Tetrahedron 65 (2009) 8143–8153

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Solid-phase synthesis of *O*-sulfated glycopeptide by the benzyl-protected glycan strategy

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ARTICLE INFO

Article history:
Received 6 July 2009
Received in revised form 27 July 2009
Accepted 28 July 2009
Available online 6 August 2009

ABSTRACT

To expand the repertoire of our benzyl-protection strategy for solid-phase glycopeptide synthesis, an *O*-sulfated glycopeptide was chosen as the synthetic target. Trisaccharyl serine derivatives (Galβ1–4-GlcNAcβ1–2-Manα1–3-Ser) carrying (4-methoxyphenyl)methyl (MPM) groups at either 3-*O* or 6-*O* of the Gal residue were prepared through three stereoselective glycosylations. Cleavage of MPM followed by reaction with $Me_3N{\cdot}SO_3$ efficiently afforded 3-*O*- and 6-*O*-sulfo-glycoserines, respectively. A preliminary debenzylation study using the sulfated glycoserines revealed that the sulfate groups persisted under 'low-acidity TfOH' conditions, when using a limited amount of TfOH and extending the reaction period. The 3-*O*-sulfo-glycoserine was then introduced into an icosapeptide modeled after an α-dystroglycan fragment by a combination of automated and manual solid-phase peptide synthesis procedures. The synthesized glycopeptide was successfully debenzylated by the low-acidity TfOH cocktail with slight damage to the sulfate functionality.

1. Introduction

Recent advances in methodology and technology have enabled the synthesis of complex glycopeptides up to the size of glycoproteins. Synthetic samples obtained in a single glycoform are necessary tools to investigate the oligosaccharide-mediated biological functions of glycoprotein. Widely used approaches to synthetic glycopeptides employ preformed oligosaccharyl amino acids as a building block in Fmoc-based solid-phase peptide synthesis (SPPS). Although on-resin peptide assembly can be performed without masking the hydroxyl groups in the oligosaccharyl moiety,[1] the hydroxyl groups are usually protected to prevent undesired O-aminoacylation. *O*-Acetylated oligosaccharides have often been used in glycopeptides synthesis. The acetyl groups are removed at the final stage of synthesis with a base, which sometimes gives rise to the concern about epimerization at the peptide backbone and β-elimination of the O-linked oligosaccharide at Ser and Thr residues. Therefore, careful pH control of the basic conditions is necessary. On the other hand, O-benzyl protection provides reactive intermediates in oligosaccharide synthesis, and the benzyl groups can be removed by hydrogenolysis under essentially neutral conditions. However, the catalytic hydrogenolysis cannot be applied, when sulfur-containing amino acid residues are involved in the glycopeptides. In 1997, we first found that benzyl groups in the oligosaccharide of glycopeptides were efficiently removed after SPPS under acidic conditions with minimum scission of glycosidic linkages.[2] Since then, we have established syntheses of several complex glycopeptides carrying *N*- and *O*-glycans by a combination of the benzyl-protection strategy and Fmoc SPPS method.[3] Remarkable advantage of the strategy has been demonstrated by the syntheses of the labile glycopeptide thioesters, a key intermediate for peptide chemical ligation.

O-Sulfation is found in the outer chain of the complex-type *N*-glycans, exemplified by sialyl-6-sulfoLe^x[Siaα2-3 Galβ1–4(6-sulfo)-(Fucα1–3)GlcNAc] and HNK-1 [(3-sulfo)-GlcAβ1–3Galβ1–4GlcNAc] epitopes. On the other hand, sulfate groups are often functionally

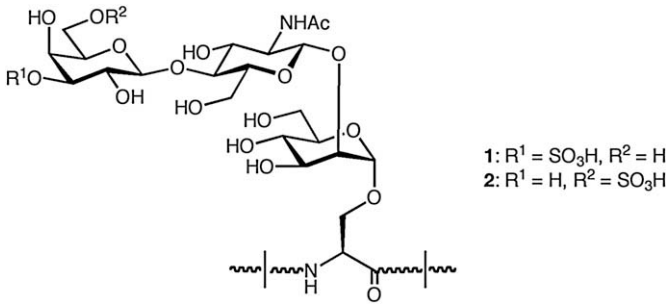

Figure 1. Structure of sulfated glycopeptide models.

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0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.07.080

equivalent to the sialic acid residue in oligosaccharide, as reported for 3-sulfoLe^x.[4]

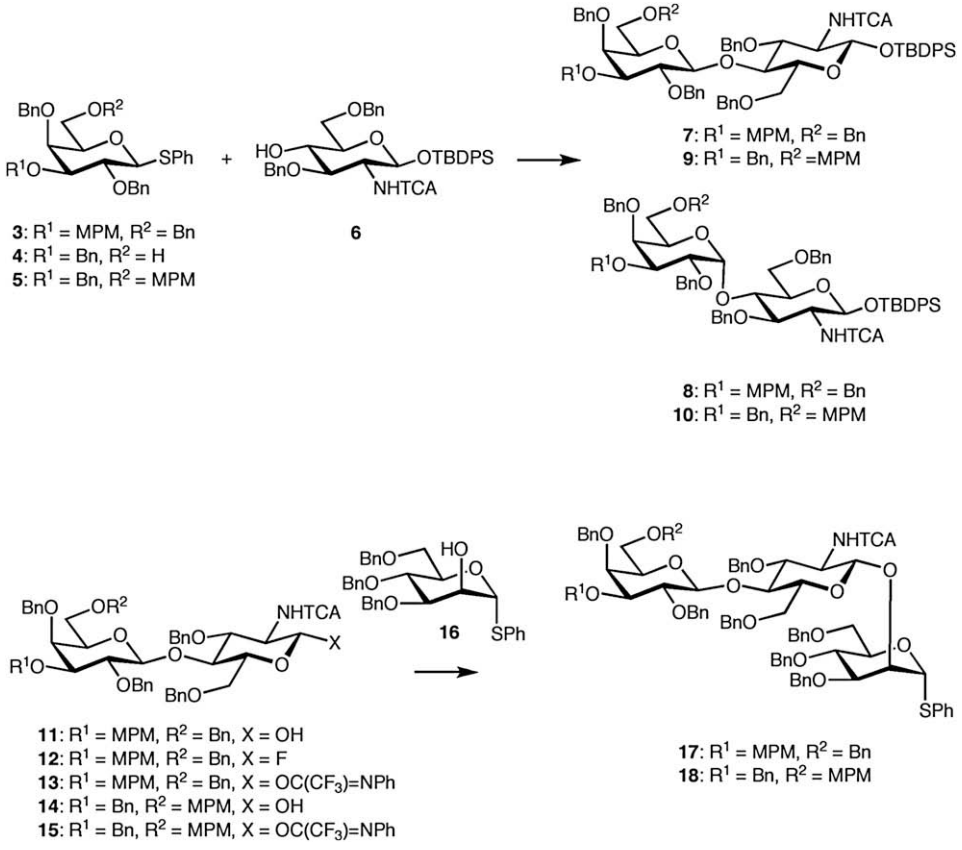
In continuation of our research on the solid-phase synthesis of complex glycopeptides, we have been particularly interested in observing whether our benzyl-protection strategy is compatible with preparation of sulfated glycopeptides. In addition, little research has been conducted so far on solid-phase synthesis using sulfated glycoamino acid.[5]

In this paper, we describe our approach to a synthetic sulfo-glycopeptide, which consists of (1) stereoselective synthesis of the benzyl-protected 3-sulfo-Galβ1–4GlcNAcβ1–2Man-Ser and 6-sulfo-Galβ1–4GlcNAcβ1–2Man-Ser, as a sulfated model of *O*-mannosyl glycans, and (2) solid-phase synthesis and debenzylation of the sulfated glycopeptide. The corresponding sialyl oligosaccharide [Siaα2–3Galβ1–4GlcNAcβ1–2Manα1–3-Ser/Thr] is known as a major oligosaccharide of α-dystroglycan,[6] whereas the trisaccharide structure is shared by the outer chain of complex-type *N*-glycans (Fig. 1).

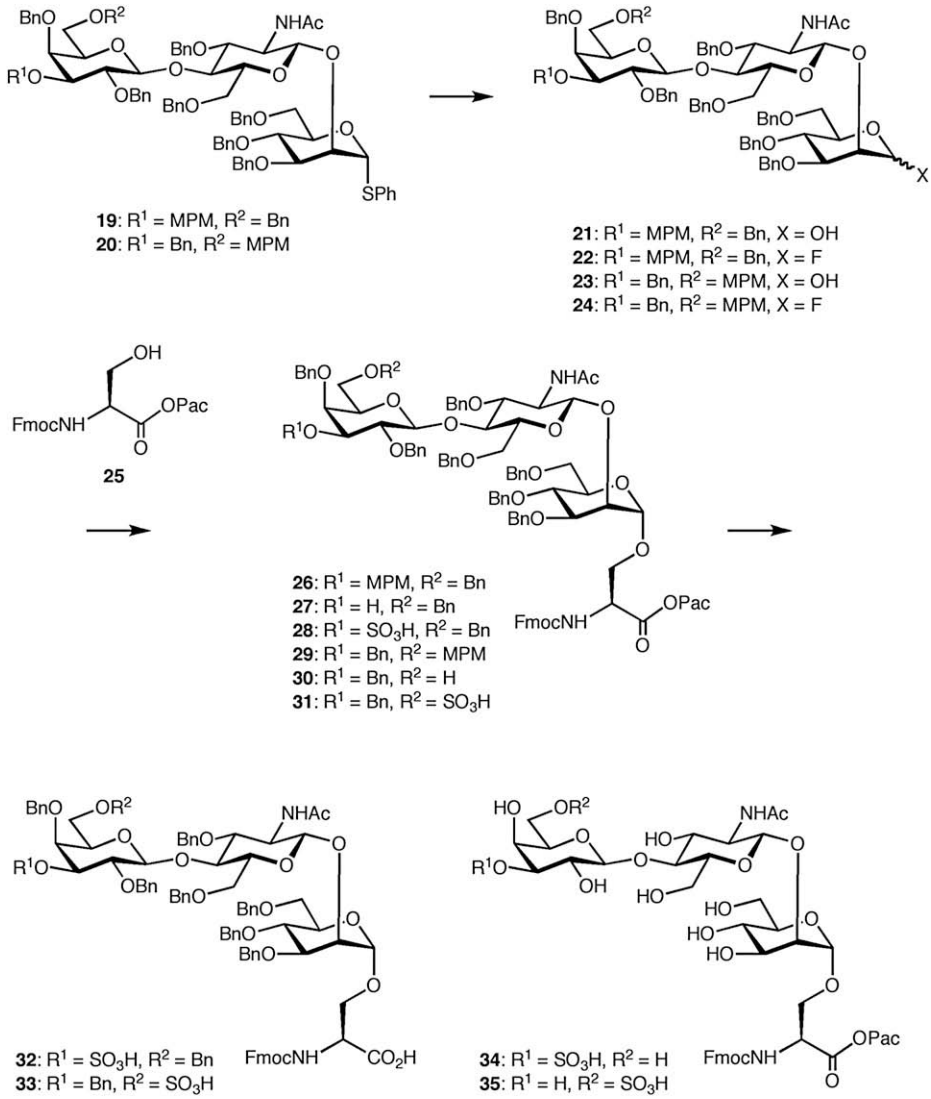
2. Synthesis of sulfated glycoserine building blocks

Our study began with preparation of the disaccharide precursors for an *N*-acetyllactosamine moiety based on the β-selective galactosylation method recently reported by this laboratory.[7] Phenyl 2,4,6-tri-*O*-benzyl-3-*O*-(4-methoxyphenyl)methyl-1-thio-β-D-galactopyranoside **3**[8] and phenyl 2,3,4-tri-*O*-benzyl-6-*O*-(4-methoxyphenyl)methyl-1-thio-β-D-galactopyranoside **5** were chosen as the glycosyl donors and reacted with *tert*-butyldiphenylsilyl 3,6-di-*O*-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside **6**.[7] The 2-trichloroacetamido sugar was preferred because of its ready conversion to GlcNAc by Zn reduction and high stereo-controlling ability in glycosylation.[3e] Compound **5** was obtained by (4-methoxyphenyl)methylation of phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-galactopyranoside **4** prepared by the reported procedure.[9] Propionitrile-mediated glycosylation of **6** with **3** gave β-glycoside **7** in 71% yield. The stereoisomer **8** was produced as a minor product (13%). The structure of the disaccharide was readily assignable by the ^{1}H NMR spectrum. The reaction of **5** and **6** also predominated in the formation of β-glycoside **9** (71%, β/α=83:17). The β-disaccharides were desilylated to hemiacetals **11** (97%) and **14** (quant), respectively, by treatment with tetra-*n*-butylammonium fluoride in the presence of AcOH, and then converted to glycosyl donors to condense with phenyl 3,4,6-tri-*O*-benzyl-1-thio-α-D-mannnopyranoside **16**.[10] Glycosylation of **16** with glycosyl fluoride **12** derived from **11** was performed by activation with Cp_2ZrCl_2–$AgClO_4$ in the standard condition[11] to produce the desired trisaccharide **17** in a moderate yield (44%). In contrast, the corresponding *N*-phenyltrifluoroacetimidate **13**, prepared by reaction with *N*-phenyltrifluoroacetimidoyl chloride and K_2CO_3,[12,13] reacted with **16** by a catalytic amount of acidic promoter, TMSOTf, to give **17** in a 91% yield. The stereochemistry of the newly formed glycosidic linkage was determined to be β by the ^{1}H signal at δ 5.15 ppm (J=8.3 Hz). Similarly, imidate **15** derived from **14** produced trisaccharide **18** (81%, β/α=97:3).

Before condensing the amino acid moiety, the trichloroacetamido group was dechlorinated under microwave-assisted conditions of Zn–AcOH in EtOAc[3i] to trisaccharides **19** (84%) and **20** (95%). Preparation of the trisaccharyl amino acid was first attempted by glycosylation of *N*-Fmoc serine phenacyl ester **25**[14] with thioglycoside **19** in the presence of NIS–TfOH in CH_2Cl_2 at −20 to 0 °C for 4.5 h. However, the product was obtained as a mixture of α/β-isomers (70%, α/β=3:2). Although other thiophilic promoters were not tested, thioglycoside **19** was transformed to other glycosyl donors such as trichloroacetimidate, *N*-phenyltrifluoroacetimidate, and fluoride via hemiacetal **21**. Among the glycosyl donors, fluoride **22** demonstrated the highest α-stereoselectivity (α/β=9:1) affording the desired **26** in 80% yield,



Scheme 1. Synthesis of trisaccharides.



Scheme 2. Synthesis of sulfated glycoserine building blocks **32** and **33**. Structure of model debenzylation products **34** and **35**.

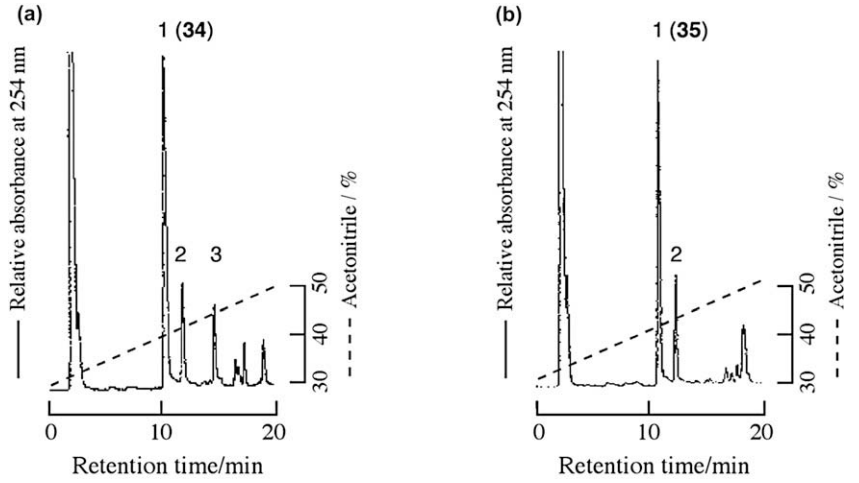


Figure 2. HPLC profiles of debenzylation products: (a) product **34** and the byproducts, (b) product **35** and the byproducts.

when the reaction was performed in the presence of a large amount of molecular sieves, which might serve as a proton scavenger retaining the acid-labile (4-methoxyphenyl)methyl group. Reaction with either trichloroacetimidate or *N*-phenyltrifluoroacetimidate gave a low yield of **26**. Thus, 6-MPM isomer **20** was converted to fluoride **24**, which was condensed with **25** to give **29** (75%) and the stereoisomer (α/β=15:1).

Having prepared the necessary frameworks, sulfation was performed after selective removal of the MPM groups from **26** and **29** with 90% CF_3CO_2H aq–CH_2Cl_2. Compound **27** was heated with excess $Me_3N\cdot SO_3$ in dimethylformamide at 60 °C for 1 h to produce sulfated product **28** in 97% yield. Successful 3-*O*-sulfation was evidenced by the lower-field shift of Gal H-3 and C-3 signals in the NMR spectra (for Gal H-3 at around δ 4.4 ppm and for C-3 at 81.7 ppm) and by the mass spectral data. 6-*O*-Sulfo-trisaccharyl serine **31** was also obtained through cleavage of MPM (**30**: 85%) and sulfation (76%). Then, both phenacyl esters were converted to carboxylic acids **32** (90%) and **33** (82%) by Zn–AcOH reduction. Before shifting to the SPPS study, we tested debenzylation of sulfated oligosaccharides **28** and **31**. When compound **28** was exposed to our standard debenzylation conditions using an excess of the low-acidity TfOH cocktail (TFA/Me_2S/*m*-cresol/TfOH, 5:3:1:1) at −15 °C for 2 h, a substantial quantity of sulfate-group-lacking product was generated, along with the desired debenzylated glycoserine. Therefore, we needed to tune the conditions appropriately. In general, an elevated temperature accelerated scission of GlcNAc–Man linkages in addition to departure of the sulfate group, whereas a lowered temperature gave rise to incomplete debenzylation. The optimum result was obtained by using a limited amount of TfOH (TfOH/benzyl group=1.5) in the TFA/Me_2S/*m*-cresol cocktail and by extending the reaction time (7 h)at −15 °C (Schemes 1 and 2).

HPLC profiles of the products obtained from **28** and **31** under these conditions are shown in Figure 2a and b, respectively. The major products (peak 1) represent the desired **34** and **35**, respectively, while the following fractions (peak 2) show the mass spectra of the sulfate-missing products (Fig. 2a: *m*/*z* 995.6, Fig. 2b: *m*/*z* 995.3). In a less-mobile fraction of the crude mixture of **34** (Fig. 2a), an incompletely debenzylated product (*m*/*z* 1188.2) is present (peak 3). Having confirmed the considerable stability of the *O*-sulfate group in the conditions with TfOH, we next considered whether the synthesized sulfo-glycoserine acts as a suitable building block in solid-phase synthesis of glycopeptide (Fig. 2).

3. Solid-phase synthesis of glycopeptide

Solid-phase synthesis was investigated targeting a model glycopeptide (**40**), which represents a mucin-like icosapeptide domain (336–355: SRIVPTPTSPAIAPPTETMA) of human α-dystroglycan[6b] with a pendent 3-*O*-sulfo-trisaccharide instead of the native sialotetrasaccharide. Starting with commercial Fmoc-CLEAR amide resin, 11 amino acids were assembled using an automated peptide synthesizer under the *Fastmoc* program, where N-deprotection was performed with 20% piperidine/1-methyl-2-pyrrolidinone (NMP), and *O*-benzotriazol-1-yl-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (HBTU) and 1-hydroxybenzotriazole (HOBt) were used to activate Fmoc amino acids in NMP. Part of the machine-made peptide resin (**37**, 27 μmol) was subjected to manual condensation with **32** (3 equiv) in a plastic tube. The reaction was carried out at an elevated temperature (50 °C) with DCC/HOBt in NMP by stirring with a vortex mixer for 7 h. Then resin **38** was again transferred to the synthesizer, by which the remaining N-terminal octapeptide was elongated. The resulting resin (**39**) was treated with reagent K (CF_3CO_2H/H_2O/thioanisole/1,2-ethanedithiol/phenol) for 1 h at 0 °C to room temperature to split the synthetic glycopeptide from the resin. The product, precipitated by an addition of ether and separated by centrifugation, was subjected to the low-acidity TfOH-promoted debenzylation reaction. The crucial reaction was performed by the use of TfOH (TfOH/benzyl group=1.7) at −15 °C for 7 h, whereas a large excess of TfOH resulted in considerable scission of the sulfate group as examined with model compound **28**.

An HPLC profile of the crude product is shown in Figure 3. The major product, negative mass spectrum of which showed the desired deprotonated molecular ion (*m*/*z* 2642.0) for **40** $[M-H]^-$, was isolated by preparative HPLC, and the yield (17%) was determined by amino acid analysis as reported earlier. From the two minor peaks, 2 and 3, eluted after **40**, mass spectra corresponding to the analogs lacking SO_3 and LacNAc groups, respectively, were obtained. Since such LacNAc-missing products were not detected in the debenzylation of **34** and **35** practiced under similar conditions, the acidic and higher-temperature conditions used in the reagent K process might also be responsible for the undesired cleavage of the GlcNAc–Man linkage. Further studies will be required to suppress this side reaction.

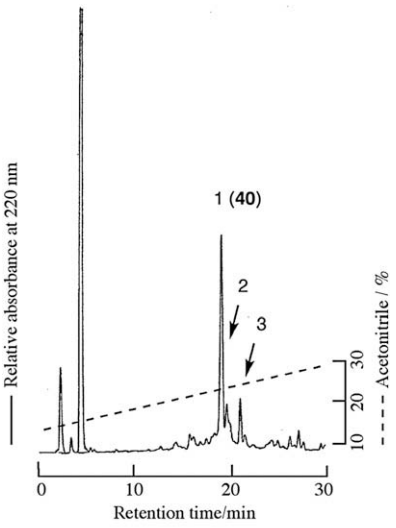


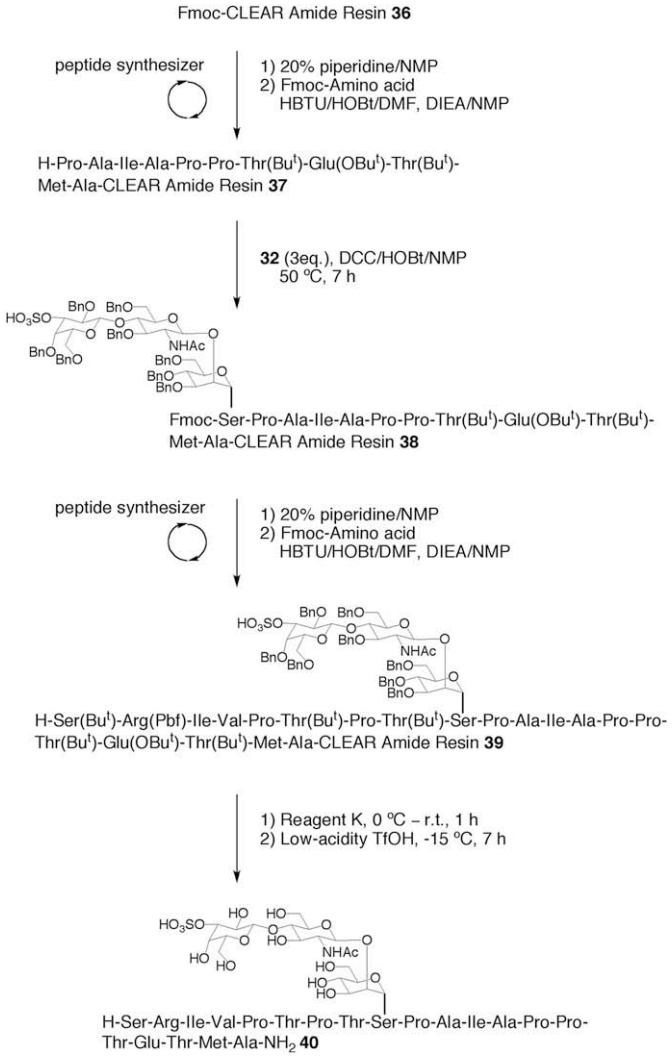
Figure 3. HPLC profile of crude glycopeptide **40**.

In summary, we have synthesized the benzyl- and MPM-protected glycoserine derivatives by three stereoselective glycosylation processes using thioglycoside, *N*-phenyltrifluoroacetimidate and fluoride methods. Selective cleavage of MPM groups followed by conventional sulfation produced 3-*O*-sulfo- and 6-*O*-sulfo-trisaccharyl serine derivatives. A preliminary study illustrated that selective debenzylation of the sulfated glycoserines was feasible under optimized low-acidity TfOH conditions. Sulfated glycoserine **32** was successfully introduced into the solid-phase synthesis of model glycopeptide **40**. Through optimized deprotection, the desired **40** was obtained as the major product in a 17% overall yield. This study also demonstrates that sulfated glycoamino acid building blocks can be utilized in the usual SPPS without masking the sulfate functionality. This benzyl-protection strategy is promising for preparation of a variety of *N*- and *O*-glycopeptide samples carrying a sulfate motif for obtaining insight into the biological importance of O-sulfation (Scheme 3).

4. Experimental

4.1. General

Specific rotation values were determined with a Jasco DIP-370 polarimeter at 20±2 °C for solutions in $CHCl_3$. Column



Scheme 3. Solid-phase synthesis of sulfated glycopeptide **40**.

chromatography was performed on silica gel PSQ 100B (Fuji Silysia). TLC and HPTLC were performed on silica gel 60 F_{254} (E. Merck). ^{1}H and ^{13}C NMR spectra were recorded with a Jeol AL400 spectrometer [^{1}H (400 MHz) and ^{13}C (100 MHz)]. For solutions in $CDCl_3$ the parts per million downfield chemical shifts are expressed from the internal Me_4Si signal. For assignment of the signals of sugar residue in oligosaccharides, the reducing terminal, the second, and the third residues are described as a, b and c, respectively. MALDI TOF mass spectra were obtained with a PerSeptive Voyager-DE PRO spectrometer (2,5-dihydroxybenzoic acid was used as a matrix). High-resolution mass spectra were obtained with an AccuTOF (JMS-T100LC) spectrometer. Microwave irradiation was carried out with a CEM *Discover* microwave reactor.

*4.1.1. Phenyl 2,3,4-tri-O-benzyl-6-O-(4-methoxyphenyl)methyl-1-thio-β-D-galactopyranoside **5**.* To a stirred mixture of **4** (1.89 g, 3.48 mmol) and 60% NaH/mineral oil (0.28 g, 6.96 mmol) in anhydrous DMF (35 ml) was added (4-methoxyphenyl)methyl chloride (0.95 ml, 7.01 mmol) at 0 °C. Then the mixture was stirred at room temperature for 2.5 h, diluted with EtOAc, successively washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was chromatographed on silica gel with toluene/EtOAc (49:1) to give **5** (1.94 g, 84%). Mp 91.5–92 °C (recrystallized from hexane/EtOAc). $[\alpha]_D$=−0.5 (*c*, 1.1). R_f 0.23 (49:1 toluene/EtOAc). ^{1}H NMR δ: 7.57–7.55 (m, 2H, Ar-*H*), 7.38–7.16 (m, 20H, Ar-*H*), 6.83 (br d, 2H, *J*=8.3 Hz, Ar-*H*), 4.95 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.77 (d, 1H, *J*=10.2 Hz, ArCH_2–), 4.72 (d, 2H, *J*=11.2 Hz, 2×ArCH_2–), 4.68 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.63 (d, 1H, *J*=9.8 Hz, H-1), 4.58 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.40 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.34 (d, 1H, *J*=11.2 Hz, ArCH_2–), 3.96 (d, 1H, *J*=2.4 Hz, H-4), 3.93 (t, 1H, *J*=9.3 Hz, H-2), 3.74 (s, 3H, CH_3O–), 3.63–3.55 (m, 4H, H-3, H-5, 2×H-6). Anal. Calcd for $C_{41}H_{42}O_6S$: C, 74.29; H, 6.39; S, 4.84. Found: C, 74.27; H, 6.43; S, 4.85.

*4.1.2. t-Butyldiphenylsilyl 2,4,6-tri-O-benzyl-3-O-(4-methoxyphenyl)-methyl-β-D-galactopyranosyl-(1→4)-3,6-di-O-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside **7** and t-butyldiphenylsilyl 2,4,6-tri-O-benzyl-3-O-(4-methoxyphenyl)methyl-α-D-galactopyranosyl-(1→4)-3,6-di-O-benzyl-2-deoxy-trichloroacetamido-β-D-glucopyranoside **8**.* A mixture of **3** (1.0 g, 1.5 mmol), **6** (750 mg, 1.0 mmol), TTBP (511 mg, 2.0 mmol), BSP (328 mg, 1.5 mmol), and dried MS 4 Å (4.0 g) in anhydrous EtCN (51 ml) was cooled at −78 °C with stirring for 30 min. To the mixture was slowly added Tf_2O (190 μl, 1.1 mmol). The mixture was stirred for 30 min at −78 °C before the reaction was quenched by adding excess satd $NaHCO_3$ aq. The insoluble materials were filtered off through Celite and washed with EtOAc. The combined filtrate and washings were washed successively with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was chromatographed on Bio-beads S X1 in toluene, and then on silica gel with toluene/EtOAc (19:1) to afford **7** (935 mg, 71%) and less polar **8** (165 mg, 13%).

*4.1.2.1. Compound **7**.* $[\alpha]_D$=−0.8 (*c*, 1.1). R_f 0.28 (19:1 toluene/EtOAc). ^{1}H NMR δ: 7.68–7.62 (m, 4H, Ar-*H*), 7.39–7.10 (m, 33H, Ar-*H*), 6.90–6.82 (m, 3H, TCAN*H*, Ar-*H*), 4.95 (d, 1H, *J*=10.2 Hz, ArCH_2–), 4.94 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.89 (d, 1H, *J*=7.3 Hz, H-1a), 4.73 (d, 1H, *J*=10.7 Hz, ArCH_2–), 4.67 (d, 1H, *J*=10.7 Hz, ArCH_2–), 4.64 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.61 (d, 1H, *J*=11.3 Hz, ArCH_2–), 4.54 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.51 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.43 (d, 1H, *J*=7.8 Hz, H-1b), 4.38 (d, 1H, *J*=12.2 Hz, ArCH_2–), 4.32 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.22 (br d, 2H, *J*=11.7 Hz, ArCH_2–), 4.04 (t, 1H, *J*=8.3 Hz, H-4a), 3.86 (d, 1H, *J*=3.4 Hz, H-4b), 3.83–3.74 (m, 5H, H-3a, H-2a, CH_3O–), 3.68 (dd, 1H, *J*=7.8, 9.8 Hz, H-2b), 3.65 (dd, 1H, *J*=3.4, 11.2 Hz, H-6a), 3.48 (br t, 1H, *J*=8.0 Hz, H-6b), 3.41–2.29 (m, 4H, H-5b, H-6a, H-6b, H-3b), 3.08 (m, 1H, H-5a), 1.06 (s, 9H, ^{t}Bu). ^{13}C NMR: δ 102.8 ($^1J_{CH}$=160.0 Hz, C-1b), 94.9 ($^1J_{CH}$=160.0 Hz, C-1a). Anal. Calcd for $C_{73}H_{78}Cl_3NO_{12}Si$: C, 67.66; H, 6.07; N, 1.08. Found: C, 67.50; H, 6.21; N, 1.05.

*4.1.2.2. Compound **8**.* $[\alpha]_D$=+12.0 (*c*, 1.0). R_f 0.35 (19:1 toluene/EtOAc). ^{1}H NMR δ: 7.71–7.65 (m, 4H, Ar-*H*), 7.38–7.12 (m, 33H, Ar-*H*), 6.87–6.80 (m, 3H, TCAN*H*–, Ar-*H*), 5.34 (d, 1H, *J*=3.9 Hz, H-1b), 4.87 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.82 (d, 1H, *J*=7.3 Hz, H-1a), 4.72 (d, 1H, *J*=10.2 Hz, ArCH_2–), 4.65 (d, 1H, *J*=12.2 Hz, ArCH_2–), 4.57 (d, 1H, *J*=12.0 Hz, ArCH_2–), 4.55 (br s, 2H, ArCH_2–), 4.52 (d, 1H, *J*=12.2 Hz, ArCH_2–), 4.51 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.35–4.31 (m, 3H, 3×ArCH_2–), 4.27 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.12–4.07 (m 2H, H-4a, H-2a), 3.93 (dd, 1H, *J*=3.4, 10.2 Hz, H-2b), 3.91 (br s, 1H, H-4b), 3.89–3.83 (m, 2H, H-3a, H-5b), 3.77 (s, 3H, CH_3O–), 3.72 (dd, 1H, *J*=2.4, 10.2 Hz, H-3b), 3.62 (dd, 1H, *J*=3.9, 10.7 Hz, H-6a), 3.50–3.45 (m, 2H, H-6b, H-6a), 3.41 (dd, 1H, *J*=5.9, 8.8 Hz, H-6b), 3.32 (m, 1H, H-5a), 1.08 (s, 9H, ^{t}Bu). ^{13}C NMR: δ 97.61 ($^1J_{CH}$=173.8 Hz, C-1b), 95.02 ($^1J_{CH}$=158.9 Hz, C-1a). Anal. Calcd for $C_{73}H_{78}Cl_3NO_{12}Si$: C, 67.66; H, 6.07; N, 1.08. Found: C, 67.38; H, 6.20; N, 1.08.

*4.1.3. t-Butyldiphenylsilyl 2,3,4-tri-O-benzyl-6-O-(4-methoxyphenyl)-methyl-β-D-galactopyranosyl-(1→4)-3,6-di-O-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside **9** and t-butyldiphenylsilyl 2,3,4-tri-O-benzyl-6-O-(4-methoxyphenyl)methyl-α-D-*

galactopyranosyl-(1→4)-3,6-di-O-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside ***10***. Reaction of **5** (178 mg, 0.27 mmol) and **6** (100 mg, 0.13 mmol) was performed using the same procedure as described for **7**. Chromatographic purification of the crude product on Bio-beads and then on silica gel gave **9** (125 mg, 71%) and less polar **10** (25 mg, 15%).

4.1.3.1. Compound ***9***. $[\alpha]_D=-4.3$ (*c*, 1.0). R_f 0.42 (2:1 hexane/EtOAc). Mp 113.0–114.0 °C (recrystallized from hexane/EtOAc). ^{1}H NMR δ: 7.70–7.63 (m, 4H, Ar-*H*), 7.40–7.10 (m, 33H, Ar-*H*), 6.90 (d, 1H, *J*=7.3 Hz, TCANH–), 6.84–6.80 (m, 2H, Ar-*H*), 4.96 (d, 1H, *J*=10.7 Hz, ArCH_2–), 4.93 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.89 (d, 1H, *J*=7.3 Hz, H-1a), 4.73 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.69 (br s, 2H, ArCH_2–), 4.67 (d, 1H, *J*=10.2 Hz, ArCH_2–), 4.54 (d, 1H, *J*=10.2 Hz, ArCH_2–), 4.50 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.44 (d, 1H, *J*=7.8 Hz, H-1b), 4.38 (d, 1H, *J*=12.2 Hz, ArCH_2–), 4.27 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.22 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.17 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.06 (t, 1H, *J*=8.3 Hz, H-4a), 3.89 (d, 1H, *J*=2.9 Hz, H-4b), 3.83 (dd, 1H, *J*=7.8, 9.2 Hz, H-3a), 3.76 (s, 3H, CH_3O–), 3.75 (br, 1H, H-2a), 3.70 (dd, 1H, *J*=7.8, 9.7, H-2b), 3.65 (dd, 1H, *J*=3.4, 11.2 Hz, H-6a), 3.47 (br t, 1H, *J*=8.3 Hz, H-6b), 3.45–3.37 (m, 2H, H-3b, H-5b), 3.32–3.29 (m, 2H, H-6a, H-6b), 3.08 (m, 1H, H-5a), 1.05 (s, 9H, ^{t}Bu). ^{13}C NMR: δ 102.8 ($^1J_{CH}$=159.7 Hz, C-1b), 94.9 ($^1J_{CH}$=164.7 Hz, C-1a). Anal. Calcd for $C_{73}H_{78}Cl_3NO_{12}Si$: C, 67.66; H, 6.07; N, 1.08. Found: C, 67.42; H, 6.10; N, 1.07.

4.1.3.2. Compound ***10***. $[\alpha]_D=+14.5$ (*c*, 1.0). R_f 0.52 (2:1 hexane/EtOAc). ^{1}H NMR δ: 7.70–7.62 (m, 4H, Ar-*H*), 7.38–7.11 (m, 33H, Ar-*H*), 6.83–6.78 (m, 3H, TCANH–, Ar-*H*), 5.33 (d, 1H, *J*=3.4 Hz, H-1b), 4.84 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.78 (d, 1H, *J*=7.3 Hz, H-1a), 4.71 (d, 1H, *J*=10.7 Hz, ArCH_2–), 4.63 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.62 (br s, 2H, ArCH_2–), 4.59 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.57 (d, 1H, *J*=10.7 Hz, ArCH_2–), 4.51 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.49 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.33 (d, 1H, *J*=12.2 Hz, ArCH_2–), 4.28 (d, 1H, *J*=12.2 Hz, ArCH_2–), 4.27 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.20 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.13–4.07 (m, 2H, H-2a, H-4a), 3.96–3.93 (m, 2H, H-2b, H-4b), 3.87–3.83 (m, 2H, H-3a, H-5b), 3.76 (s, 3H, CH_3O–), 3.72 (dd, 1H, *J*=2.9, 10.2 Hz, H-3b), 3.58 (m, 1H, H-6a), 3.48–3.43 (m, 2H, H-6b, H-6a), 3.37 (br dd, 1H, H-6b), 3.34 (m, 1H, H-5a), 1.07 (s, 9H, ^{t}Bu). ^{13}C NMR: δ 97.55 ($^1J_{CH}$=173.8 Hz, C-1b), 95.1 ($^1J_{CH}$=158.9 Hz, C-1a). MALDI TOF MS: calcd for $C_{73}H_{78}Cl_3NO_{12}Si$: *m*/*z* 1316.4 $(M+Na)^+$. Found: *m*/*z* 1317.1. Anal. Calcd for $C_{73}H_{78}Cl_3NO_{12}Si$: C, 67.66; H, 6.07; N, 1.08. Found: C, 67.63; H, 6.11; N, 1.13.

4.1.4. 2,4,6-Tri-O-benzyl-3-O-(4-methoxyphenyl)methyl-β-D-galactopyranosyl-(1→4)-3,6-di-O-benzyl-2-deoxy-2-trichloroacetamido-α-D-glucopyranose ***11***. A solution of 1 M TBAF/THF (3.2 ml, 3.2 mmol) was added to a cold mixture of **7** (1.0 g, 0.8 mmol) and AcOH (0.46 ml, 8.0 mmol) in freshly distilled THF (14 ml) on an ice-water bath with stirring. The mixture was stirred for 2 days at room temperature, then diluted with EtOAc, washed successively with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was chromatographed on silica gel with toluene/EtOAc (5:1) to give **11** (0.85 g, 99%) as an α-anomer rich mixture. R_f 0.15 (9:1 toluene/EtOAc). ^{1}H NMR δ: 7.32–7.10 (m, 27H, Ar-*H*), 6.88–6.83 (m, 3H, TCANH–, Ar-*H*), 5.37 (br t, 1H, *J*=3.5 Hz, H-1a), 5.02 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.94 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.83 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.78 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.65 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.61 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.52 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.51 (d, 1H, *J*=12.2 Hz, ArCH_2–), 4.35 (d, 1H, *J*=7.3 Hz, H-1b), 4.34 (d, 1H, *J*=12.2 Hz, ArCH_2–), 4.30 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.20 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.10 (m, 1H, H-2a), 4.01–3.97 (m, 2H, H-5a, H-4a), 3.87 (d, 1H, *J*=2.4 Hz, H-4b), 3.86–3.71 (m, 3H, H-2b, H-3a, H-6a), 3.79 (s, 3H, CH_3O–), 3.60 (br d, 1H, *J*=9.7 Hz, H-6a), 3.44–3.33 (m, 3H, H-3b, H-5b, H-6b), 3.28 (dd, *J*=4.9, 8.3 Hz, H-6b), 3.16 (br, 1H, –OH). Anal. Calcd for $C_{57}H_{60}Cl_3NO_{12}$: C, 64.74; H, 5.72; N, 1.32. Found: C, 64.64; H, 5.79; N, 1.32.

4.1.5. 2,4,6-Tri-O-benzyl-3-O-(4-methoxyphenyl)methyl-β-D-galactopyranosyl-(1→4)-3,6-di-O-benzyl-2-deoxy-2-trichloroacetamido-α-D-glucopyranosyl fluoride ***12***. To a stirred solution of **11** (149 mg, 0.14 mmol) in anhydrous THF (5.5 ml) was added DAST (37 μl, 0.28 mmol) at 0 °C. Then the mixture was stirred at room temperature for 30 min before adding CH_3OH to quench excess reagent, and evaporating the solvent in vacuo. The residue was extracted with EtOAc, washed successively with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was chromatographed on silica gel with toluene/EtOAc (10:1) to afford **12** (135 mg, 91%) as α/β mixture (α/β=7.4:1). R_f 0.49 (9:1 toluene/EtOAc). ^{1}H NMR δ: 7.32–7.14 (m, 27H, Ar-*H*), 6.85 (d, 2H, *J*=8.8 Hz, Ar-*H*), 6.63 (d, 1H, *J*=8.3 Hz, TCANH–), [6.30 (d, 0.14H, *J*=7.3 Hz, TCANH–)], 5.75 (dd, 1H, *J*=2.4, 53.6 Hz, H-1a), 5.03 (d, 1H, *J*=10.7 Hz, ArCH_2–), 4.95 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.83 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.74 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.67–4.60 (m, 3H, 3×ArCH_2–), 4.55 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.52 (d, 1H, *J*=10.2 Hz, ArCH_2–), 4.38 (d, 1H, *J*=12.1 Hz, ArCH_2–), 4.37 (d, 1H, *J*=7.8 Hz, H-1b), 4.33 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.24 (d, 1H, *J*=12.1 Hz, ArCH_2–), 4.17–4.02 (m, 2H, H-4a, H-2a), 3.92–3.69 (m, 5H, H-5a, H-4b, H-2b, H-3a, H-6a), 3.80 (s, 3H, CH_3O–), 3.56 (dd, 1H, *J*=1.4, 11.2 Hz, H-6a), 3.48–3.32 (m, 4H, H-6b, H-3b, H-6b, H-5b). Anal. Calcd for $C_{57}H_{59}Cl_3FNO_{11}$: C, 64.62; H, 5.61; N, 1.32. Found: C, 64.65; H, 5.62; N, 1.41.

4.1.6. 2,3,4-Tri-O-benzyl-3-O-(4-methoxyphenyl)methyl-β-D-galactopyranosyl-(1→4)-3,6-di-O-benzyl-2-deoxy-2-trichloroacetamido-D-glucopyranosyl (N-phenyl)-2,2,2-trifluoroacetimidate ***13***. A mixture of **11** (438 mg, 0.42 mmol), *N*-phenyltrifluoroacetimidoyl chloride (172 mg, 0.84 mmol), and K_2CO_3 (115 mg, 0.84 mmol) in acetone (4.2 ml) was stirred at room temperature for 30 min. The insoluble material was filtered off and the filtrate was concentrated in vacuo. The residue was chromatographed on silica gel with toluene/EtOAc (15:1) to afford **13** (506 mg, 99%) as a mixture of α/β and/or *syn*/*anti* isomers. R_f 0.56 (9:1 toluene/EtOAc). ^{1}H NMR: δ 7.35–7.16 (m, 29H, Ar-*H*), 7.08 (m, 1H, Ar-*H*), 6.89–6.79 (m, 4H, Ar-*H*), 6.61 and 6.31 (2d, 1H, *J*=7.8 Hz, H-1a), 5.01 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.97 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.86 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.77 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.68–4.52 (m, 5H, 5×ArCH_2–), 4.42–4.23 (m, 4H, H-1b, 3×ArCH_2–), 4.16–4.09 (m, 2H, H-2a, H-4a), 3.89 (d, 1H, *J*=2.4 Hz, H-4b), 3.86–3.72 (m, 4H, H-2b, H-3a, H-5a, H-6a), 3.80 (s, 3H, CH_3O–), 3.55–3.32 (m, 5H, H-6a, H-5b, H-3b, 2×H-6b). Anal. Calcd for $C_{65}H_{64}Cl_3F_3N_2O_{12}$: C, 63.55; H, 5.25; N, 2.28. Found: C, 63.50; H, 5.38; N, 2.23.

4.1.7. 2,3,4-Tri-O-benzyl-6-O-(4-methoxyphenyl)methyl-β-D-galactopyranosyl-(1→4)-3,6-di-O-benzyl-2-deoxy-2-trichloroacetamido-α-D-glucopyranose ***14***. Compound **9** (212 mg, 0.16 mmol) was desilylated with TBAF/AcOH in THF in a similar manner as described for **11**. The crude product was purified by chromatography on silica gel with toluene/EtOAc (5:1) to give **14** (170 mg, 99%) as an α-anomer rich mixture. R_f 0.14 (9:1 toluene/EtOAc). ^{1}H NMR: δ 7.32–7.11 (m, 26H, Ar-*H*), 6.86–6.80 (m, 3H, TCANH–, Ar-*H*), 5.33 (br t, 1H, *J*=3.4 Hz, H-1a), 5.02 (d, 1H, *J*=10.7 Hz, ArCH_2–), 4.93 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.82 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.78 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.71 (d, 1H, *J*=12.2 Hz, ArCH_2–), 4.67 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.59 (d, 1H, *J*=10.7 Hz, ArCH_2–), 4.51 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.48 (d, 1H, *J*=12.1 Hz, ArCH_2–), 4.32 (d, 1H, *J*=8.3 Hz, H-1b), 4.30 (d, 1H, *J*=12.7 Hz, ArCH_2–), 4.23 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.17 (d, 1H, *J*=12.7 Hz, ArCH_2–), 4.13 (m, 1H, H-2a), 4.04–3.93 (m, 2H, H-5a, H-4a), 3.88 (d, 1H, *J*=2.4 Hz, H-4b), 3.82–3.70 (m, 3H, H-6a, H-3a, H-2b), 3.77 (s, 3H, CH_3O–), 3.63–3.58

(m, 2H, –O*H*, H-6a), 3.42–3.32 (m, 2H, H-3b, H-5b), 3.26 (dd, 1H, *J*=4.9, 8.0 Hz, H-6b). Anal. Calcd for $C_{57}H_{60}Cl_3NO_{12}$: C, 64.74; H, 5.72; N, 1.32. Found: C, 64.61; H, 5.77; N, 1.31.

4.1.8. 2,3,4-Tri-O-benzyl-6-O-(4-methoxyphenyl)methyl-β-D-galactopyranosyl-(1→4)-3,6-di-O-benzyl-2-deoxy-2-trichloroacetamido-D-glucopyranosyl (N-phenyl)-2,2,2-trifluoroacetimidate ***15****.* Compound **14** (158 mg, 0.15 mmol) was reacted with *N*-phenyltrifluoroacetimidoyl chloride (62 mg, 0.30 mmol), and K_2CO_3 (41 mg, 0.30 mmol) in acetone (1.5 ml) as described for **13**. The crude product was chromatographed on silica gel with toluene/EtOAc (15:1) to give **15** (176 mg, 96%). R_f 0.63 (9:1 toluene/EtOAc). ^{1}H NMR: δ 7.35–7.06 (m, 30H, Ar-*H*), 6.84–6.75 (m, 4H, Ar-*H*), 6.62 and 6.29 (2d, 1H, *J*=7.8 Hz, H-1a), 5.01 (d, 1H, *J*=10.7 Hz, ArC*H*$_2$–), 4.94 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.85 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.77 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.73 (d, 1H, *J*=12.2 Hz, ArC*H*$_2$–), 4.68 (d, 1H, *J*=11.7 Hz, ArC*H*$_2$–), 4.64 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.54 (d, 1H, *J*=11.7 Hz, ArC*H*$_2$–), 4.52 (d, 1H, *J*=11.7 Hz, ArC*H*$_2$–), 4.38 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.37 (d, 1H, *J*=8.3 Hz, H–1b), 4.27 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.19 (d, 1H, *J*=11.7 Hz, ArC*H*$_2$–), 4.25–4.09 (m, 2H, H-2a, H-4a), 3.90 (d, 1H, *J*=2.9 Hz, H-4b), 3.89–3.76 (m, 4H, H-6a, H-3a, H-2b, H-5a), 3.78 (s, 3H, C*H*$_3$O–), 3.55 (br d, 1H, *J*=10.7 Hz, H-6a), 3.45 (m, 1H, H-6b), 3.39–3.31 (m, 3H, H-5b, H-3b, H-6b). Anal. Calcd for $C_{65}H_{64}Cl_3F_3N_2O_{12}$: C, 63.55; H, 5.25; N, 2.28. Found: C, 63.80; H, 5.34; N, 2.16.

4.1.9. Phenyl 2,4,6-tri-O-benzyl-3-O-(4-methoxyphenyl)methyl-β-D-galactopyranosyl-(1→4)-3,6-di-O-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl-(1→2)-3,4,6-tri-O-benzyl-1-thio-α-D-mannnopyranoside ***17.***

4.1.9.1. Procedure A (reaction of ***13*** *and* ***16****).* To a stirred mixture of **13** (109 mg, 88 μmol) and **16** (48 mg, 88 μmol) in anhydrous CH_2Cl_2 (3 ml) was added TMSOTf (0.8 μl, 4.4 μmol) at −78 °C. Then the temperature was raised to −40 °C. The mixture was stirred for 2 h before adding satd $NaHCO_3$ aq to quench the reaction, diluted with EtOAc, and filtrated through Celite. The combined filtrate and washings (EtOAc) were successively washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was chromatographed on Bio-beads S X1 in toluene, and then on silica gel with toluene/EtOAc (9:1) to give **17** (127 mg, 91%).

4.1.9.2. Procedure B (reaction of ***12*** *and* ***16****).* A mixture of Cp_2ZrCl_2 (35 mg, 0.12 mmol), $AgClO_4$ (25 mg, 0.12 mmol), and dried molecular sieves 4 Å powder (500 mg) in anhydrous CH_2Cl_2 (2 ml) was stirred at room temperature under Ar for 30 min and then cooled at −20 °C. To the stirred mixture was added a mixture of **12** (114 mg, 0.11 mmol) and **16** (72 mg, 0.13 mmol) in anhydrous CH_2Cl_2 (3 ml). Then the stirring was continued for 30 min, before the reaction was quenched with aq $NaHCO_3$. The mixture was diluted with EtOAc and filtered through Celite. The combined filtrate and washings (EtOAc) were successively washed with satd $NaHCO_3$, water, and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was chromatographed on silica gel with toluene/EtOAc (95:5) to give **17** (75 mg, 44%). $[\alpha]_D$=+32.1 (*c*, 1.0). R_f 0.39 (9:1 toluene/EtOAc). ^{1}H NMR: δ 7.37–7.35 (m, 2H, Ar-*H*), 7.25–7.02 (m, 46H, TCAN*H*–, Ar-*H*), 6.78–6.76 (m, 2H, Ar-*H*), 5.46 (d, 1H, *J*=2.0 Hz, H-1a), 5.15 (d, 1H, *J*=8.3 Hz, H-1b), 4.98 (d, 1H, *J*=10.2 Hz, ArC*H*$_2$–), 4.98 (d, 1H, *J*=11.7 Hz, ArC*H*$_2$–), 4.75 (d, 1H, *J*=10.7 Hz, ArC*H*$_2$–), 4.73 (d, 1H, *J*=11.7 Hz, ArC*H*$_2$–), 4.71 (d, 1H, *J*=11.7 Hz, ArC*H*$_2$–), 4.66 (d, 1H, *J*=10.7 Hz, ArC*H*$_2$–), 4.59 (d, 1H, *J*=12.2 Hz, ArC*H*$_2$–), 4.56 (d, 1H, *J*=11.7 Hz, ArC*H*$_2$–), 4.49–4.29 (m, 11H, 8×ArC*H*$_2$–, H-1c, H-2a, H-3b), 4.20 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.17 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.15 (m, 1H, H-5a), 3.95 (br t, 1H, *J*=9.3 Hz, H-4b), 3.85 (br t, 1H, *J*=9.3 Hz, H-4a), 3.80 (d, 1H, *J*=2.4 Hz, H-4c), 3.77 (dd, 1H, H-3a), 3.72 (s, 3H, C*H*$_3$O–), 3.71–3.65 (m, 3H, H-2c, H-6a, H-6b), 3.61–3.56 (m, 2H, H-6a, H-6b), 3.48–3.43 (m, 2H, H-5b, H-6c), 3.35–3.25 (m, 4H, H-2b, H-3c, H-5c, H-6c). ^{13}C NMR: δ 102.7 ($^1J_{CH}$=162.2 Hz, C-1c), 97.0 ($^1J_{CH}$=164.7 Hz, C-1b), 86.2 ($^1J_{CH}$=168.0 Hz, C-1a). MALDI TOF MS: calcd for $C_{90}H_{92}Cl_3NO_{16}S$: *m*/*z* 1602.5 $(M+Na)^+$, 1618.5 $(M+K)^+$. Found: *m*/*z* 1602.5 and 1618.4. Anal. Calcd for $C_{90}H_{92}Cl_3NO_{16}S$: C, 68.32; H, 5.86; N, 0.89; Cl, 6.72; S, 2.03. Found: C, 68.15; H, 5.92; N, 0.95; Cl, 6.75; S, 2.04.

4.1.10. Phenyl 2,3,4-tri-O-benzyl-6-O-(4-methoxyphenyl)methyl-β-D-galactopyranosyl-(1→4)-3,6-di-O-benzyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranosyl-(1→2)-3,4,6-tri-O-benzyl-1-thio-α-D-mannnopyranoside ***18****.* Disaccharyl donor **15** (0.97 g, 0.79 mmol) and acceptor **16** (0.47 g, 0.87 mmol) were reacted in the presence of TMSOTf (7.2 μl, 0.04 mmol) at −40 °C for 3 h according to the procedure A described for **17**. The crude product was purified by chromatography on Bio-beads S X1 in toluene, and then on silica gel with toluene/EtOAc (9:1) to give **18** (1.10 g, 83%). $[\alpha]_D$=+31.9 (*c*, 1.1). R_f 0.40 (9:1 toluene/EtOAc). ^{1}H NMR: δ 7.45–7.42 (m, 2H, Ar-*H*), 7.35–7.10 (m, 46H, TCAN*H*–, Ar-*H*), 6.83–6.81 (m, 2H, Ar-*H*), 5.53 (d, 1H, *J*=1.5 Hz, H-1a), 5.22 (d, 1H, *J*=8.3 Hz, H-1b), 5.06 (d, 1H, *J*=10.2 Hz, ArC*H*$_2$–), 4.96 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.82 (d, 1H, *J*=10.7 Hz, ArC*H*$_2$–), 4.79 (br s, 2H, ArC*H*$_2$–), 4.76 (d, 1H, *J*=10.7 Hz, ArC*H*$_2$–), 4.71 (br s, 2H, ArC*H*$_2$–), 4.56–4.39 (m, 10H, 7×ArC*H*$_2$–, H-1c, H-2a, H-3b), 4.33 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.27–4.22 (m, 2H, ArC*H*$_2$–, H-5a), 4.18 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.02 (br t, 1H, *J*=9.3 Hz, H-4b), 3.92 (br t, 1H, *J*=9.2 Hz, H-4a), 3.89 (d, 1H, *J*=2.0 Hz, H-4c), 3.86–3.82 (m, 2H, H-3a, H-6b), 3.77 (s, 3H, C*H*$_3$O–), 3.79–3.63 (m, 3H, H-2c, H-6b, H-6a), 3.68–3.63 (m, 2H, H-6a, H-6b), 3.54–3.49 (m, 2H, H-5b, H-6c), 3.42–3.34 (m, 4H, H-5c, H-3c, H-6c, H-2b). ^{13}C NMR: δ 102.7 ($^1J_{CH}$=161.4 Hz, C-1c), 97.0 ($^1J_{CH}$=164.7 Hz, C-1b), 86.1 ($^1J_{CH}$=168.0 Hz, C-1a). Anal. Calcd for $C_{90}H_{92}Cl_3NO_{16}S$: C, 68.32; H, 5.86; N, 0.89; Cl, 6.72; S, 2.03. Found: C, 68.10; H, 5.89; N, 0.86; Cl, 6.62; S, 2.05.

4.1.11. Phenyl 2,4,6-tri-O-benzyl-3-O-(4-methoxyphenyl)methyl-β-D-galactopyranosyl-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl-(1→2)-3,4,6-tri-O-benzyl-1-thio-α-D-mannnopyranoside ***19****.* A mixture of **17** (564 mg, 0.36 mmol), powdered Zn (3.5 g, 53.6 mmol), and AcOH (3.5 ml, 61.3 mmol) in EtOAc (35 ml) was placed in a round-bottom flask equipped with a reflux condenser. The atmosphere was replaced with a balloon of Ar. The reaction mixture was stirred under microwave irradiation at 150 W for 30 min. The microwave machine was controlled so as to continuously irradiate the flask during this period. The mixture was diluted with EtOAc and filtered through Celite. The combined filtrate and washings (EtOAc) were successively washed with satd $NaHCO_3$, water, and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was chromatographed on silica gel with toluene/EtOAc (4:1) to afford **19** (465 mg, 88%). $[\alpha]_D$=+32.1 (*c*, 1.0). R_f 0.11 (7:1 toluene/EtOAc). ^{1}H NMR: δ 7.44–7.15 (m, 47H, Ar-*H*), 6.86–6.83 (m, 2H, Ar-*H*), 5.61 (d, 1H, *J*=6.8 Hz, AcN*H*–), 5.57 (d, 1H, *J*=1.5 Hz, H-1a), 5.20 (d, 1H, *J*=7.8 Hz, H-1b), 4.96 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.96 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.89 (d, 1H, *J*=10.7 Hz, ArC*H*$_2$–), 4.80–4.69 (m, 3H, 3×ArC*H*$_2$–), 4.62 (d, 1H, *J*=12.2 Hz, ArC*H*$_2$–), 4.58 (d, 1H, *J*=12.2 Hz, ArC*H*$_2$–), 4.55–4.35 (m, 10H, 8×ArC*H*$_2$–, H-1c, H-3b), 4.29 (d, 1H, *J*=12.2 Hz, ArC*H*$_2$–), 4.25 (d, 1H, *J*=12.2 Hz, ArC*H*$_2$–), 4.16 (m, 1H, H-5a), 4.03 (br t, 1H, *J*=9.3 Hz, H-4a), 3.90 (br t, 1H, *J*=9.3 Hz, H-4b), 3.86–3.69 (m, 4H, H-4c, H-3a, H-6b, H-6a), 3.80 (s, 3H, C*H*$_3$O–), 3.63 (dd, 1H, *J*=1.5, 10.5 Hz, H-6a), 3.58 (m, 1H, H-5b), 3.52 (br t, 1H, *J*=7.8 Hz, H-6c), 3.42–3.35 (m, 3H, H-3c, H-5c, H-6c), 3.06 (m, 1H, H-2b), 1.63 (s, 3H, Ac). MALDI TOF MS: calcd for $C_{90}H_{95}NO_{16}S$: *m*/*z* 1500.6 $(M+Na)^+$, 1516.6 $(M+K)^+$. Found: *m*/*z* 1500.5 and 1516.4. Anal.

Calcd for $C_{90}H_{95}NO_{16}S$: C, 73.10; H, 6.48; N, 0.95. Found: C, 73.00; H, 6.57; N, 0.93.

*4.1.12. Phenyl 2,3,4-tri-O-benzyl-6-O-(4-methoxyphenyl)methyl-β-D-galactopyranosyl-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl-(1→2)-3,4,6-tri-O-benzyl-1-thio-α-D-mannnopyranoside **20**.* Compound **18** (101 mg, 0.06 mmol) was dechlorinated with Zn (630 mg) and AcOH (0.63 ml) in EtOAc under microwave irradiation at 150 W for 1 h as described for **19**. The crude product was purified by column chromatography on silica gel with toluene/EtOAc (4:1) to give **20** (95 mg, 99%). $[\alpha]_D$=+33.8 (*c*, 1.0). R_f 0.11 (7:1 toluene/EtOAc). ^{1}H NMR: δ 7.44–7.13 (m, 47H, Ar-*H*), 6.82 (br d, 2H, *J*=8.3 Hz, Ar-*H*), 5.59 (d, 1H, *J*=1.5 Hz, H-1a), 5.58 (d, 1H, *J*=7.3 Hz, AcN*H*–), 5.21 (d, 1H, *J*=8.3 Hz, H-1b), 4.98 (d, 1H, *J*=11.7 Hz, ArC*H*$_2$–), 4.95 (d, 1H, *J*=11.7 Hz, ArC*H*$_2$–), 4.90 (d, 1H, *J*=10.7 Hz, ArC*H*$_2$–), 4.81–4.76 (m, 3H, 3×ArC*H*$_2$–), 4.71 (d, 1H, *J*=12.2 Hz, ArC*H*$_2$–), 4.69 (d, 1H, *J*=12.2 Hz, ArC*H*$_2$–), 4.55–4.36 (m, 10H, 8×ArC*H*$_2$–, H-1c, H-3b), 4.32 (d, 1H, *J*=10.7 Hz, ArC*H*$_2$–), 4.30 (d, 1H, *J*=11.7 Hz, ArC*H*$_2$–), 4.19 (d, 1H, *J*=11.2 Hz, ArCH$_2$–), 4.17 (m, 1H, H-5a), 4.02 (br t, 1H, *J*=8.8 Hz, H-4a), 3.92 (br t, 1H, *J*=8.8 Hz, H-4b), 3.88 (d, 1H, *J*=2.4 Hz, H-4c), 3.83 (dd, 1H, *J*=2, 9, 10.7 Hz, H-3a), 3.82–3.70 (m, 3H, H-2c, H-6b, H-6a), 3.76 (s, 3H, C*H*$_3$O–), 3.63 (dd, 1H, *J*=1.5, 10.7 Hz, H-6a), 3.58 (m, 1H, H-5b), 3.51 (m, 1H, H-6c), 3.43–3.35 (m, 3H, H-3c, H-5c, H-6c), 3.07 (m, 1H, H-2b), 1.63 (s, 3H, Ac). ^{13}C NMR: δ 102.9 (C-1c), 97.2 (C-1b), 85.1 (C-1a). Anal. Calcd for $C_{90}H_{95}NO_{16}S$: C, 73.10; H, 6.48; N, 0.95. Found: C, 73.03; H, 6.66; N, 0.97.

*4.1.13. 2,4,6-Tri-O-benzyl-3-O-(4-methoxyphenyl)methyl-β-D-galactopyranosyl-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl-(1→2)-3,4,6-tri-O-benzyl-D-mannopyranose **21**.* To a stirred solution of **19** (484 mg, 0.33 mmol) in acetone/water (6:1, 6.6 ml) was added *N*-bromosuccimide (175 mg, 1.0 mmol). The mixture was stirred at room temperature for 30 min, before extracting with EtOAc. The extract was washed successively with 5% $Na_2S_2O_3$ aq and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was chromatographed on silica gel with hexane/EtOAc (3:7) to give **21** (107 mg, 98%) as an anomeric mixture. R_f 0.26 (2:3 hexane/EtOAc). ^{13}C NMR: δ 103.0 (C-1c), 102.5 and 97.5 (C-1a), 92.4 and 91.8 (C-1b). MALDI TOF MS: calcd for $C_{84}H_{91}NO_{17}$: *m*/*z* 1408.6 $(M+Na)^+$, 1424.6 $(M+K)^+$. Found: *m*/*z* 1409.4 and 1425.4. Anal. Calcd for $C_{84}H_{91}NO_{17}\cdot 1.5H_2O$: C, 71.37; H, 6.70; N, 0.99. Found: C, 71.14; H, 6.50; N, 1.02.

*4.1.14. 2,4,6-Tri-O-benzyl-3-O-(4-methoxyphenyl)methyl-β-D-galactopyranosyl-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl-(1→2)-3,4,6-tri-O-benzyl-α/β-D-mannopyranosyl fluoride **22** (α/β).* To a stirred solution of **21** (556 mg, 0.4 mmol) in anhydrous CH_2Cl_2 (11 ml) was added (diethylamino)sulfur trifluoride (105 μl, 0.8 mmol) at 0 °C. The mixture was stirred for 30 min, before the reaction was quenched with aq $NaHCO_3$. The product was extracted with $CHCl_3$, washed successively with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was chromatographed on silica gel with toluene/EtOAc (3:1) to afford **22α** (466 mg, 83%) and **22β** (82 mg, 15%).

*4.1.14.1. Compound **22α**.* $[\alpha]_D$=+11.6 (*c*, 1.0). R_f 0.32 (2:3 hexane/EtOAc). ^{1}H NMR: δ 7.34–7.17 (m, 42H, Ar-*H*), 6.86–6.82 (m, 2H, Ar-*H*), 5.60 (br d, 1H, J_{H-F}=50.7 Hz, H-1a), 5.55 (d, 1H, *J*=6.8 Hz, AcN*H*–), 5.22 (br d, 1H, *J*=7.8 Hz, H-1b), 4.99 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.97 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.88 (d, 1H, *J*=10.7 Hz, ArC*H*$_2$–), 4.80–4.75 (m, 3H, 3×ArC*H*$_2$–), 4.64 (br s, 2H, ArC*H*$_2$–), 4.58–4.24 (m, 12H, H-1c, H-2a, H-3b, 9×ArCH$_2$–), 4.04 (br t, 1H, *J*=9.7 Hz, H-4a), 3.95–3.80 (m, 5H, H-3a, H-4b, H-4c, H-5a, H-6b), 3.77 (s, 3H, C*H*$_3$O–), 3.76–3.72 (m, 3H, H-6a, H-6b, H-2c), 3.65 (br d, 1H, *J*=10.2 Hz, H-6a), 3.60 (m, 1H, H-5b), 3.52 (m, 1H, H-6c), 3.43–3.37 (m, 3H, H-3c, H-5c, H-6c), 3.02 (m, 1H, H-2b), 1.63 (s, 3H, Ac). ^{13}C NMR: δ 106.0 (J_{C-F}=220.9 Hz, C-1a) 102.9 (C-1c), 97.7 (C-1b). MALDI TOF MS: calcd for $C_{84}H_{90}FNO_{16}$: *m*/*z* 1410.6 $(M+Na)^+$, 1426.6 $(M+K)^+$. Found: *m*/*z* 1410.6 and 1426.6. Anal. Calcd for $C_{84}H_{90}FNO_{16}\cdot 2H_2O$: C, 70.82; H, 6.65; N, 0.98. Found: C, 70.72; H, 6.47; N, 1.12.

*4.1.14.2. Compound **22β**.* $[\alpha]_D$=−8.0 (*c*, 1.0). R_f 0.12 (2:3 hexane/EtOAc). ^{1}H NMR: δ 7.30–7.13 (m, 42H, Ar-*H*), 6.83 (br d, 2H, *J*=8.3 Hz, Ar-*H*), 5.49 (d, 1H, *J*=7.8 Hz, AcN*H*–), 5.30 (br d, 1H, J_{H-F}=51.2 Hz, H-1a), 4.98 (d, 1H, *J*=7.8 Hz, H-1b), 4.95 (d, 1H, *J*=11.7 Hz, ArC*H*$_2$–), 4.94 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.83–4.76 (m, 3H, 3×ArC*H*$_2$–), 4.72 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.64 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.61 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.58 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.53 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.52 (br s, 2H, ArC*H*$_2$–), 4.46–4.33 (m, 5H, 4×ArC*H*$_2$–, H-1c), 4.27–4.20 (m, 3H, 2×ArC*H*$_2$–, H-2a), 4.11 (br t, 1H, H-3b), 3.93 (br t, 1H, *J*=8.8 Hz, H-4b), 3.86 (d, 1H, *J*=2.9 Hz, H-4c), 3.79 (s, 3H, C*H*$_3$O–), 3.82–3.64 (m, 7H, H-2c, H-3a, H-4a, 2×H-6a, 2×H-6b), 3.56 (m, 1H, H-5b), 3.50–3.43 (m, 2H, H-2b, H-6c), 3.42–3.36 (m, 3H, H-3c, H-5c, H-6c), 1.82 (s, 3H, Ac). ^{13}C NMR: δ 106.4 (J_{C-H}=218.3 Hz, C-1a), 102.9 (C-1c), 100.3 (C-1b). MALDI TOF MS: calcd for $C_{84}H_{90}FNO_{16}$: *m*/*z* 1410.6 $(M+Na)^+$, 1426.6 $(M+K)^+$. Found: *m*/*z* 1410.8 and 1426.8. Anal. Calcd for $C_{84}H_{90}FNO_{16}\cdot 2H_2O$: C, 70.82; H, 6.65; N, 0.98. Found: C, 70.85; H, 6.47; N, 1.06.

*4.1.15. 2,3,4-Tri-O-benzyl-6-O-(4-methoxyphenyl)methyl-β-D-galactopyranosyl-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl-(1→2)-3,4,6-tri-O-benzyl-D-mannopyranose **23**.* According to the procedure described for **21**, thioglycoside **20** (438 mg, 0.30 mmol) was converted to hemiacetal **23** by treatment with NBS in aq acetone. The crude product was purified by chromatography on silica gel with hexane/EtOAc (3:7) to give **23** (375 mg, 91%). R_f 0.25 (2:3 hexane/EtOAc). ^{13}C NMR: δ 103.0 and 102.5 (C-1c), 97.4 (C-1b), 92.4 and 91.7 (C-1a). MALDI TOF MS: calcd for $C_{84}H_{91}NO_{17}$: *m*/*z* 1408.6 $(M+Na)^+$, 1424.6 $(M+K)^+$. Found: *m*/*z* 1409.5 and 1424.6. HRMS: calcd for $C_{84}H_{91}NNaO_{17}$: *m*/*z* 1408.6184. Found: *m*/*z* 1408.6129.

*4.1.16. 2,3,4-Tri-O-benzyl-6-O-(4-methoxyphenyl)methyl-β-D-galactopyranosyl-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl-(1→2)-3,4,6-tri-O-benzyl-D-mannopyranosyl fluoride **24**.* Hemiacetal **23** (375 mg, 0.27 mmol) was treated with DAST in CH_2Cl_2, as described for **22**. The crude product was chromatographed on silica gel with toluene/EtOAc (3:1) to afford **24α** (310 mg, 83%) and **24β** (56 mg, 15%).

*4.1.16.1. Compound **24α**.* $[\alpha]_D$=+5.9 (*c*, 1.0). R_f 0.25 (2:3 hexane/EtOAc). ^{1}H NMR: δ 7.33–7.14 (m, 42H, Ar-*H*), 6.82 (br d, 2H, *J*=8.8 Hz, Ar-*H*), 5.59 (d, 1H, J_{H-F}=50.2 Hz, H-1a), 5.57 (d, 1H, *J*=6.8 Hz, AcN*H*–), 5.22 (d, 1H, *J*=8.3 Hz, H-1b), 4.98 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.93 (d, 1H, *J*=11.7 Hz, ArC*H*$_2$–), 4.87 (d, 1H, *J*=10.7 Hz, ArC*H*$_2$–), 4.80 (br s, 2H, ArC*H*$_2$–), 4.77 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.71 (br s, 2H, ArC*H*$_2$–), 4.57–4.42 (m, 8H, 7×ArC*H*$_2$–, H-1c), 4.35 (d, 1H, *J*=8.3 Hz, H-3b), 4.33 (d, 1H, *J*=11.7 Hz, ArC*H*$_2$–), 4.30 (d, 1H, *J*=12.2 Hz, ArC*H*$_2$–), 4.25 (d, 1H, H-2a), 4.20 (d, 1H, *J*=11.2 Hz, ArC*H*$_2$–), 4.04 (br t, 1H, *J*=9.7 Hz, H-4a), 3.92 (br t, 1H, *J*=9.3 Hz, H-4b), 3.89–3.70 (m, 7H, H-4c, H-3a, H-5a, H-6a, H-2c, 2×H-6b), 3.76 (s, 3H, C*H*$_3$O–), 3.65 (br d, 1H, *J*=9.3 Hz, H-6a), 3.59 (m, 1H, H-5b), 3.51 (m, 1H, H-6c), 3.43–3.38 (m, 3H, H-3c, H-5c, H-6c), 3.03 (m, 1H, H-2b), 1.64 (s, 3H, Ac). ^{13}C NMR: δ 106.0 (J_{C-F}= 221.5 Hz, C-1a), 102.9 (C-1c), 97.7 (C-1b). Anal. Calcd for $C_{84}H_{90}FNO_{16}\cdot 0.5H_2O$: C, 72.19; H, 6.56; N, 1.00. Found: C, 72.24; H, 6.64; N, 0.91.

*4.1.16.2. Compound **24β**.* $[\alpha]_D$=−12.3 (*c*, 1.0). R_f 0.11 (2:3 hexane/EtOAc). ^{1}H NMR: δ 7.33–7.31 (m, 42H, Ar-*H*), 6.82 (br d, 2H, *J*=8.8 Hz, Ar-*H*), 5.50 (d, 1H, *J*=7.8 Hz, AcN*H*–), 5.30 (d, 1H,

J_{H-F}=51.2 Hz, H-1a), 4.99 (d, 1H, J=8.3 Hz, H-1b), 4.95 (d, 1H, J=11.2 Hz, ArCH_2–), 4.94 (d, 1H, J=11.7 Hz, ArCH_2–), 4.84–4.77 (m, 3H, 3×ArCH_2–), 4.73 (d, 1H, J=11.2 Hz, ArCH_2–), 4.71 (d, 1H, J=11.7 Hz, ArCH_2–), 4.68 (d, 1H, J=11.7 Hz, ArCH_2–), 4.59 (d, 1H, J=11.2 Hz, ArCH_2–), 4.53–4.42 (m, 5H, 4×ArCH_2–, H-1c), 4.39 (d, 1H, J=11.7 Hz, ArCH_2–), 4.34–4.18 (m, 5H, 4×ArCH_2–, H-2a), 4.12 (br t, 1H, J=9.3 Hz, H-2a), 3.94 (t, 1H, J=8.8 Hz, H-4b), 3.89 (d, 1H, J=2.4 Hz, H-4c), 3.78 (s, 3H, CH_3O–), 3.79–3.65 (m, 6H, H-2c, H-3a, 2×H-6a, 2×H-6b), 3.54 (m, 1H, H-5b), 3.53–3.46 (m, 2H, H-2b, H-6c), 3.43–3.35 (m, 3H, H-3c, H-5c, H-6c), 1.82 (s, 3H, Ac). HRMS: calcd for $C_{84}H_{90}FNNaO_{16}$: m/z 1410.6141. Found: m/z 1410.6120.

4.1.17. N-(9-Fluorenylmethoxycarbonyl)-O-[2,4,6-tri-O-benzyl-3-O-(4-methoxyphenyl)methyl-β-D-galactopyranosyl-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl-(1→2)-3,4,6-tri-O-benzyl-α-D-mannopyranosyl]-L-serine phenacyl ester ***26.***

4.1.17.1. Procedure A (reaction of ***22*** *and* ***25****).* A mixture of Cp_2ZrCl_2 (160 mg, 0.55 mmol), $AgClO_4$ (228 mg, 1.10 mmol), and dried molecular sieves 4 Å (3.3 g) in anhydrous CH_2Cl_2 (5 ml) was stirred at room temperature under Ar for 30 min, and then cooled at −40 °C. To the mixture was added a mixture of **22** (378 mg, 0.27 mmol) and **25** (148 mg, 0.33 mmol) in anhydrous CH_2Cl_2 (6 ml). The reaction mixture was stirred for 3 h by raising the temperature (−40 to 0 °C). The reaction was quenched by adding satd $NaHCO_3$ aq. The mixture was diluted with $CHCl_3$ and filtered through Celite. The combined filtrate and washings ($CHCl_3$) were washed successively with satd $NaHCO_3$ aq, water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude product was chromatographed on Bio-beads S X1 in toluene, and then on silica gel with toluene/EtOAc (3:1) to give **26** (397 mg, 80%). In a less polar fraction the β-glycoside isomer was obtained (42 mg, 9%).

4.1.17.2. Procedure B (reaction of ***19*** *and* ***25****).* A mixture of **19** (50 mg, 34 μmol), **25** (18 mg, 40 μmol), *N*-iodosuccimide (12 mg, 53 μmol), and dried molecular sieves 3 Å (100 mg) in anhydrous CH_2Cl_2 (1 ml) was stirred at −20 °C under Ar for 30 min. Then TfOH (0.45 μl, 5 μmol) was added to the mixture, which was stirred at −20 to 0 °C for 4.5 h before adding satd $NaHCO_3$ aq to quench the reaction. The mixture was diluted with $CHCl_3$ and filtered through Celite. The filtrate and washings ($CHCl_3$) were washed successively with 10% $Na_2S_2O_3$ aq and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was chromatographed on Bio-beads S X1 in toluene, and then on silica gel with toluene/EtOAc (3:1) to give **26** (25 mg, 41%). The β-isomer (18 mg, 29%) was also obtained.

4.1.17.3. Compound ***26****.* $[\alpha]_D$=+4.7 (*c*, 1.0). R_f 0.26 (2:1 toluene/EtOAc). ^{1}H NMR: δ 7.87 (br d, 2H, J=7.3 Hz, Ar-*H*), 7.73 (br d, 2H, J=7.3 Hz, Ar-*H*), 7.59 (br d, 2H, J=7.3 Hz, Ar-*H*), 7.47–7.16 (m, 49H, Ar-*H*), 6.83 (br d, 2H, J=8.8 Hz, Ar-*H*), 5.87 (d, 1H, J=8.8 Hz, FmocN*H*–), 5.79 (d, 1H, J=7.3 Hz, AcN*H*–), 5.53 (d, 1H, J=16.1 Hz, PhCOCH_2–), 5.26 (d, 1H, J=16.6 Hz, PhCOCH_2–), 5.15 (d, 1H, J=7.8 Hz, H-1b), 4.97–4.93 (m, 3H, H-1a, 2×ArCH_2–), 4.81 (br d, 2H, J=11.2 Hz, 2×ArCH_2–), 4.74 (d, 1H, J=11.2 Hz, ArCH_2–), 4.71 (d, 1H, J=11.2 Hz, ArCH_2–), 4.69 (m, 1H, Ser-αH), 4.63 (d, 1H, J=11.7 Hz, ArCH_2–), 4.60 (d, 1H, J=11.2 Hz, ArCH_2–), 4.56–4.22 (m, 16H, 10×ArCH_2–, H-1c, H-2a, H-3b, Ar$_2$CHCH_2–, Ar$_2$C*H*–), 4.15 (m, 1H, Ser-βH), 4.02 (m, 1H, Ser-βH), 3.98–3.64 (m, 10H, H-4b, H-3a, H-4c, H-2c, H-4a, H-5a, 2×H-6a, 2×H-6b), 3.79 (s, 3H, CH_3O–), 3.58 (m, 1H, H-5b), 3.51 (br t, 1H, J=9.7 Hz, H-6c), 3.40–3.30 (m, 5H, H-2b, H-3c, H-5c, H-6c, H-2b), 1.71 (s, 3H, Ac).

^{13}C NMR: δ 102.8 ($^1J_{C-H}$=160.6 Hz, C-1c), 99.1 ($^1J_{C-H}$=169.7 Hz, C-1a), 98.4 ($^1J_{C-H}$=162.2 Hz, C-1b). MALDI TOF MS: calcd for $C_{110}H_{112}N_2O_{22}$: m/z 1835.7 $(M+Na)^+$, 1851.7 $(M+K)^+$. Found: m/z 1835.6 and 1851.4. Anal. Calcd for $C_{110}H_{112}N_2O_{22}$: C, 72.83; H, 6.22; N, 1.54. Found: C, 72.55; H, 6.30; N, 1.54.

4.1.17.4. β-Isomer. $[\alpha]_D$=−18.2 (*c*, 1.4). R_f 0.34 (2:1 toluene/EtOAc). ^{1}H NMR: δ 7.89 (br d, 2H, J=7.3 Hz, Ar-*H*), 7.70 (br d, 2H, J=6.3 Hz, Ar-*H*), 7.62 (br, 2H, Ar-*H*), 7.36–7.10 (m, 49H, Ar-*H*), 6.83 (br d, 2H, J=8.8 Hz, Ar-*H*), 6.46 (d, 1H, J=7.8 Hz, FmocN*H*–), 6.07 (d, 1H, J=8.3 Hz, AcN*H*–), 5.39 (br s, 2H, PhCOCH_2–), 4.89 (d, 1H, J=7.3 Hz, H-1b), 4.96–4.87 (m, 3H, 3×ArCH_2–), 4.76–4.69 (m, 4H, Ser-αH, 3×ArCH_2–), 4.65–4.14 (m, 20H, 2×Ser-βH, H-1c, H-1a, H-3b, 12×ArCH_2–, Ar$_2$CHCH_2–, Ar$_2$C*H*–), 3.90–3.21 (m, 17H, H-2b, H-4c, H-4a, H-4b, H-2a, H-3a, H-2c, H-5a, H-5b, 2×H-6a, 2×H-6b, H-3c, 2×H-6c, H-5c), 3.79 (s, 3H, CH_3O–), 1.86 (s, 3H, Ac). ^{13}C NMR: δ 103.1 ($^1J_{C-H}$=162.2 Hz, C-1c), 101.9 ($^1J_{C-H}$=156.4 Hz, C-1a), 99.9 ($^1J_{C-H}$=158.1 Hz, C-1b). MALDI TOF MS: calcd for $C_{110}H_{112}N_2O_{22}$: m/z 1835.7 $(M+Na)^+$, 1851.7 $(M+K)^+$. Found: m/z 1836.1 and 1852.1. HRMS: calcd for $C_{110}H_{112}N_2NaO_{22}$: m/z 1835.7604. Found: m/z 1835.7666.

4.1.18. N-(9-Fluorenylmethoxycarbonyl)-O-[2,4,6-tri-O-benzyl-β-D-galactopyranosyl-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl-(1→2)-3,4,6-tri-O-benzyl-α-D-mannopyranosyl]-L-serine phenacyl ester ***27****.* To a solution of **26** (340 mg, 0.19 mmol) in CH_2Cl_2 (6.5 ml) was added 90% TFA aq (6.5 ml) at −10 °C. The mixture was stirred at the temperature for 30 min, and carefully neutralized by addition of satd $NaHCO_3$ aq. The mixture was extracted with EtOAc. The extract was washed successively with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was chromatographed on silica gel with toluene/EtOAc (3:1–1:1). The product was further purified by HPLC in Mightysil (250×20 mm) with a program of recycled elution of 40% EtOAc/$CHCl_3$ to give **27** (290 mg, 85%). $[\alpha]_D$=+2.5 (*c*, 1.0). R_f 0.18 (5:3 toluene/EtOAc). ^{1}H NMR: δ 7.86 (br d, 2H, J=7.8 Hz, Ar-*H*), 7.73 (br d, 2H, J=7.3 Hz, Ar-*H*), 7.59 (d, 2H, J=7.3 Hz, Ar-*H*), 7.47 (br d, 1H, J=7.3 Hz, Ar-*H*), 7.39–7.17 (m, 45H, Ar-*H*), 5.89 (d, 1H, J=8.8 Hz, FmocN*H*–), 5.84 (d, 1H, J=7.3 Hz, AcN*H*–), 5.53 (d, 1H, J=16.6 Hz, PhCOCH_2–), 5.26 (d, 1H, J=16.1 Hz, PhCOCH_2–), 5.17 (d, 1H, J=8.3 Hz, H-1b), 4.96 (br s, 1H, H-1a), 4.95 (d, 1H, J=11.2 Hz, PhCH_2–), 4.83–4.74 (m, 4H, 4×PhCH_2–), 4.68 (m, 1H, Ser-αH), 4.60–4.21 (m, 17H, 11×PhCH_2–, H-1c, H-2a, H-3b, Ar$_2$CHCH_2–, Ar$_2$C*H*–), 4.13 (m, 1H, Ser-βH), 4.03 (m, 4H, Ser-βH, H-3a, H-4a, H-4b), 3.83–3.65 (m, 6H, H-4c, H-5a, 2×H-6a, 2×H-6b), 3.58 (m, 1H, H-5b), 3.55–3.39 (m, 5H, H-2c, H-3c, H-5c, 2×H-6c), 3.27 (m, 1H, H-2b), 1.72 (s, 3H, Ac). ^{13}C NMR: δ 102.8 (C-1c), 99.2 (C-1a), 98.2 (C-1b). Anal. Calcd for $C_{102}H_{104}N_2O_{21}\cdot 0.5H_2O$: C, 71.94; H, 6.21; N, 1.65. Found: C, 71.90; H, 6.31; N, 1.59.

4.1.19. N-(9-Fluorenylmethoxycarbonyl)-O-[2,4,6-tri-O-benzyl-3-O-sulfo-β-D-galactopyranosyl-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl-(1→2)-3,4,6-tri-O-benzyl-α-D-mannopyranosyl]-L-serine phenacyl ester ***28****.* A mixture of **27** (277 mg, 0.16 mmol) and $Me_3N\cdot SO_3$ (453 mg, 3.2 mmol) in anhydrous DMF (28 ml) was stirred at 60 °C for 1 h under Ar. Most of the solvent was evaporated with toluene under reduced pressure. The residue was chromatographed on silica gel with $CHCl_3$/MeOH/AcOH (36:4:1) to afford **28** (282 mg, 97%). R_f 0.36 (36:4:1 $CHCl_3$/MeOH/AcOH). ^{1}H NMR (CD_3OD): δ 7.78 (br d, 2H, J=7.3 Hz, Ar-*H*), 7.61 (br d, 2H, J=7.3 Hz, Ar-*H*), 7.51–7.41 (m, 4H, Ar-*H*), 7.32–7.00 (m, 45H, Ar-*H*), 5.43 (d, 1H, J=16.6 Hz, PhCOCH_2–), 5.24 (d, 1H, J=16.6 Hz, PhCOCH_2–), 5.03 (d, 1H, J=11.2 Hz, PhCH_2–), 4.90–4.79 (m, 4H, H-1a, H-1b, 2×PhCH_2–), 4.72–4.66 (m, 2H, 2×PhCH_2–), 4.60–4.51 (m, 3H, Ser-αH, 2×PhCH_2–), 4.43–3.35 (m, 6H, H-1c, H-3c, 4×PhCH_2–), 4.30–4.17 (m, 7H, H-2a, 4×PhCH_2–, Ar$_2$CHCH_2–), 4.17–3.97 (m, 4H, PhCH_2–, Ar$_2$C*H*–, 2×Ser-βH), 3.87–3.23 (m, 16H, H-3a, H-4a, H-5a, 2×H-6a, H-2b, H-3b, H-4b, H-5b, 2×H-6b, H-2c, H-4c, H-5c, 2×H-6c), 1.78 (s, 3H, Ac). ^{13}C NMR: δ 103.2 (C-1c), 99.9 (C-1b), 99.2 (C-1a).

MALDI TOF MS: calcd for $C_{102}H_{103}N_2Na_2O_{24}S$: *m/z* 1817.6, for $C_{102}H_{103}KN_2NaO_{24}S$: *m/z* 1833.6. Found: *m/z* 1816.3 and 1832.3. Anal. Calcd for $C_{102}H_{103}N_2NaO_{24}S\cdot H_2O$: C, 67.54; H, 5.83; N, 1.54. Found: C, 67.81; H, 5.88; N, 1.55.

4.1.20. N-(9-Fluorenylmethoxycarbonyl)-O-[2,3,4-tri-O-benzyl-6-O-(4-methoxyphenyl)methyl-β-D-galactopyranosyl-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl-(1→2)-3,4,6-tri-O-benzyl-α-D-mannopyranosyl]-L-serine phenacyl ester ***29****.* In a similar procedure described for **26**, fluoride **24** (276 mg, 0.20 mmol) and **25** (115 mg, 0.26 mmol) were reacted with Cp_2ZrCl_2 (119 mg, 0.41 mmol), $AgClO_4$ (166 mg, 0.80 mmol) and MS 4 Å (2.7 g) in anhydrous CH_2Cl_2 (8 ml) at −40 to 0 °C for 2 h under Ar. The crude product was chromatographed on Bio-beads S X1 in toluene, and then on silica gel with toluene/EtOAc (2:1) to give **29** (272 mg, 75%) and the β-isomer (18 mg, 5%).

4.1.20.1. Compound ***29****.* $[\alpha]_D$=+2.8 (*c*, 1.0). R_f 0.25 (2:1 toluene/EtOAc). ^{1}H NMR: δ 7.87 (d, 2H, *J*=7.8 Hz, Ar-*H*), 7.73 (d, 2H, *J*=7.8 Hz, Ar-*H*), 7.59 (d, 2H, *J*=7.3 Hz, Ar-*H*), 7.46 (d, 2H, *J*=7.3 Hz, Ar-*H*), 7.38–7.12 (m, 47H, Ar-*H*), 6.82 (d, 2H, *J*=8.8 Hz, Ar-*H*), 5.87 (d, 1H, *J*=8.8 Hz, FmocN*H*–), 5.79 (d, 1H, *J*=7.3 Hz, AcN*H*–), 5.53 (d, 1H, *J*=16.1 Hz, PhCOCH_2–), 5.26 (d, 1H, *J*=16.6 Hz, PhCOCH_2–), 5.16 (d, 1H, *J*=7.8 Hz, H-1b), 4.98 (br s, 1H, H-1a), 4.96 (d, 1H, *J*=11.2 Hz, ArCH_2–), 4.95 (d, 1H, *J*=11.7 Hz, ArCH_2–), 4.81 (br d, 2H, *J*=10.7 Hz, 2×ArCH_2–), 4.75–4.64 (m, 7H, 6×ArCH_2–, Ser-αH), 4.57–4.14 (m, 15H, 8×ArCH_2–, H-1c, H-2a, H-3b, Ar_2CHCH_2–, Ar_2C*H*–, Ser-βH), 4.02–3.28 (m, 17H, Ser-βH, H-4b, H-3a, H-4c, H-2c, H-4a, H-5a, 2×H-6a, 2×H-6b, H-5b, H-5c, H-3c, H-2b, 2×H-6c), 3.77 (s, 3H, CH_3O–), 1.70 (s, 3H, Ac). ^{13}C NMR: δ 102.8 ($^1J_{C-H}$=162.2 Hz, C-1c), 99.1 ($^1J_{C-H}$=169.7 Hz, C-1a), 98.4 ($^1J_{C-H}$=163.0 Hz C-1b). Anal. Calcd for $C_{110}H_{112}N_2O_{24}\cdot 4H_2O$: C, 70.05; H, 6.41; N, 1.49. Found: C, 69.87; H, 6.09; N, 1.58.

4.1.20.2. β-Isomer. $[\alpha]_D$=−19.8 (*c*, 0.9). R_f 0.32 (2:1 toluene/EtOAc). ^{1}H NMR: δ 7.88 (br d, 2H, *J*=6.8 Hz, Ar-*H*), 7.70 (br d, 2H, *J*=6.3 Hz, Ar-*H*), 7.61 (br, 2H, Ar-*H*), 7.36–7.11 (m, 49H, Ar-*H*), 6.81 (br d, 2H, *J*=8.8 Hz, Ar-*H*), 6.45 (br d, 1H, *J*=7.3 Hz, FmocN*H*–), 6.08 (br d, 1H, *J*=7.8 Hz, AcN*H*–), 5.39 (br s, 2H, PhCOCH_2–), 4.99–4.84 (m, 4H, H-1b, 3×ArCH_2–), 4.81–4.63 (m, 6H, Ser-αH, 5×ArCH_2–), 4.55–3.99 (m, 18H, 2×Ser-βH, H-1a, H-1c, H-3b, 10×ArCH_2–, Ar_2CHCH_2–, Ar_2C*H*–), 3.75–3.17 (m, 16H, H-4b, H-3a, H-4c, H-2c, H-4a, H-5a, 2×H-6a, 2×H-6b, H-5b, H-5c, H-3c, H-2b, 2×H-6c), 3.83 (s, 3H, CH_3O–), 1.87 (s, 3H, Ac). ^{13}C NMR: δ 103.0 ($^1J_{C-H}$=161.4 Hz, C-1c), 101.9 ($^1J_{C-H}$=158.1 Hz, C-1a), 99.8 ($^1J_{C-H}$=159.7 Hz, C-1b). MALDI TOF MS: calcd for $C_{110}H_{112}N_2O_{22}$: *m/z* 1835.7 $(M+Na)^+$. Found: *m/z* 1836.4. HRMS: calcd for $C_{110}H_{112}N_2NaO_{22}$: *m/z* 1835.7604. Found: *m/z* 1835.7672.

4.1.21. N-(9-Fluorenylmethoxycarbonyl)-O-[2,3,4-tri-O-benzyl-β-D-galactopyranosyl-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl-(1→2)-3,4,6-tri-O-benzyl-α-D-mannopyranosyl]-L-serine phenacyl ester ***30****.* Compound **29** (340 mg, 0.19 mmol) was stirred with 90% TFA aq (6.5 ml) in CH_2Cl_2 (6.5 ml) at −10 °C for 30 min. The reaction was worked-up as described for **27**, and the crude product was purified by column chromatography and then by HPLC to afford **30** (290 mg, 85%). $[\alpha]_D$=+7.7 (*c*, 1.0). R_f 0.18 (5:3 toluene/EtOAc). ^{1}H NMR: δ 7.85 (d, 2H, *J*=7.3 Hz, Ar-*H*), 7.71 (d, 2H, *J*=7.3 Hz, Ar-*H*), 7.59 (d, 2H, *J*=7.3 Hz, Ar-*H*), 7.47–7.17 (m, 47H, Ar-*H*), 5.90–5.86 (m, 2H, FmocN*H*–, AcN*H*–), 5.52 (d, 1H, *J*=16.1 Hz, PhCOCH_2–), 5.24 (d, 1H, *J*=16.6 Hz, PhCOCH_2–), 5.19 (d, 1H, *J*=7.8 Hz, H-1b), 4.99–4.93 (m, 3H, H-1a, 2×PhCH_2–), 4.85–4.81 (m, 2H, 2×PhCH_2–), 4.76 (br s, 2H, PhCH_2–), 4.71 (br s, 2H, PhCH_2–), 4.68 (m, 1H, Ser-αH), 4.58–4.42 (m, 8H, 7×PhCH_2–, H-1c), 4.37–4.21 (m, 6H, PhCH_2–, H-2a, H-3b, Ar_2CHCH_2–, Ar_2C*H*–), 4.14 (br dd, 1H, *J*=3.0, 10.3 Hz, Ser-βH), 4.01 (br dd, 1H, *J*=2.9, 10.3 Hz, Ser-βH), 3.96–3.89 (m, 3H, H-3a, H-4b, H-4a), 3.81–3.64 (m, 7H, H-2c, H-4c, H-5a, 2×H-6a, 2×H-6b), 3.62–3.53 (m, 2H, H-5b, H-6c), 3.39 (dd, 1H, *J*=2.4, 9.8 Hz, H-3c), 3.30 (dd, 1H, *J*=4.4, 11.2 Hz, H-6c), 3.23 (br d, 1H, *J*=8.8 Hz, H-2b), 3.18 (dd, 1H, *J*=4.4, 7.8 Hz, H-5c), 1.73 (s, 3H, Ac). ^{13}C NMR: δ 102.8 (C-1c), 99.1 (C-1a), 98.2 (C-1b). Anal. Calcd for $C_{102}H_{104}N_2O_{21}\cdot H_2O$: C, 71.56; H, 6.24; N, 1.64. Found: C, 71.52; H, 6.22; N, 1.74.

4.1.22. N-(9-Fluorenylmethoxycarbonyl)-O-[2,3,4-tri-O-benzyl-6-O-sulfo-β-D-galactopyranosyl-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl-(1→2)-3,4,6-tri-O-benzyl-α-D-mannopyranosyl]-L-serine phenacyl ester ***31****.* In a similar manner as described for **28**, compound **30** (170 mg, 0.10 mmol) was treated with $Me_3N\cdot SO_3$ (279 mg, 2.00 mmol) in DMF (17 ml), and the product was purified by chromatography on silica gel to give **31** (125 mg, 76%). R_f 0.44 (38:2:1 $CHCl_3$/MeOH/AcOH). ^{1}H NMR ($CDCl_3$–CD_3OD): δ 7.86 (d, 2H, *J*=8.3 Hz, Ar-*H*), 7.74 (d, 2H, *J*=7.3 Hz, Ar-*H*), 7.68 (m, 2H, Ar-*H*), 7.61 (m, 2H), 7.45–7.10 (m, 45H, Ar-*H*), 5.55 (d, 1H, *J*=16.6 Hz, PhCOCH_2–), 5.33 (d, 1H, *J*=16.6 Hz, PhCOCH_2–), 5.00 (br s, 1H, H-1a), 4.97–4.92 (m, 2H, 2×PhCH_2–), 4.80 (d, 1H, *J*=11.2 Hz, PhCH_2–), 4.76–4.67 (m, 8H, 6×PhCH_2–, H-1b, Ser-αH), 4.54–4.19 (m, 12H, 7×PhCH_2–, H-1c, H-2a, Ar_2CHCH_2–, H-6c), 4.12–3.35 (m, 19H, Ar_2C*H*–, 2×Ser-βH, H-6c, H-3b, H-3a, H-2c, H-2b, H-4a, H-4b, H-4c, H-5a, H-5b, H-5c, 2×H-6a, 2×H-6b, H-3c), 1.85 (s, 3H, Ac). ^{13}C NMR: δ 102.1 (C-1c), 99.0 (C-1b), 97.9 (C-1a). MALDI TOF MS: calcd for $C_{102}H_{103}N_2Na_2O_{24}S$: *m/z* 1817.6, for $C_{102}H_{103}KN_2NaO_{24}S$: *m/z* 1833.6. Found: *m/z* 1818.2, 1834.0. HRMS: calcd for $C_{102}H_{103}N_2Na_2O_{24}S$: *m/z* 1817.6416. Found: *m/z* 1817.6411.

4.1.23. N-(9-Fluorenylmethoxycarbonyl)-O-[2,4,6-tri-O-benzyl-3-O-sulfo-β-D-galactopyranosyl-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl-(1→2)-3,4,6-tri-O-benzyl-α-D-mannopyranosyl]-L-serine ***32****.* A mixture of **28** (217 mg, 0.12 mmol), powdered Zn (1.85 g, 28.3 mmol), and AcOH (1.85 ml, 32.3 mmol) in CH_2Cl_2 (17 ml) was stirred at room temperature for 5 h. Then the insoluble material was filtered through Celite and washed with $CHCl_3$/MeOH (9:1). The filtrate and washings were concentrated with toluene. The residue was chromatographed on silica gel with $CHCl_3$/MeOH/AcOH (36:4:1) to give **32** (196 mg, 97%). R_f 0.38 (18:2:1 $CHCl_3$/MeOH/AcOH). ^{1}H NMR (CD_3OD): δ 7.72 (br d, 2H, *J*=7.3 Hz, Ar-*H*), 7.62–7.56 (m, 2H, Ar-*H*), 7.47 (br d, 2H, *J*=7.3 Hz, Ar-*H*), 7.37–7.10 (m, 42H, Ar-*H*), 5.13 (d, 1H, *J*=11.7 Hz, PhCH_2–), 5.00 (br d, 2H, *J*=11.2 Hz, 2×PhCH_2–), 4.85–4.62 (m, 5H, H-1b, H-1a, 3×PhCH_2–), 4.56–4.42 (m, 6H, H-3c, H-1c, 4×PhCH_2–), 4.41–4.11 (m, 11H, Ser-αH, 6×PhCH_2–, ArCHCH_2–, H-2a, Ar_2C*H*–), 4.06–3.90 (m, 5H, Ser-βH, H-3b, H-3a, H-6a), 3.82–3.31 (m, 13H, H-4a, H-5a, H-6a, H-2b, H-4b, H-5b, 2×H-6b, H-2c, H-4c, H-5c, 2×H-6c). ^{13}C NMR: δ 102.3 (C-1c), 98.9 and 98.0 (C-1a, C-1b). MALDI TOF MS: calcd for $C_{94}H_{97}N_2Na_2O_{23}S$: *m/z* 1699.6, for $C_{94}H_{97}KN_2NaO_{23}S$: *m/z* 1715.6. Found: *m/z* 1699.9, 1715.9. HRMS: calcd for $C_{94}H_{97}N_2Na_2O_{23}S$: *m/z* 1699.5998. Found: *m/z* 1699.5950.

4.1.24. N-(9-Fluorenylmethoxycarbonyl)-O-[2,3,4-tri-O-benzyl-6-O-sulfo-β-D-galactopyranosyl-(1→4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl-(1→2)-3,4,6-tri-O-benzyl-α-D-mannopyranosyl]-L-serine ***33****.* Compound **31** (125 mg, 0.07 mmol) was treated with Zn (1.05 g, 16.1 mmol) and AcOH (1.05 ml, 18.4 mmol) in CH_2Cl_2 (10 ml) as described for **32**. The crude product was chromatographed on silica gel with $CHCl_3$/MeOH/AcOH (38:2:1) to afford **33** (95 mg, 82%). R_f 0.15 (38:2:1 $CHCl_3$/MeOH/AcOH). ^{1}H NMR (CD_3OD/$CDCl_3$): δ 7.74 (br d, 2H, *J*=7.3 Hz, Ar-*H*), 7.62 (br, 2H, Ar-*H*), 7.37–7.16 (m, 36H, Ar-*H*), 4.96–4.63 (m, 14H, H-1a, H-1b, H-1c, Ser-αH, 10×PhCH_2–), 4.60–4.10 (m, 12H, 6×PhCH_2–, Ar_2CHCH_2–, Ar_2C*H*–, 2×Ser-βH, H-6c), 4.05–3.35 (m, 17H, H-2a, H-3a, H-4a, H-5a, 2×H-6a, H-2b, H-3b, H-4b, H-5b, 2×H-6b, H-2c, H-4c, H-5c, H-6c), 3.40 (br d, 1H, *J*=10.7 Hz, H-3c), 1.84 (s, 3H, Ac). ^{13}C NMR:

δ 100.4 (C-1c), 97.2 and 96.8 (C-1a, C-1b). MALDI TOF MS: calcd for $C_{94}H_{97}N_2Na_2O_{23}S$: *m*/*z* 1699.6, for $C_{94}H_{97}KN_2NaO_{23}S$: *m*/*z* 1715.6. Found: *m*/*z* 1699.7 and 1715.7. HRMS: calcd for $C_{94}H_{97}KN_2NaO_{23}S$: *m*/*z* 1715.5737. Found: *m*/*z* 1715.5745.

*4.1.25. Debenzylation (for **34** and **35**).* Sulfo-glycoserine **34**/**35** (5.0 mg, 2.8 μmol) was dissolved in a mixture of TFA/DMS/*m*-cresol (5:3:1, 54 μl) and the mixture was stirred at −15 °C. On the other hand, a mixture of TFA/DMS/*m*-cresol (5:3:1) containing TfOH (10% v/v) was also cooled at −15 °C. Then the TfOH mixture (30 μl, 34 μmol) was added to the reactant mixture. The resultant mixture was stirred for 7 h at −15 °C, before the reaction was quenched by adding cold (−80 °C) ether (180 μl) containing pyridine (2.8 μl, 35 μmol). The mixture diluted with additional cold ether was vigorously stirred with a vortex mixer. The precipitate was separated by centrifugation, the ethereal layer was decanted, and the residual precipitate was washed further five times with ether by vortex mixing, centrifugation, and decantation. The crude product was dried under vacuum, dissolved in 50% aq CH_3CN, and analyzed by HPLC using a reversed column (Inertsil ODS-SP, 4.6×150 mm) with a gradient elution of aq CH_3CN containing 0.1% TFA (Fig. 2).

*4.1.26. Glycopeptide **40**.* Commercial Fmoc-CLEAR amide resin (521 mg, 0.25 mmol) was subjected to an automated synthesis of the peptide to produce an undecapeptide (PAIAPPTETMA)-resin by the *Fastmoc* program of the synthesizer, using 20% piperidine/NMP for N-deprotection and HBTU/HOBt as the condensing agent. *t*-Bu group was employed for the protection of Thr and Glu, respectively. A part of the peptide resin (84 mg, 27 μmol) was transferred into a polypropylene test tube, to which a solution of **32** (90 mg, 80 μmol) in NMP (1.4 ml), 0.1 M HOBt/NMP (81 μl, 81 μmol), and 0.1 M DCC/NMP (81 μl, 81 μmol) were added. The mixture was stirred for 7 h with a vortex mixer at 50 °C in an oven, and filtered. The resin was washed several times with NMP and CH_2Cl_2, and again submitted to the automated procedure using the synthesizer to complete the icosapeptide chain. To the resin dried in vacuo, was added an ice-cooled solution of reagent K (TFA/phenol/water/thioanisole/ethanedithiol, 33:2:2:2:1, 1.5 ml). The mixture was stirred with the vortex mixer at 0 °C to room temperature for 1 h. Then the resin was filtered off, and the volatile materials in the mixture were evaporated in a stream of N_2. Ether was added to the residue to precipitate the product, which was separated by centrifugation. The precipitate was washed several times by suspending in ether and then centrifuging to give a crude product, to which was added a mixture of TFA/DMS/*m*-cresol (5:3:1, 288 μl), and the mixture was cooled at −15 °C. TfOH (32 μl, 0.36 mmol) was added to the mixture and the plastic vessel was shaken in the cooling bath. The reaction mixture was left at −15 °C for 7 h, before the reaction was terminated by the addition of ether cooled at −80 °C. The mixture was centrifuged to separate the debenzylated product, which was washed three times with ether and centrifuged as mentioned above to give a precipitate. The crude product was dissolved in 50% CH_3CN aq water, and purified by preparative HPLC. The major fraction was collected and lyophilized to afford **40** (16.6 mg, 17% overall yield based on the amino acid analysis). MALDI TOF MS (negative): calcd for $C_{109}H_{182}N_{25}O_{46}S_2$ $[M-H]^-$: *m*/*z* 2641.2. Found: *m*/*z* 2642.0. Amino acid analysis: $Thr_{5.29}$ $Ser_{2.58}$ $Glu_{1.57}$ $Pro_{6.24}$ $Ala_{4.23}$ $Val_{1.41}$ $Met_{0.89}$ $Ile_{2.28}$ $Arg_{1.32}$.

Acknowledgements

This work was supported by a grant-in-aid for creative scientific research (17GS0420) from the Japan Society for the Promotion of Science, and in part by a grant-in-aid for scientific research from the Ministry of Education, Sports, Science and Technology of Japan (20380069). We thank the chemical analysis team at Riken for the combustion analyses, and Prof. J. Tamura, Tottori University, for the helpful discussion on the preparation of sulfated samples. We also thank Tokai University for its support via a grant-in-aid for high technology research.

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