

(18) Ness, R. K.; Fletcher, Jr., H. G.; Hudson, C. S. *J. Am. Chem. Soc.* **1950**, *72*, 2200.

139.2. Anal. Calcd for $C_{90}H_{102}0_{17}NF_3Si$: C,69.52; H, 6.61; N,0.90. Found: C, 69.02; H, 6.44; N, 0.98.

[*p*-(Trifluoroacetamido)phenyl]ethyl 2-*O*-Benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl)-4-*O*-[3,4,6-tri-*O*-benzyl-2-*O*-(chloroacetyl)-*β*-D-glucopyranosyl]-6-*O*-(*tert*-butyldimethylsilyl)-α-D-glucopyranoside (11). Bromine (48 μL, 0.93 mmol) was added at rt to a solution of **8** (492 mg, 0.86 mmol) in CH_2Cl_2 (10 mL). After 10 min, toluene was added, the solution was concentrated, and the residue was coevaporated twice with toluene. The residue in CH_2Cl_2 (4 mL) was added to a solution of **5** (745 mg, 0.66 mmol) in CH_2Cl_2 (4 mL) containing molecular sieves (4 Å). The mixture was stirred under argon for 30 min at rt, and then the temperature was lowered to −20 °C and silver triflate (290 mg, 1.1 mmol) was added. After 30 min triethylamine was added and the stirring was continued for 20 min. The mixture was diluted with CH_2Cl_2, filtered through Celite, and concentrated. The residue was purified by silica gel chromatography (toluene:EtOAc 20:1) to give **11** (935 mg, 86%): ^{13}C NMR ($CDCl_3$) δ −5.2, −5.1, 18.3, 26.0, 35.2, 40.7, 61.9, 68.0, 69.1, 69.2, 71.4, 73.0, 73.1, 73.5, 74.4, 74.7, 74.8, 74.9, 75.4, 75.7, 76.6, 77.1, 77.6, 78.1, 78.2, 82.0, 82.7, 84.9, 96.0, 97.6, 102.2, 120.9−138.9, 166.0.

Ethyl 3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-1-thio-*β*-D-glucopyranoside (12). Acetic anhydride (20 mL) was added to a solution of ethyl 2-azido-2-deoxy-1-thio-*β*-D-glucopyranoside[19] (1.1 g, 4.4 mmol) in pyridine (30 mL). After 1 h, the solution was concentrated and the residue was purified by silica gel chromatography (toluene:EtOAc 12:1) to yield **12** (1.81 g, 92%): mp 69−70 °C (diethyl ether−*n*-hexane); $[\alpha]_D$ −40° (*c* 1.1, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 15.0, 20.6, 20.7, 25.1, 62.2, 63.6, 68.3, 74.5, 75.8, 84.5, 169.6, 169.9, 170.6. Anal. Calcd for $C_{14}H_{21}O_7N_3S$: C,44.80; H, 5.64; N, 11.19. Found: C, 44.75; H, 5.51; N, 11.11.

[*p*-(Trifluoroacetamido)phenyl]ethyl 2-*O*-Benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl)-4-*O*-[2-*O*-(3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranosyl]-6-*O*-(*tert*-butyldimethylsilyl)-α-D-glucopyranoside (13). Bromine (34 μL, 0.66 mmol) was added to a solution of **12** (113 mg, 0.30 mmol) in CH_2Cl_2 (4 mL). After 30 min, toluene was added, the mixture was concentrated, and the residue was coevaporated twice with toluene. The residue in CH_2Cl_2 (5 mL) was added to a solution of **10** (236 mg, 0.15 mmol) in CH_2Cl_2 (5 mL) containing molecular sieves (4 Å). The mixture was stirred under argon for 30 min at rt, after which time the temperature was lowered to −30 °C and silver triflate (97 mg, 0.38 mmol) was added. After 30 min, triethylamine was added, and the stirring was continued for 20 min. The mixture was diluted with CH_2Cl_2, filtered through Celite, and concentrated. The residue was purified by silica gel chromatography (toluene:EtOAc 12:1) to give **13** (152 mg, 54%). Starting material **10** (64 mg, 27%) was recovered by further elution (toluene:EtOAc 9:1). **13**: $[\alpha]_D$ +67° (*c* 0.6, $CHCl_3$); NMR ($CDCl_3$) ^{13}C, δ −5.3, −5.0, 18.4, 20.5, 20.7, 20.8, 26.0, 35.3, 60.9, 61.2, 62.1, 66.9, 68.0, 68.4, 69.1, 69.5, 70.2, 71.7, 72.7 (2 C), 72.9, 73.1, 73.3, 73.6, 74.4, 74.9 (2 C), 75.1 (3 C), 75.5, 76.3, 78.4, 78.6, 82.4, 83.0 (2 C), 84.9, 96.0 ($J_{C,H}$ = 164.0 Hz), 96.1 ($J_{C,H}$ = 166.1 Hz), 99.0 ($J_{C,H}$ = 166.1 Hz), 102.1 ($J_{C,H}$ = 170.6 Hz), 120.5−139.1, 154.3, 154.9, 169.6, 170.0, 170.5; ^{1}H, δ 3.00 (dd, $J_{1''',2'''}$ = 3.3 Hz, $J_{2''',3'''}$ = 10.6 Hz 1H, H-2‴), 5.53 (d, $J_{1''',2'''}$ = 3.3 Hz, 1H, H-1‴). Anal. Calcd for $C_{102}H_{117}O_{24}N_4F_3Si$: C, 65.58; H, 6.31; N, 3.05. Found: C, 66.92; H, 6.23; N, 3.23.

To a stirred mixture of **10** (0.73 g, 0.47mmol) and **12** (0.26 g, 0.70 mmol) in diethyl ether (30 mL) containing molecular sieves (4 Å) were added NIS (0.18 g, 0.79 mmol) and silver tfiflate (24 mg, 0.09 mmol). After 3 h, triethylamine was added, and the mixture was diluted with CH_2Cl_2, filtered through Celite, and washed with $Na_2S_2O_3$, $NaHCO_3$, and water. The organic phase was dried, filtered, concentrated, and purified by silica gel chromatography (toluene:EtOAc 12:1) to give **13** (534 mg, 61%). Starting material **10** (212 mg, 29%) could be recovered by further eluation (toluene:EtOAc 9:1).

[*p*-(Trifluoroacetamido)phenyl]ethyl 2-*O*-Benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl)-4-*O*-[2-*O*-(3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranosyl]-α-D-glucopyranoside (14). **13** (620 mg, 0.33 mmol) was dissolved in CH_3CN (4 mL), HOAc (80%, aqueous, 8 mL) was added, and the solution was stirred at 40 °C for 18 h, concentrated, and then purified by silica gel chromatography (toluene:EtOAc 4:1) to give **14** (492 mg, 85%): $[\alpha]_D$ +73 ° (*c* 1.2, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 20.5, 20.7, 20.8, 35.3 , 60.8, 61.1, 61.9, 67.0, 67.9, 68.6, 69.1, 69.4, 70.2, 71.3, 72.5, 72.8, 73.3 (2 C), 73.6 (2C), 74.3, 74.8, 74.9, 75.1 (2 C), 75.6, 76.4, 78.3, 78.5, 82.3, 82.8, 83.0, 84.9, 96.3, 96.4, 99.0, 102.2, 120.5−139.1, 154.3, 154.9, 169.6, 170.0, 170.5. Anal. Calcd for $C_{96}H_{103}O_{24}N_4F_3$: C,65.74; H, 5.92; N,3.19. Found: C, 65.57; H, 5.90; N,3.23.

[*p*-(Trifluoroacetamido)phenyl]ethyl 2-*O*-Benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl)-4-*O*-(2-*O*-(3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranosyl)-6-*O*-(3,4,6-tri-*O*-benzyl-2-*O*-(chloroacetyl)-*β*-D-glucopyranosyl)-α-D-glucopyranoside (15). Bromine (12 μL, 0.24 mmol) was added at 0 °C to a solution of **8** (120 mg, 0.21 mmol) in CH_2Cl_2 (4 mL). After 10 min, toluene was added, the solution was concentrated, and the residue was coevaporated twice with toluene. The residue in CH_2Cl_2 (5mL) was added to a solution of **14** (244 mg, 0.14 mmol) in CH_2Cl_2 (5 mL) containing molecular sieves (4 Å). The mixture was stirred under argon for 30 min at rt, and then the temperature was lowered to −35 °C and silver triflate (71 mg, 0.28 mmol) was added. After 30 min, triethylamine was added, and the stirring was continued for 20 min. The mixture was diluted with CH_2Cl_2, filtered through Celite, and concentrated. Purification of the residue by silica gel chromatography (toluene:EtOAc 8:1) gave **15** (250 mg, 79%): $[\alpha]_D$ +66 ° (*c* 1.0 , $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 20.5, 20.6, 20.8, 35.2, 40.8, 60.5, 61.2, 67.2, 67.9, 68.3, 68.5, 68.9, 69.1, 69.6, 70.0, 71.8, 72.3, 73.5, 73.9, 74.3, 74.6, 74.8, 74.9, 75.2, 75.3, 75.6, 76.0, 78.1, 78.4, 82.2, 82.7, 83.0 83.1, 85.0, 96.1 (2C), 97.7, 101.6, 102.5, 120.6−138.8, 154.3, 154.9, 165.9, 169.5, 169.9, 170.6. Anal. Calcd for $C_{125}H_{132}O_{30}N_4F_3Cl$: C, 66.35; H, 5.88; N, 2.48. Found: C, 66.27; H, 5.88; N, 2.46.

[*p*-(Trifluoroacetamido)phenyl]ethyl 2-*O*-Benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl)-4-*O*-[2-*O*-(3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranosyl]-6-*O*-(3,4,6-tri-*O*-benzyl-*β*-D-glucopyranosyl)-α-D-glucopyranoside (16). Hydrazine dithiocarbonate[12] (100 mg, 1.3 mmol) in DMF (10 mL) was added to a solution of **15** (600 mg, 0.27 mmol) in DMF (10 mL). After 30 min, the solution was diluted with CH_2Cl_2 and washed with 1 M H_2SO_4, $NaHCO_3$, and water. The organic phase was dried and concentrated, and the residue was purified by silica gel chromatography (toluene:EtOAc 6:1) to give **16** (459 mg, 79%): $[\alpha]_D$ +56° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 21.5, 21.7, 21.8, 36.3, 61.9, 62.1, 68.1, 69.0, 69.5, 69.9, 70.0, 70.4, 71.1, 71.3, 73.3, 73.8, 74.4, 74.6, 75.2, 75.5, 75.8, 76.0, 76.1, 76.7, 79.4, 79.9, 83.0, 83.8, 84.1, 85.5, 85.9, 97.3, 97.6, 99.8, 103.2, 104.5, 121.6−140.0, 170.5, 171.0, 171,5. Anal. Calcd for $C_{123}H_{131}O_{29}N_4F_3$: C, 67.57; H, 6.04; N, 2.56. Found: C, 67.55; H, 6.03; N, 2.52.

[*p*-(Trifluoroacetamido)phenylethyl 4-*O*-[2-*O*-(2-Acetamido-2-deoxy-α-D-glucopyranosyl)-*β*-D-glucopyranosyl]-3-*O*-*β*-D-glucopyranosyl-6-*O*-*β*-D-glucopyranosyl-α-D-glucopyranoside (17). A solution of **15** (250 mg, 0.11 mmol) in CH_2Cl_2 (2 mL) and MeOH (10 mL) was treated with a catalytic amount of 1 M sodium methoxide. After 6 h, the mixture was neutralized with Dowex 50 (H^+) resin, filtered, concentrated, and purified by silica gel chromatography (toluene:EtOAc 2:1). The residue was dissolved in EtOAc/MeOH/HOAc (2:2:1, 15 mL) and hydrogenolyzed over 10% Pd/C (50 mg) at 120 psi for 20 h. The mixture was filtered and concentrated and the residue treated with acetic anhydride (38 μL, 0.41 mmol) in MeOH (2 mL). After 2 h the solution was concentrated, dissolved in water, and washed with diethyl ether. The water phase was concentrated and the residue desalted on a BioGel

(19) Buskas, T.; Garegg, P. J.; Konradsson, P.; Maloisel, J.-L. *Tetrahedron: Assymetry*, **1994**, *5*, 2187.

P-2 column to give after lyophilization **17** (64 mg, 53%): $[\alpha]_D$ +67° (*c* 1.0, H_2O); NMR (D_2O) ^{13}C, δ 23.1, 35.3, 54.4, 54.6, 61.4, 67.3, 69.1, 70.1, 70.2, 70.3, 70.5, 70.7, 71.7, 72.2, 72.4, 72.5, 72.6, 73.6, 74.0, 75.2, 76.0, 76.2, 76.5, 76.7, 76.8, 77.7, 96.6, 98.7, 101.2, 102.7, 102.9, 122.9, 130.5, 133.9, 138.3, 174.5; ^1H, δ 2.08 (3H, s), 2.96−4.13 (32H, m), 4.44 (1H, d, $J_{1,2}$ = 8.1 Hz), 4.75 (1H, d, $J_{1,2}$ = 8 Hz), 4.80 (1H, d, $J_{1,2}$ = 8 Hz), 4.93 (1H, d, $J_{1,2}$ = 3.7 Hz), 5.22 (1H, d, $J_{1,2}$ = 3.3 Hz), 7.37 (2H, d, J = 8.1 Hz), 7.51 (2H, d, J = 8.1 Hz); HRMS calcd for $C_{42}H_{63}O_{27}N_2F_3$ $[M - H]^+$ 1083.3492, found 1083.3496.

Methyl 2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-*β*-D-galactopyranosyl)-1-thio-*β*-D-glucopyranoside (19). A solution of methyl 1-thio-*β*-D-lactoside[13] (**18**, 1.15 g, 3.09 mmol) in DMF (10 mL) was added to a suspension of sodium hydride (60%, 1.3 g, 32.5 mmol) in DMF (5 mL) followed by a solution of benzyl bromide (3.6 mL, 30.3 mmol) in DMF (10 mL). After 2 h, MeOH (10 mL) was added, and stirring was continued for 30 min. The mixture was diluted with toluene, washed with water, dried, and concentrated. Purification of the residue by silica gel chromatography (light petroleum bp 40−60 °C−EtOAc 5:1) gave **19** (2.80 g, 90%): mp 82−84 °C (diethyl ether−*n*-hexane); $[\alpha]_D$ +6.5° (*c* 1.1, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 12.6, 68.0, 68.3, 72.6, 73.0, 73.4, 73.6, 74.7, 75.3, 75.5, 76.4, 79.5, 80.4, 82.5, 84.8, 85.2, 102.7, 127.1−139.9. Anal. Calcd for $C_{62}H_{66}O_{10}S$: C,74.23; H, 6.63. Found: C, 74.10; H, 6.70.

Methyl 2,3,6-Tri-*O*-benzyl-4-*O*-(4,6-*O*-benzylidene-*β*-D-galactopyranosyl)-1-thio-*β*-D-glucopyranoside (20). A solution of methyl 4-*O*-(4,6-*O*-benzylidene-*β*-D-galactopyranosyl)-1-thio-*β*-D-glucopyranoside[13] (1.18 g, 2.56 mmol) in DMF (20 mL) was added to a suspension of sodium hydride (60%, 0.77 g, 19.2 mmol) in DMF (3 mL) followed by a solution of benzyl bromide (2.1 mL, 17.9 mmol) in DMF (5 mL). After 2 h, MeOH (5 mL) was added, and stirring was continued for 30 min. The mixture was diluted with toluene, washed with water, dried, and concentrated. Purification of the residue by silica gel chromatography (light petroleum bp 40−60 °C:EtOAc 4:1) gave **20** (1.83 g, 78%): mp 124−126 °C (EtOAc−*n*-hexane); $[\alpha]_D$ +7.2° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 12.7, 66.4, 68.3, 68.9, 71.6, 72.9, 73.7, 75.4, 75.5, 76.0, 77.2, 78.8, 79.4, 79.6, 80.5, 84.9, 85.2, 101.4, 102.7, 126.6−138.8. Anal. Calcd for $C_{55}H_{58}O_{10}S$: C,72.50; H, 6.42. Found: C, 72.43; H, 6.54.

Methyl 2,3,6-Tri-*O*-benzyl-4-*O*-(2,3,6-tri-*O*-benzyl-*β*-D-galactopyranosyl)-1-thio-*β*-D-glucopyranoside (21). Sodium cyanoborohydride (0.91, 14.6 mmol) was added at 0 °C to a stirred mixture of **20** (1.31g, 1.40 mmol) and molecular sieves (4 Å) in THF (20 mL), followed by HCl in diethyl ether (saturated) until gas evolution ceased. After 20 min, CH_2Cl_2 (4 mL) and water (2 mL) were added, and the mixture was filtered through Celite. The organic layer was washed with water, $NaHCO_3$, and water, dried, and concentrated. Purification of the residue by silica gel chromatography (toluene:EtOAc 15:1) gave **21** (0.74 g, 56%): mp 65−67 °C (diethyl ether−*n*-hexane); $[\alpha]_D$ +18° (*c* 1.0, $CHCl_3$); NMR ($CDCl_3$) ^{13}C δ 12.6, 66.1, 68.2, 68.4, 72.0, 72.8, 73.0, 73.5, 75.2, 75.4, 75.5, 76.2, 79.4 (2 C), 79.6, 80.4, 84.7, 85.1, 102.4, 127.3−138.9 Anal. Calcd for $C_{55}H_{60}O_{10}S$: C, 72.34; H, 6.62. Found: C, 72.24; H, 6.67.

Methyl 2,3,6-Tri-*O*-benzyl-4-*O*-[2,3,6-tri-*O*-benzyl-4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-*β*-D-galactopyranosyl]-1-thio-*β*-D-glucopyranoside (22). Silver triflate (159 mg, 0.62 mmol) was added at −60 °C to a stirred mixture of 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl chloride[14] (330 mg, 0.59 mmol) and **20** (270 mg, 0.30 mmol) in diethyl ether (15 mL) containing molecular sieves (4 Å). After 1 h at −60 °C, the reaction was left to attain −10 °C during 3 h, and then triethylamine (1 mL) was added and the stirring was continued for 20 min. The mixture was diluted with CH_2Cl_2, filtered through Celite, and concentrated. Purification of the residue by silica gel chromatography twice (toluene−EtOAc 25:1 and then light petroleum bp 40−60 °C−EtOAc 5:1) gave **2** (262 mg, 62%): $[\alpha]_D$+32° (*c* 1.2, $CHCl_3$); NMR ($CDCl_3$) ^{13}C, δ 12.6, 67.7, 67.8, 68.3, 69.5, 72.1, 72.4, 73.0, 73.2, 73.3, 73.7, 74.8, 75.1, 75.3, 75.4, 76.6, 76.8, 79.4, 80.3, 81.6, 84.5, 85.2, 100.7, 102.7, 127.1−139.0; ^1H, δ 5.19 (1H, d, $J_{1'',2''}$ = 2.9 Hz, H-1″), 5.27 (1H, d, $J_{1',2'}$ = 10.6 Hz, H-1′). Anal. Calcd for $C_{89}H_{94}O_{15}S$: C, 74.45; H, 6.60. Found: C, 73.92; H, 6.51.

[*p*-(Trifluoroacetamido)phenyl]ethyl 2-*O*-Benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl)-4-*O*-[2-*O*-(3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranosyl]-6-*O*-[3,4,6-tri-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl)-*β*-D-glucopyranosyl]-α-D-glucopyranoside (23). Bromine (17 *μ*L, 0.34 mmol) was added at 0 °C to a solution of ethyl 2,3,4,6-tetra-*O*-benzyl-1-thio-*β*-D-glucopyranoside[15] (188 mg, 0.31 mmol) in CH_2Cl_2 (10 mL). After 10 min, toluene was added, the solution was concentrated, and the residue was coevaporated twice with toluene. The residue in diethyl ether (5 mL) was added to a solution of **16** (226 mg, 0.10 mmol) in diethyl ether (5 mL) containing molecular sieves (4 Å). The mixture was stirred under argon for 30 min at rt, whereafter the temperature was lowered to −35 °C and silver triflate (106 mg, 0.41 mmol) was added. After 30 min, triethylamine was added, and the stirring was continued for 20 min. The mixture was diluted with CH_2Cl_2, filtered through Celite, and concentrated. Purification of the residue by silica gel chromatography (toluene:EtOAc 10:1) gave **23** (210 mg, 75%): $[\alpha]_D$ +76° (*c* 1.0, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 20.5, 20.6, 20.8, 34.9, 60.7, 60.9, 67.0, 67.9, 68.6, 68.7, 69.1, 69.6, 69.9, 70.2, 71.3, 71.8, 72.3, 73.0, 73.1, 73.6, 73.7, 74.4, 74.6, 74.9, 75.2, 75.6, 76.1, 77.0, 77.8, 78.0, 78.7, 80.3, 81.8, 82.6, 82.8, 82.9, 83.3, 84.9, 94.4, 95.3, 96.6, 97.7, 102.2, 103.5, 120.7−139.0, 169.5, 170.0, 170.4. Anal. Calcd for $C_{157}H_{165}O_{34}N_4F_3$: C, 69.61; H, 6.14; N, 2.07. Found: C, 69.50; H, 6.01; N, 2.07.

[*p*-(Trifluoroacetamido)phenyl]ethyl 2-*O*-Benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl)-4-*O*-[2-*O*-(3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranosyl]-6-*O*-[3,4,6-tri-*O*-benzyl-2-*O*-[4-*O*-(2,3,4,6-tetra-*O*-benzyl-*β*-D-galactopyranosyl)-2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl]-*β*-D-glucopyranosyl]-α-D-glucopyranoside (24). The bromosugar of **19** (215 mg, 0.21 mmol) was prepared as described and coupled to **16** (241 mg, 0.11 mmol) as described for compound **23** above to give, after silica gel chromatography twice (toluene−EtOAc 10:1 then light petroleum bp 40−60 °C−EtOAc 5:2), **24** (240 mg, 69%): $[\alpha]_D$ +58° (*c* 1.1, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 20.5, 20.6, 20.7, 35.1, 60.3, 60.7, 60.8, 67.0, 67.9, 68.6, 69.0, 69.3, 69.9, 70.3, 71.2, 71.8, 72.3, 72.7, 72.8, 73.2, 73.5, 73.6, 73.8, 74.1, 74.5, 74.7, 75.1, 75.3, 75.5, 76.8, 78.0, 78.5, 78.6, 79.1, 79.8, 80.1, 82.5, 82.9, 84.9, 94.0, 95.6, 96.5, 97.7, 102.1, 103.0, 103.6, 121.2−139.4, 154.2, 154.8, 169.4, 169.9, 170.3. Anal. Calcd for $C_{184}H_{193}O_{39}N_4F_3$: C, 70.35; H, 6.19; N, 1.78. Found: C, 70.33; H, 6.21; N, 1.76.

[*p*-(Trifluoroacetamido)phenyl]ethyl 2-*O*-Benzyl-3-*O*-(2,3,4,6-tetra-*O*-benzyl-*β*-D-glucopyranosyl)-4-*O*-[2-*O*-(3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-3,4,6-tri-*O*-benzyl-*β*-D-glucopyranosyl]-6-*O*-[3,4,6-tri-*O*-benzyl-2-*O*-[4-*O*-[4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-2,3,6-tri-*O*-benzyl-*β*-D-galactopyranosyl]-2,3,6-tri-*O*-benzyl-α-D-glucopyranosyl]-*β*-D-glucopyranosyl]-α-D-glucopyranoside (24). The bromosugar of **22** (346 mg, 0.24 mmol) was prepared and coupled to **16** (275 mg, 0.13 mmol) as described for compound **23** above to give, after silica gel chromatography twice (toluene−EtOAc 10:1 then light petroleum bp 40−60°C−EtOAc 3:1), **25** (282 mg, 63%): $[\alpha]_D$ +64° (*c* 0.8, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 20.5, 20.6, 20.8, 35.0, 60.7, 60.9, 67.0, 67.7, 67.9, 68.4, 68.5, 68.7, 69.0, 69.3, 69.4, 69.9, 70.1, 70.3, 71.2, 71.9, 72.2, 72.9, 73.1, 73.5, 73.6, 73.8, 74.1, 74.4, 74.6, 74.7, 74.9, 75.2, 75.3, 75.6, 76.0, 76.9, 77.3, 78.0, 78.4, 78.6, 79.5, 79.7, 80.1, 81.5, 82.5, 82.9, 83.0, 84.9, 94.0, 95.6, 96.5, 97.6, 100.9, 102.1, 103.1, 103.7, 121.2−139.5, 154.2, 154.7, 169.5, 169.9, 170.4. Anal. Calcd for $C_{211}H_{221}O_{44}N_4F_3$: C, 70.91; H, 6.23; N, 1.57. Found: C, 70.98; H, 6.27; N, 1.44.

[*p*-(Trifluoroacetamido)phenyl]ethyl 4-*O*-[2-*O*-(2-Acetamido-2-deoxy-α-D-glucopyranosyl)-*β*-D-glucopyranosyl]-3-*O*-*β*-D-glucopyranosyl-6-*O*-[2-*O*-(α-D-glucopyranosyl)-*β*-D-glucopyranosyl]-α-D-glucopyranoside (26). 23 (190 mg, 0.07 mmol) was deprotected and desalted as described for compound **17** above to give **26** (46 mg, 53%): $[\alpha]_D$ +73 ° (*c* 0.6, H_2O); NMR (D_2O) ^{13}C, δ 23.4, 35.4, 54.4, 61.0, 61.5, 61.7, 69.2, 69.7, 70.3, 70.5, 70.9, 72.3, 72.5, 72.7, 73.0, 73.5, 73.8, 74.4, 75.2, 75.4, 76.5, 76.6, 76.8, 80.2 97.4, 98.9 (3 C), 103.1, 103.7, 122.9, 130.5, 134.1, 137.9, 157.3, 157.9, 174.9; ^1H, δ 4.57 (1H,

d, $J_{1,2}$ = 7.7 Hz), 4.92 (1H, d, $J_{1,2}$ = 3.7 Hz), 4.93 (1H, d, $J_{1,2}$ = 7.7 Hz), 4.99 (1H, d, $J_{1,2}$ = 7.3 Hz), 5.12 (1H, d, $J_{1,2}$ = 3.3 Hz), 5.34 (1H, d, $J_{1,2}$ = 3.7 Hz); HRMS calcd for $C_{48}H_{73}O_{32}N_2F_3$ [M − H]$^+$ 1245.4021, found 1245.4003.

[*p*-(Trifluoroacetamido)phenyl]ethyl 4-*O*-[2-*O*-(2-Acetamido-2-deoxy-α-D-glucopyranosyl)-*β*-D-glucopyranosyl]-6-*O*-[2-*O*-(4-O-*β*-D-galactopyranosyl-α-D-glucopyranosyl)-*β*-D-glucopyranosyl]-3-*O*-*β*-D-glucopyranosyl-α-D-glucopyranoside (27). **24** (210 mg, 0.07 mmol) was deprotected and desalted as described for compound **17** above to yield **27** (34 mg, 36%): $[\alpha]_D$ +75 ° (*c* 0.9, H_2O); NMR (D_2O)^{13}C, δ 23.4, 35.4 , 54.4, 60.9, 61.5, 61.7, 61.8, 69.3, 69.6, 70.3, 70.5, 70.9, 71.1, 72.0, 72.2, 72.7, 73.0, 73.3, 73.7, 74.4, 75.1, 75.3, 76.1, 76.5, 76.8, 79.5, 80.1, 97.1, 98.9 (3 C), 103.1, 103.6, 103.8, 122.9, 130.5, 134.0, 137.9, 157.2, 174.9; ^{1}H, δ 4.38 (1H, d, $J_{1,2}$ = 7.7 Hz), 4.58 (1H, d, $J_{1,2}$ = 7.7 Hz), 4.92 (1H, d, $J_{1,2}$ = 7.3 Hz), 4.93 (1H, d, $J_{1,2}$ = 3.7 Hz), 4.98 (1H, d, $J_{1,2}$ = 7.3 Hz), 5.12 (1H, d, $J_{1,2}$ = 3.3 Hz), 5.34 (1H, d, $J_{1,2}$ = 4.0 Hz); HRMS calcd for $C_{54}H_{83}O_{37}N_2F_3$ [M − H]$^+$ 1407.4549, found 1407.4548.

[*p*-(Trifluoroacetamido)phenyl]ethyl 4-*O*-[2-*O*-(2-Acetamido-2-deoxy-α-D-glucopyranosyl)-*β*-D-glucopyranosyl]-6-*O*-[2-*O*-[4-*O*-(4-*O*-α-D-galactopyranosyl-*β*-D-galactopyranosyl)-α-D-glucopyranosyl]-3-*O*-*β*-D-glucopyranosyl-*β*-D-glucopyranosyl]-α-D-glucopyranoside (28). **25** (272 mg, 0.08 mmol) was deprotected and desalted as described for **17** to give **28** (43 mg, 36%): $[\alpha]_D$ +84° (*c* 1.0, H_2O); NMR (D_2O) ^{13}C, δ 23.4, 35.4 , 54.4, 60.9, 61.1, 61.3, 61.5, 61.7, 69.3, 69.7, 69.9, 70.3, 70.5, 70.9, 71.2, 71.5, 71.6, 72.1, 72.2, 72.7, 72.9, 73.8, 74.4, 75.1, 75.3, 76.2, 76.4, 76.5, 76.6, 76.8,78.1, 79.8, 80.1 97.1, 98.9, 101.0, 103.2, 103.6, 104.0, 122.9, 130.5, 134.0, 137.9, 174.9; ^{1}H, δ 4.45 (1H, d, $J_{1,2}$ = 7.7 Hz), 4.58 (1H, d, $J_{1,2}$ = 7.7 Hz), 4.94 (3H, m), 4.98 (1H, d, $J_{1,2}$ = 7.7 Hz), 5.12 (1H, d, $J_{1,2}$ = 3.3 Hz), 5.34 (1H, d, $J_{1,2}$ = 3.7 Hz); FABMS calcd for $C_{60}H_{93}O_{42}N_2F_3$ [M + H]$^+$ 1570.5, found 1571.1.

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