JOC Article

An Orthogonally Protected α,α-Bis(aminomethyl)-β-alanine Building Block for the Construction of Glycoconjugates on a Solid Support

Johanna Katajisto,* Tuomas Karskela, Petri Heinonen, and Harri Lönnberg

Department of Chemistry, University of Turku, FIN-20014 Turku, Finland

jokrka@utu.fi

Received June 13, 2002

Synthetic glycoclusters are extensively used as mimetics of naturally occurring, multivalent carbohydrate ligands in various glycobiological applications. Their preparation, however, is far from trivial, and it still is a limiting factor in the study of carbohydrate binding. We herein report the synthesis of an orthogonally protected building block, *N*-Alloc-*N*′-Boc-*N*″-Fmoc-α,α-bis(aminomethyl)-β-alanine (**1**), and its use in the preparation of triantennary peptide glycoclusters (**21**−**24**) on a solid support. The assembly of the clusters involves removal of the amino protections of the solid-supported branching unit **1** in the order Fmoc, Boc, and Alloc, and subsequent coupling of peracetylated *O*-(glycopyranosyl)-*N*-Fmoc-L-serine pentafluorophenyl esters (galactose, glucose, mannose, and ribose) to each amino group exposed.

Introduction

Multivalency of the interactions between carbohydrates and carbohydrate-binding proteins[1] or nucleic acids[2] has recently become a subject of considerable interest. To learn more about the factors governing the strength of these cluster effects, a variety of multivalent oligosaccharide and glycoconjugate mimetics, including glycoclusters,[3] glycodendrimers,[4] glycopeptides,[5] cyclodextrin-based glycoclusters,[6] and glycopolymers[7] have been synthesized. Typically these syntheses involve coupling of a single type of sugar moiety to a multivalent scaffold. However, in nature a number of different sugar ligands may be essential for a biological recognition process. Despite this, only a few procedures that allow the construction of glycoclusters from different sugar moieties have been described. Lindhorst et al. recently reported a synthesis of "mixed type" oligosaccharide mimetics based on an orthogonally derivatized galactoside scaffold.[8] This kind of synthesis based on the use of an orthogonally derivatized or protected core molecule should provide, when carried out on a polymeric support, an opportunity to combine the benefits of the solid-phase synthesis and the efficiency of parallel synthesis upon creation of diverse glycocluster libraries.

We now report on a straightforward procedure that allows construction of triantennary peptide glycoclusters by parallel synthesis on a solid support. The key building block is orthogonally protected α,α-bis(aminomethyl)-β-alanine (**1**) that bears conventional Fmoc, Boc, and Alloc protective groups on the three amino functions and a free carboxylic acid group for the attachment to a solid support (Figure 1). The applicability of **1** as a solid-supported scaffold[9] has been demonstrated by preparing four clusters containing six different fully acetylated glycopyranosyl groups. The synthesis involved acylation of each of the amino functions of support-bound **1** with an appropriate *O*-glycosyl-*N*-Fmoc-L-serine pentafluo

(1) (a) Lee, Y. C.; Lee, R. T. *Acc. Chem. Res.* **1995**, *28*, 321. (b) Whitesides, G. M.; Mammen, M.; Choi, S. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2754.

(2) Sreedhara, A.; Cowan, J. A. *J. Biol. Inorg. Chem.* **2001**, *6*, 166.

(3) (a) Lindhorst, T. K.; Dubber, M.; Krallmann-Wenzel, U.; Ehlers, S. *Eur. J. Org. Chem.* **2000**, 2027. (b) Liu, B.; Roy, R. *J. Chem. Soc., Perkin Trans. 1* **2001**, 773. (c) Liu, B.; Roy, R. *Chem. Commun.* **2002**, 594. (d) Dominique, R.; Roy, R. *Tetrahedron Lett.* **2002**, *43*, 395.

(4) (a) Roy, R.; Park, W. K. C.; Wu, Q.; Whang, S. *Tetrahedron Lett.* **1995**, *36*, 4377. (b) Pagé, D.; Aravind, S.; Roy, R. *Chem. Commun.* **1996**, 1913. (c) Jayaraman, N.; Stoddart, J. F. *Tetrahedron Lett.* **1997**, *38*, 6767, (d) Jayaraman, N.; Nepogodiev, S. A.; Stoddart, J. F. *Chem. Eur. J.* **1997**, *3*, 1193. (e) Dubber, M.; Lindhorst, T. K. *Carbohydr. Res.* **1998**, *310*, 35. (f) Langer, P.; Ince, S. J.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3913. (g) Roy, R.; Kim, J. M. *Angew. Chem., Int. Ed.* **1999**, *38*, 369. (h) Grandjean, C.; Rommens, R.; Gras-Masse, H.; Melnyk, O. *Tetrahedron Lett.* **1999**, *40*, 7235. (i) Grandjean, C.; Rommens, R.; Gras-Masse, H.; Melnyk, O. *Angew. Chem., Int. Ed.* **2000**, *39*, 1068. (j) Sadalapure, K.; Lindhorst, T. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 2010. (k) Turnbull, W. B.; Pease, A. R.; Stoddart, J. F. *ChemBioChem* **2000**, *1*, 70. (l) Vrasidas, I.; De Mol, N. J.; Liskamp, R. M. J.; Pieters, R. J. *Eur. J. Org. Chem.* **2001**, 4685. (m) McWatt, M.; Boons, G. J. *Eur. J. Org. Chem.* **2001**, 2535. (n) Turnbull, W. B. *Rev. Mol. Biotech.* **2002**, *90*, 23. (o) Bezouška, K. *Rev. Mol. Biotech.* **2002**, *90*, 269. (p) Roy, R.; Baek, M. *Rev. Mol. Biotech.* **2002**, *90*, 291.

(5) Seeberger, P. H. *Solid Support Oligosaccharide Synthesis and Combinatorial Carbohydrate Libraries*; John Wiley & Sons: New York, 2001; Chapter 13, p 257.

(6) (a) García-López, J. J.; Hernández-Mateo, F.; Isac-García, J.; Kim, J. M.; Roy, R.; Santoyo-González, F.; Vargas-Berenguel, A. *J. Org. Chem.* **1999**, *64*, 522. (b) Roy, R.; Hernández-Mateo, F.; Santoyo-González, F. *J. Org. Chem.* **2000**, *65*, 8743. (c) Furuike, T.; Aiba, S.; Nishimura, S. *Tetrahedron* **2000**, *56*, 9909.

(7) (a) Mortel, K. H.; Weatherman, R. V.; Kiessling, L. L. *J. Am. Chem. Soc.* **1996**, *118*, 2297. (b) Manning, D. D.; Strong, L. E.; Hu, X.; Beck, P. J.; Kiessling, L. L. *Tetrahedron* **1997**, *53*, 11937. (c) Strong, L. E.; Kiessling, L. L. *J. Am. Chem. Soc.* **1999**, *121*, 6193.

(8) Patel, A.; Lindhorst, T. K. *Eur. J. Org. Chem.* **2002**, 79.

(9) For a recent example of flexible solid-phase bound scaffolds, see: (a) Heinonen, P.; Rosenberg, J.; Lönnberg, H. *Eur. J. Org. Chem.* **2000**, *21*, 3647. (b) Virta, P.; Rosenberg, J.; Karskela, T.; Heinonen, P.; Lönnberg, H. *Eur. J. Org. Chem.* **2001**, *18*, 3467. (c) Farcy, N.; De Muynck, H.; Madder, A.; Hosten, N.; De Clercq, P. *Org. Lett.* **2001**, *3*, 4299.

10.1021/jo026053b CCC: $22.00
Published on Web 10/19/2002

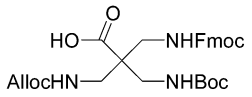
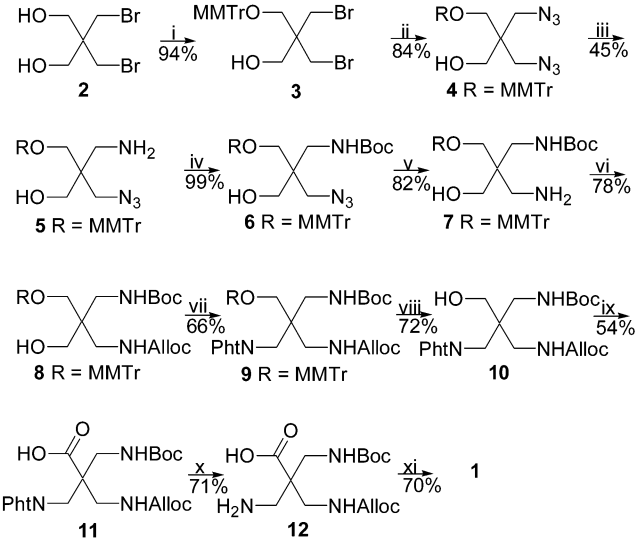


FIGURE 1. Branching agent **1**.

SCHEME 1[a]



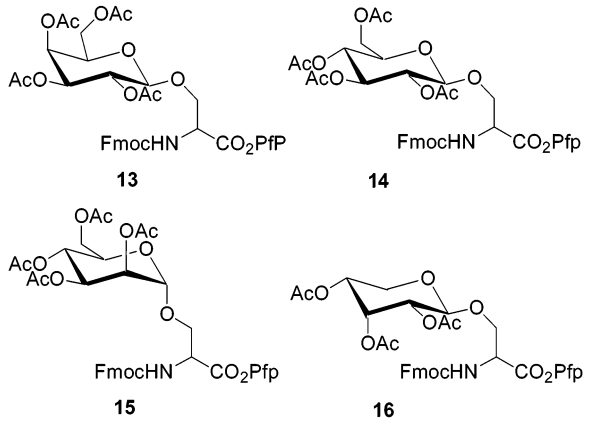
[a] Conditions: (i) MMTrCl, pyridine, (ii) NaN_3, LiCl, DMF, pyridine, (iii) $NaBH_4$, $HS(CH_2)_3SH$, NEt_3, *i*PrOH, (iv) Boc_2O, NaOH, MeCN, (v) PPh_3, NH_3, aq, (vi) AllocCl, NEt_3, dioxane, (vii) phthalimide, PPh_3, DEAD, THF, (viii) I_2, MeOH, CH_2Cl_2, (ix) CrO_3, H_2SO_4, H_2O, acetone, (x) NH_2NH_2, allyl alcohol, DMF, dioxane, (xi) FmocCl, K_2CO_3, H_2O, MeCN.

rophenyl ester after exposing them by removal of the three orthogonal protective groups in the order Fmoc, Boc, and Alloc.

Results and Discussion

***N*-Alloc-*N′*-Boc-*N″*-Fmoc-α,α-bis(aminomethyl)-*β*-alanine (1) (Scheme 1).** The orthogonally protected bis(aminomethyl)-*β*-alanine building block (**1**) was synthesized from commercially available 2,2-bis(bromomethyl)-1,3-propanediol (**2**). The 4-methoxytritylation (MMTr) of one of the hydroxy groups to give **3** was followed by displacement of the bromo substituents with an azide ion yielding **4**. The next step, selective reduction of one of the azido groups of **4** with a combination of sodium borohydride (2 equiv) and 1,3-propanedithiol (0.1 equiv), was the key step of the synthesis. A 24-h treatment at room temperature afforded monoamine **5** in a 45% yield. Despite the relatively low yield this reaction still remarkably shortens the route to the desired tridimensionally, orthogonally protected end product, and hence increases the overall yield. Furthermore, the remaining unreacted starting material (55%) could easily be recycled. When prolonged reaction time or larger excess of the reducing agents was used, a mixture of mono- and diamine products was obtained. Attemps to use alternative reduction methods, such as $SnCl_4$ or PPh_3, either failed completely or caused over-reduction to the diamine. Next, the free amino function was protected with a Boc group to give **6**, and the remaining azido group was then reduced by the Staudinger reaction to yield **7**.[10] Protection of the amino group with allyloxycarbonyl chloride (AllocCl) gave **8**. The third amino function was introduced in a phthaloyl (Pht) protected form by the Mitsunobu reaction to afford **9**.[11] The MMTr group of **9** was removed with iodine in methanol giving **10**,[12] and the deblocked hydroxy function was then transformed to a carboxy group by Jones oxidation to obtain **11**. The concentration of sulfuric acid in the reaction mixture was carefully tuned and hence no sign of the cleavage of the Boc protection was observed. The isolation and purification of **11**, however, turned out to be somewhat difficult, which explains, at least in part, the low yield (54%) for this step. The phthaloyl protection was finally replaced in two steps with Fmoc protection to ensure easier deblocking upon the solid support applications. The hydrazinolysis of the phthaloyl protection proceeded cleanly giving compound **12**, when allyl alcohol was added to the reaction mixture, preventing the loss of the Alloc protection. The Fmoc protection of the deblocked amino group completed the synthesis of **1**.

CHART 1. The Synthesized *O*-Glycosylated *N*-Fmoc-L-serine Pentafluorophenyl Esters (13-16)

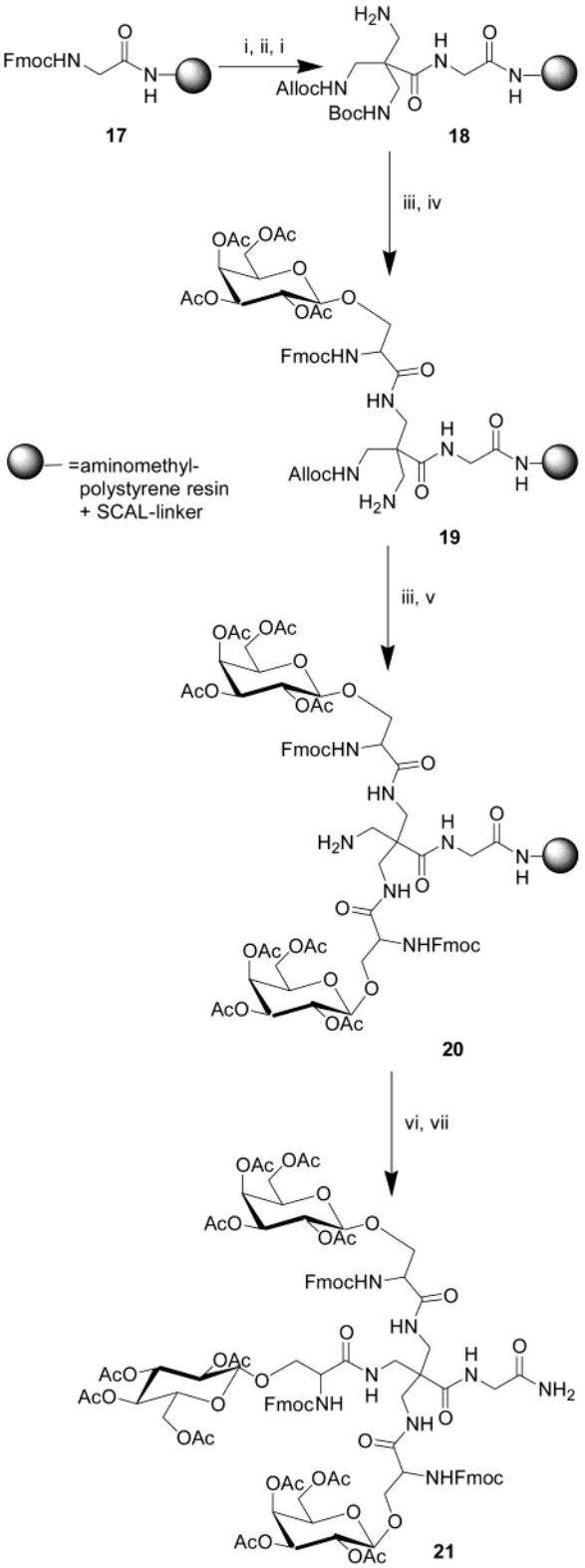


Glycosylated Building Blocks. The pentafluorophenyl ester of *N*-Fmoc-L-serine (Fmoc-Ser-OPfp)[13] was glycosylated with four different *trans*-1,2-glycopyranosyl peracetates [*β*-galactose (*β*-Gal), *β*-glucose (*β*-Glc), α-mannose (α-Man), *β*-ribose (*β*-Rib)] which were either commercially available or easily prepared by acetylation with Ac_2O in pyridine.[14] The conventional boron trifluoride promoted glycosidation in dichloromethane (DCM)[15] afforded the *O*-glycosylated *N*-Fmoc-L-serine pentafluorophenyl esters (Chart 1) in 15 to 41% yields (not optimized).

Carbohydrate Clusters. To assemble the branched glycocluster **21** on a solid support (Scheme 2), an aminomethyl polystyrene support was first derivatized with a safety catch acid labile linker (SCAL, Figure 2), as described previously.[16] A loading of 120 μmol g^{-1} was obtained. The Fmoc group was removed (25% piperidine in DMF), and the support-bound linker was elongated with one *N*-Fmoc-glycine unit to afford **17**. The Fmoc

(10) Staudinger, H.; Meyer, J. *Helv. Chim. Acta* **1919**, *2*, 635.
(11) Mitsunobu, O.; Yamada, M.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 935.
(12) Wahlström, J. L.; Ronald, R. C. *J. Org. Chem.* **1998**, *63*, 6021.
(13) Kisfaludy, L.; Schön, I. *Synthesis* **1983**, 325.
(14) Behrend, R.; Roth, P. *Ann.* **1904**, 359.
(15) (a) Salvador, L. A.; Elofsson, M.; Kihlberg, J. *Tetrahedron* **1995**, *51*, 5643. (b) Kihlberg, J.; Åhman, J.; Walse, B.; Drakenberg, T.; Nilsson, A.; Söderberg-Ahlm, C.; Bengtsson, B.; Olsson, H. *J. Med. Chem.* **1995**, *38*, 161.
(16) Pátek, M.; Lebl, M. *Tetrahedron. Lett.* **1991**, *32*, 3891.

SCHEME 2[a]



[a] Conditions: (i) piperidine, DMF, (ii) **1**, HATU, NEt*i*Pr$_2$, DMF, (iii) **13**, 1-hydroxybenzotriazole (HOBt), DMF, (iv) TFA, DCM, (v) Pd(OAc)$_2$, Bu$_3$SnH, PPh$_3$, AcOH, DMF, (vi) **14**, HOBt, DMF, (vii) 0.1% HBr in AcOH, TFA, DCM.

protection was again removed, and the orthogonally protected branching unit **1** was coupled to the exposed amino function. The first three coupling steps were all performed by making use of a standard *O*-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU) activation.[17] The Fmoc protected amino group was then deblocked to give **18**, and the first pentafluorophenyl activated *O*-glycosylserine building block (**13**) was introduced. Subsequently, the Boc protection was removed from the solid-supported branching unit (25% TFA in DCM) to afford **19** and the second galactosylated serine building block (**13**) was coupled to the exposed amino group. Finally, the Alloc protection was removed via a palladium-catalyzed hydrostannolysis by Bu$_3$SnH giving **20**.[18] The reaction conditions were carefully tuned in order to avoid the cleavage of the Fmoc protections. Slightly acidic reaction conditions and short reaction times were found to be optimal. Coupling with the third glycosylated serine building block (**14**) then afforded the desired resin-bound glycocluster. Cleavage from the support by consecutive treatments with 0.1% HBr in AcOH (2 h at room temperature) and 50% TFA in DCM (2 h at room temperature), followed by semi-preparative HPLC purification, gave the protected glycocluster **21** in a 10% overall yield. After HPLC purification, the product was characterized by HPLC/Electrospray Ionization (ESI)-MS (Table 1; entry 1), HRMS, and ^{1}H and ^{13}C NMR spectroscopy (including PDQF and HMBC spectra). When NMR spectra on the glycocluster

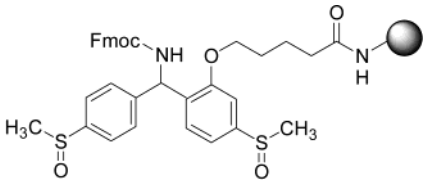
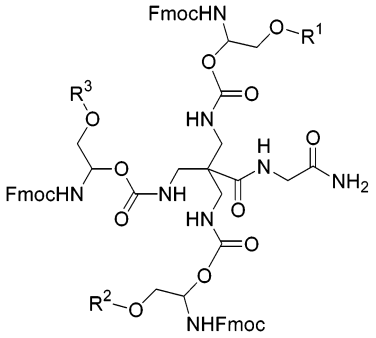


FIGURE 2. Aminomethyl polystyrene support derivatized with a SCAL linker.

TABLE 1. The Synthesized Glycoclusters 21−24 and Their Required (M_{req}) and Found ($[M + H]^+_{found}$, LC/ESI-MS) Relative Molecular Masses



21-24

entry	glyco-cluster	PerAc-R R^1	PerAc-R R^2	PerAc-R R^3	$[M + H]^+_{found}$	M_{req}
1	**21**	β-D-Gal	β-D-Gal	β-D-Glc	2123.7	2122.1
2	**22**	β-D-Gal	β-D-Rib	α-D-Man	2051.5	2050.0
3	**23**	β-D-Gal	β-D-Glc	α-D-Man	2123.6	2122.1
4	**24**	β-D-Rib	β-D-Gal	β-D-Glc	2051.5	2050.0

(17) (a) Carpino, L. A. *J. Am. Chem. Soc.* **1993**, *115*, 4397. (b) Carpino, L. A.; El-Faham, A.; Minor, C.; Albericio, F. *J. Chem. Soc., Chem. Commun.* **1994**, 201.

(18) (a) Guibé, F.; Dangles, O.; Balavoine, G. *Tetrahedron Lett.* **1986**, *27*, 2365. (b) Guibé, F.; Zhang, H. X.; Balavoine, G. *Tetrahedron Lett.* **1988**, *29*, 623.

21 were recorded, elevation of the temperature (90 °C) was necessary to get an instructive spectrum without the signal broadening. No sign of anomerization of the sugar residues during the total synthesis of **21** could be detected. The ^{1}H NMR spectrum of **21** exhibited a signal at δ 4.64 ppm due to the anomeric proton of the β-D-galactose residues. The signal due to the anomeric proton of the β-D-glucose residue could be observed as part of a complex signal containing several other protons at 4.18−4.30 ppm. No signals referring to the α-anomeric protons (expectedly at a lower field) could be observed.

The universality of the procedure developed for the construction of diverse glycoclusters was demonstrated by preparing three other glycoclusters (**22**−**24**) in a smaller scale by essentially the same procedure. Analytical RP-HPLC purification of the crude products yielded chromatographically pure compounds, which were identified by HPLC/ESI-MS (Table 1; entries 2−4). Glycoclusters derived from three different sugars, such as compounds **22**−**24**, contain an additional chiral center in the branching unit **1**, and hence the products are obtained as a mixture of two diastereomers, which, however, could not be separated by HPLC.

As a further extension of the present study, the conversion of the synthesized glycoclusters into a globally deprotected form was demonstrated by using glycocluster **22** as a model compound. Deprotection of the amino acid moiety was effected by Fmoc removal (20% piperidine in DMF), and the amino groups exposed were capped by acetylation. The glycocluster was then detached from the solid support and subjected to deacylation by the conventional base-catalyzed transesterification in methanolic sodium methoxide.[19] The completion of the deprotection was verified by HPLC/ESI-MS.

Experimental Section

General Methods and Materials. See the Supporting Information for detailed information. The NMR spectra were recorded at 200, 400, or 500 MHz. ^{1}H NMR spectra were recorded, unless otherwise stated, in deuteriochloroform, and the chemical shifts are given in ppm from internal TMS. The coupling constants are reported in hertz. ^{13}C NMR spectra were recorded, unless otherwise stated, in deuteriochloroform. The mass spectra were recorded using EI, ESI or FAB ionization methods.

Of the 1,2-*trans*-glycosyl peracetates used as starting materials, β-D-galactose pentaacetate, α-D-mannose pentaacetate, and β-D-ribose tetraacetate were commercial products, while β-D-glucose pentaacetate was prepared by acetylating the corresponding monosaccharide with Ac_2O in pyridine.[14]

2,2-Bis(bromomethyl)-3-(4-methoxytrityloxy)propanol (3). 2,2-Bis(bromomethyl)-1,3-propanediol (**2**, 30.0 g, 115 mmol) was dried by repeated coevaporation with dry pyridine, and it was then dissolved in dry pyridine (200 mL). 4-Methoxytrityl chloride (17.7 g, 57.3 mmol) was added to this solution and the reaction mixture was stirred overnight at room temperature. Pyridine was removed in vacuo, and the residue was subjected to normal DCM/aq $NaHCO_3$ workup. The organic phase was dried with Na_2SO_4 and evaporated to dryness, and the oily residue was purified by silica gel chromatography with DCM as an eluent. Compound **3** was obtained as a white solid foam in a 94% yield (29.0 g). The ^{1}H and ^{13}C NMR spectra were identical with those published in the literature.[9a] HRMS (EI): M^+ calcd 532.0249, obsd 532.0256.

2,2-Bis(azidomethyl)-3-(4-methoxytrityloxy)propanol (4). Compound **3** (29.0 g, 54.3 mmol), NaN_3 (17.7 g, 272 mmol), and a catalytic amount of LiCl were dissolved in a mixture of pyridine and DMF (400 mL, 1:4, v/v). The mixture was refluxed for 5 h and solvents were removed by evaporation under reduced pressure. The residue was dissolved in DCM, washed with water, dried with Na_2SO_4, and evaporated to dryness. The oily crude product was purified by silica gel chromatography (DCM) to afford **4** as a colorless oil in an 84% yield (20.9 g). The ^{1}H and ^{13}C NMR spectra were identical with those published in the literature.[9a] HRMS (EI): M^+ calcd 458.2066, obsd 458.2062.

2-Aminomethyl-2-azidomethyl-3-(4-methoxytrityloxy)-propanol (5). Compound **4** (19.2 g, 41.8 mmol), 1,3-propanedithiol (0.4 mL, 4 mmol), and triethylamine (TEA; 11.6 mL, 83.6 mmol) were dissolved in 2-propanol (300 mL). $NaBH_4$ (1.90 g, 50.2 mmol) was portionwise added under vigorous stirring, and the mixture was shaken overnight at room temperature. The solvent was evaporated and the residue was dissolved in DCM. The solution was washed with 10% NaOH in brine. The organic phase was dried with Na_2SO_4 and evaporated to dryness. The crude product was purified by silica gel chromatography (CH_2Cl_2/MeOH/TEA 92:6:2, v/v/v), yielding **5** as a colorless oil in a 45% yield (7.9 g). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.18−7.41 (m, 12H), 6.82 (d, 2H), 3.77 (s, 3H), 3.63 (s, 2H), 3.49 (q_{AB}, 2H, J = 12.2 Hz), 3.05 (s, 2H), 2.79 (q_{AB}, 2H, J = 12.6 Hz,), 2.14 (br s, 2H); ^{13}C NMR (DMSO-d_6, 50 MHz) δ 158.1, 144.4, 135.0, 130.0, 127.9, 127.8, 126.7, 113.1, 85.3, 61.9, 61.3, 54.9, 52.0, 45.7, 44.7; HRMS (EI) M^+ calcd 432.2161, obsd 432.2164.

2-Azidomethyl-2-(*tert*-butyloxycarbonyl)aminomethyl-3-(4-methoxytrityloxy)propanol (6). Compound **5** (2.86 g, 6.6 mmol) was dissolved in acetonitrile (50 mL), and aq NaOH (1 M, 9.9 mL, 9.9 mmol) and Boc_2O (1.59 g, 7.3 mmol) were added. After the reaction was complete according to TLC (10% MeOH in DCM), DCM (20 mL) was added and the mixture was washed with aq $NaHCO_3$ and dried with Na_2SO_4. The solvent was evaporated, and the resulting crude product was chromatographed on a silica gel column eluting with a mixture of EtOAc and petroleum ether (3:7, v/v). Compound **6** was obtained as a white solid foam in a 99% yield (3.46 g). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.44−7.48 (m, 4H), 7.30−7.35 (m, 6H), 7.19−7.26 (m, 2H), 6.86 (d, 2H), 4.11 (m, 1H), 3.80 (s, 3H), 3.67 (t, 1H, J = 8.6 Hz,), 3.49 (q_{AB}, 2H, J = 11.9 Hz,), 3.34 (t, 1H, J = 9.0 Hz,), 3.17−3.22 (m, 2H), 3.11 (dd, 1H, J = 14.4 and 7.8 Hz), 2.87 (dd, 1H, J = 14.4 and 5.8 Hz,), 2.80 (d, 1H, J = 9.3 Hz,), 1.40 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.6, 157.5, 144.2, 143.9, 130.3, 128.3, 128.2, 127.9, 127.9, 113.2, 86.4, 79.9, 60.9, 55.2, 52.0, 45.8, 40.1, 28.2; HRMS (EI) M^+ calcd 532.2686, obsd 532.2685.

2-Aminomethyl-2-(*tert*-butyloxycarbonyl)aminomethyl-3-(4-methoxytrityloxy)propanol (7). Compound **6** (7.3 g, 13.7 mmol) and triphenylphosphine (10.8 g, 41.4 mmol) were dissolved in dry THF. The mixture was stirred at room temperature and the formation of iminophosphorane intermediate was monitored by TLC (30% EtOAc in petroleum ether). Upon completion of the reaction, water (1.2 mL, 68.5 mmol) and 33% aq ammonia (1 mL) were added, and the mixture was refluxed for 3 h. The solvent was removed by evaporation. Purification of the crude product on a silica gel column (5% MeOH in DCM) gave **7** as an almost colorless oil in an 82% (5.71 g) yield. The ^{1}H and ^{13}C NMR spectra were identical with those published in the literature.[9c] HRMS (ESI) $[M + H]^+$ calcd 507.2859, obsd 507.2869.

2-(Allyloxycarbonyl)aminomethyl-2-(*tert*-butyloxycarbonyl)aminomethyl-3-(4-methoxytrityloxy)propanol (8). Compound **7** (5.71 g, 11.3 mmol) and triethylamine (1.88 mL, 13.5 mmol) were dissolved in dioxane (60 mL). The solution was cooled to 0 °C and AllocCl (1.44 mL, 13.5 mmol) was added dropwise under vigorous stirring. The reaction was monitored by TLC (5% MeOH in CH_2Cl_2). Upon completion of the reaction, the solution was evaporated to dryness, the residue

(19) Kihlberg, J.; Sjölin, P. *Tetrahedron lett.* **2000**, *41*, 4435.

was subjected to DCM/aq $NaHCO_3$ workup, and the organic phase was dried with Na_2SO_4. Purification by silica gel chromatography (30% EtOAc in petroleum ether) gave **8** as a white solid foam in a 78% (5.18 g) yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.46 (d, 4H), 7.20−7.35 (m, 8H), 6.84 (d, 2H), 5.82−5.93 (m, 1H), 5.12−5.28 (m, 2H), 4.80 (t, 1H, J = 8.1 Hz), 4.50 (d, 2H, J = 5.6 Hz), 4.06 (t, 1H, J = 7.4 Hz), 3.78 (s, 3H,), 3.39 (d, 2H, J = 7.5 Hz,), 3.08−3.25 (m, 2H), 3.00 (q_{AB}, 2H, J = 9.4 Hz,), 2.61−2.71 (m, 2H), 1.38 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.6, 157.7, 157.6, 144.2, 144.1, 135.2, 132.7, 130.2, 128.3, 128.2, 128.1, 127.9, 127.0, 117.6, 113.3, 86.2, 79.6, 65.7, 61.3, 55.2, 46.1, 40.1, 39.3, 28.3; HRMS (EI) M^+ calcd 590.2992, obsd 590.2992.

***N*-(Alloxycarbonyl)-*N*′-(*tert*-butyloxycarbonyl)-2-(4-methoxytrityloxy)methyl-2-phthalimidomethylpropane-1,3-diamine (9).** Compound **8** (5.18 g, 8.77 mmol) was coevaporated twice with dry benzene. The residue was dissolved in dry THF (50 mL) together with triphenylphosphine (3.91 g, 14.9 mmol) and phthalimide (2.19 g, 14.9 mmol), and then DEAD (2.32 mL, 14.9 mmol) was slowly added. The mixture was refluxed for 7 h. The solvent was removed by evaporation, and the residue was purified by silica gel chromatography (0 to 2% MeOH in DCM) yielding **9** as a pale yellow solid foam in a 66% (4.18 g) yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.75−7.85 (m, 4H), 7.10−7.40 (m, 12H), 6.80 (d, 2H), 5.87−5.97 (m, 2H), 5.52 (t, 1H, J = 6.6 Hz), 5.30 (dd, 1H, J = 1.5 and 17.3 Hz), 5.21 (dd, 1H, J = 1.4 and 10.5 Hz), 4.54 (d, 2H, J = 5.5 Hz), 3.79 (s, 3H), 3.69 (s, 2H), 3.24−3.36 (m, 4H), 3.04−3.14 (m, 2H), 1.42 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.1, 158.4, 156.9, 156.5, 143.8, 134.9, 134.2, 134.1, 133.0, 131.8, 130.3, 128.3, 127.7, 126.8, 123.5, 123.4, 86.8, 79.1, 64.9, 55.1, 45.8, 42.4, 41.6, 40.3, 28.3; HRMS (EI) M^+ calcd 719.3207, obsd 719.3203.

2-(Alloxycarbonyl)aminomethyl-2-(*tert*-butyloxycarbonyl)aminomethyl-3-phthalimidopropan-ol (10). Compound **9** (3.91 g, 5.56 mmol) was stirred in a mixture of methanolic iodine (44 mL, 1% iodine in MeOH) and DCM (30 mL) at room temperature. When the reaction was complete according to TLC (30% EtOAc in petroleum ether), excess of DCM (30 mL) was added, and the mixture was washed several times with neutral aq. Na_2SO_3 (10%, m/v). The organic phase was dried over Na_2SO_4 and evaporated to dryness. Purification of the crude product by silica gel chromatography (30% EtOAc in petroleum ether) gave **10** as a pale yellow solid foam in a 72% yield (1.80 g). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.85−7.89 (m, 2H), 7.76−7.79 (m, 2H), 6.39 (t, 1H, J = 6.6 Hz), 6.03 (t, 1H, J = 6.4 Hz), 5.90−5.99 (m, 1H), 5.32 (dd, 1H, J = 1.5 and 17.3 Hz), 5.22 (dd, 1H, J = 1.1 and 10.3 Hz), 4.59 (d, 2H, J = 5.5 Hz), 4.32 (t, 1H, J = 7.7 Hz), 3.57 (s, 2H), 3.12−3.27 (m, 4H), 2.82−2.94 (m, 2H), 1.45 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.7, 157.6, 157.5, 134.5, 132.8, 131.6, 123.7, 117.8, 79.9, 65.9, 46.1, 40.8, 40.1, 38.2, 28.3; HRMS (EI) M^+ calcd 447.2006, obsd 447.2009.

2-(Alloxycarbonyl)aminomethyl-2-(*tert*-butyloxycarbonyl)aminomethyl-3-phthalimidopropanoic Acid (11). A solution of CrO_3 (805 mg, 8.05 mmol) and H_2SO_4 (0.43 mL, 8.05 mmol) in water (5.80 mL, 322 mmol) was added dropwise to a solution of **10** (1.80 g, 4.02 mmol) in acetone (20 mL) at 0 °C. The mixture was stirred for 5 h at room temperature. The oxidizing reagents had, however, to be added to complete the reaction. After the consumption of **10** was complete according to TLC (10% MeOH in DCM), the mixture was filtered, MeOH (4 mL) and water (4 mL) were added, and the solution was concentrated by evaporation. DCM (50 mL) was added, the mixture was washed with brine, and then water layers were extracted with DCM. The combined organic phases were dried over Na_2SO_4 and then evaporated to dryness. The product was separated by silica gel chromatography (5% MeOH in DCM) to give **11** as a white solid foam in a 54% yield (1.05 g). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.83−7.85 (m, 2H), 7.72−7.74 (m, 2H), 6.26 (br s, 1H), 5.87−5.97 (m, 1H), 5.81 (br s, 1H), 5.30 (dd, 1H, J = 1.5 and 17.1 Hz), 5.20 (dd, 1H, J = 1.3 and 10.5 Hz), 4.58 (d, 2H, J = 5.5 Hz), 3.94 (br s, 2H), 3.34−3.58 (m, 4H), 1.45 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.3, 168.8, 156.8, 134.3, 132.8, 131.6, 123.7, 123.6, 117.7, 79.9, 65.9, 41.3, 40.7, 39.5, 28.3; HRMS (ESI) $[M + H]^+$ calcd 462.1864, obsd 462.1871.

2-(Alloxycarbonyl)aminomethyl-2-(*tert*-butyloxycarbonyl)aminomethyl-3-aminopropanoic Acid (12). Compound **11** (1.30 g, 2.82 mmol) was dissolved in a mixture of allyl alcohol (1.4 mL), dioxane (2.2 mL), and DMF (0.8 mL). Hydrazine monohydrate (0.55 mL, 11.3 mmol) was added, and the mixture was stirred overnight at room temperature. All volatile components were removed by evaporation, and the residue was suspended in DCM. The mixture was filtered and evaporated to dryness, and the product was separated by silica gel chromatography (10 to 30% MeOH in DCM) to yield 0.66 g (71%) of a white solid foam. ^{1}H NMR ($CDCl_3$:CD_3OD; v/v 3:1, 400 MHz) δ 6.49 (br, 1H), 6.03 (br, 1H), 5.74−5.84 (m, 1H), 5.21 (dd, 1H, J = 1.1 and 17.1 Hz), 5.10 (dd, 1H, J = 1.0 and 10.5 Hz), 4.44 (br s, 2H), 3.28 (m, 2H), 3.05 (m, 2H), 2.69−2.79 (m, 2H), 1.32 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.8, 158.0, 132.0, 127.3, 117.0, 79.9, 65.5, 42.0, 41.3, 39.9, 27.6; HRMS (ESI) $[M + H]^+$ calcd 332.1816, obsd 332.1821.

2-(Alloxycarbonyl)aminomethyl-2-(*tert*-butyloxycarbonyl)aminomethyl-3-(9-fluorenylmethoxycarbonyl)aminopropanoic Acid (1). Compound. **12** (0.66 g, 1.99 mmol) was dissolved in a mixture of acetonitrile (15 mL) and water (5 mL). FmocCl (0.54 g, 2.09 mmol) in acetonitrile (7 mL) and K_2CO_3 (0.69 g, 4.98 mmol) in water (10 mL) were added to this solution. After stirring the mixture overnight at room temperature, the solvents were evaporated and the residue was dissolved in water. The solution was acidified with AcOH and extracted several times with DCM. The combined organic layers were washed with aqueous 50% NaCl, dried over Na_2SO_4, and evaporated to dryness. The resulting oil was purified by silica gel chromatography (30 to 50% EtOAc in petroleum ether). The appropriate fractions were pooled and evaporated, and the residue was dissolved in a minimum amount of DCM and coevaporated with hexane, giving **1** as white amorphous solid in a 70% yield (0.77 g). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.73 (d, 2H, J = 7.9 Hz), 7.58 (d, 2H, J = 7.8 Hz), 7.37 (t, 2H, J = 6.6 Hz), 7.29 (t, 2H, J = 6.6 Hz), 6.33 (br s, 1H), 6.21 (br s, 1H), 6.21 (br s, 1H), 5.83−5.92 (m, 1H), 5.74 (br s, 1H), 5.28 (dd, 1H, J = 1.3 and 17.6 Hz), 5.19 (dd, 1H, J = 1.5 and 10.9 Hz), 4.54 (d, 2H, J = 5.6 Hz), 4.32 (d, J = 7.4 Hz, 2H), 4.19 (t, 1H, J = 7.4 Hz), 3.29−3.34 (m, 6H), 1.42 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.0, 157.6, 157.1, 143.7, 141.2, 132.6, 127.6, 127.0, 125.1, 119.9, 117.7, 79.9, 67.2, 65.9, 47.0, 40.9, 40.7, 40.2, 28.2; HRMS (ESI) $[M + H]^+$ calcd 554.2497, obsd 554.2520.

***N*-(9-Fluorenylmethoxycarbonyl)-3-*O*-(2,3,4,6-tetra-*O*-acetyl-*β*-D-galactopyranosyl)-L-serine Pentafluorophenyl Ester (13).** Compound **13** was prepared according to the procedure reported previously.[15] The fully protected pentafluorophenyl ester of galactosylserine (**13**) was obtained as a white amorphous solid in a 41% yield. The ^{1}H and ^{13}C NMR spectra were in accordance with published data. HRMS (ESI) $[M + H]^+$ calcd 824.1972, obsd 824.1951.

***N*-(9-Fluorenylmethoxycarbonyl)-3-*O*-(2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl)-L-serine Pentafluorophenyl Ester (14).** Compound **14** was obtained, starting from an anomeric mixture of 1,2,3,4,5-penta-*O*-acetyl-D-glucopyranoses (1 g, 2.6 mmol), by a slightly modified procedure described for **13**. Boron trifluoride etherate (3 molar equiv, 0.77 mL, 6.2 mmol) was added under nitrogen to a solution of pentafluorophenyl ester of *N*-(9-fluorenylmethoxycarbonyl)-L-serine[9] (1.2 molar equiv, 1.2 g, 2.5 mmol) and 1,2,3,4,5-penta-*O*-acetyl-α,*β*-D-glucopyranose (800 mg, 2.1 mmol) in dry DCM (20 mL). The reaction was allowed to proceed at room temperature for 24 h. The reaction mixture was diluted with DCM (20 mL), and the solution was washed with water (15 mL). The aqueous phase was extracted with DCM (15 mL), and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo.

The residue was purified by column chromatography, eluting first with a 1:6 (v/v) mixture of EtOAc and toluene and then with a 6:5 (v/v) mixture of EtOAc in petroleum ether. The yield of the pure β-anomer was 15%. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.77 (d, 2H, J = 7.0 Hz), 7.61 (d, 2H, J = 7.0 Hz), 7.41 (t, 2H, J = 7.0 Hz), 7.32 (t, 2H, J = 7.5 Hz), 5.69 (d, 1H, J = 8.5 Hz), 5.23 (t, 1H, J = 9.4 Hz), 5.09 (t, 1H, J = 9.7 Hz), 4.98 (dd, AB type, 1H, J = 9.4 and 8.1 Hz), 4.87 (m, 1H), 4.54 (m, 2H), 4.43 (m, 2H), 4.11−4.26 (m, 3H), 3.99 (dd, 1H, J = 3.5 and 10.5 Hz), 3.68 (m, 1H), 2.05, 2.03, 1.98 (3s, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.7, 170.6, 170.2, 169.4, 169.3, 166.1 155.8, 143.6, 143.5, 141.4, 141.3, 127.8, 127.1, 125.0, 124.9, 120.1, 100.7, 72.5, 72.1, 71.1, 69.8, 68.2, 67.3, 61.7, 54.2, 47.1, 20.6, 20.5; HRMS (ESI) [M + H]$^+$ calcd 824.1972, obsd 824.1996.

***N*-(9-Fluorenylmethoxycarbonyl)-3-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-L-serine Pentafluorophenyl Ester (15):**[20] Compound **15** was prepared as described for **14**, using 1,2,3,4,5-penta-*O*-acetyl-α-D-mannopyranose (1 g, 2.6 mmol) as a starting material. Compound **15** was obtained as white amorphous solid in a 35% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.76 (d, 2H, J = 7.5 Hz), 7.63 (d, 2H, J = 6.2 Hz), 7.40 (t, 2H, J = 7.3 Hz,), 7.31 (t, 2H, J = 7.3 Hz), 6.03 (d, 1H, J = 8.5 Hz), 5.24−5.33 (m, 2H), 4.99 (m, 1H), 4.88 (br s, 1H), 4.48 (m, 3H), 4.12−4.28 (m, 4H), 4.08 (dd, 1H), 3.99 (m, 1H), 2.01, 2.04, 2.06, 2.17 (4s, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 169.8, 169.7, 166.2, 155.7, 143.5, 141.3, 127.8, 127.1, 125.0, 120.0, 99.0, 69.9, 69.4, 69.1, 68.6, 67.6, 65.9, 62.4, 54.4, 47.0, 21.4, 20.6, 20.8; HRMS (ESI) [M + H]$^+$ calcd 824.1972, obsd 824.2007.

***N*-(9-Fluorenylmethoxycarbonyl)-3-*O*-(2,3,4-tri-*O*-acetyl-β-D-ribopyranosyl)-L-serine Pentafluorophenyl Ester (16).** Compound **16** was prepared as described for **14**, using 1,2,3,4-tetra-*O*-acetyl-β-D-ribopyranose (500 mg, 1.6 mmol) as a starting material. The product was obtained as white amorphous solid in a 38% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.76 (d, 2H, J = 7.5 Hz), 7.62 (d, 2H, J = 7.5 Hz), 7.40 (t, 2H, J = 7.5 Hz), 7.32 (t, 2H, J = 7.5 Hz), 5.79 (d, 1H, J = 8.9 Hz), 5.36 (t, 1H, J = 3.4 Hz), 5.14 (m 1H), 5.08 (t, 1H, J = 3.2 Hz), 4.96 (m, 1H), 4.79 (d, 1H, J = 3.6 Hz), 4.38−4.57 (m, 3H), 4.26 (t, 1H), 3.94−3.80 (m, 3H), 2.12, 2.11, 2.08 (3s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.1, 169.9, 169.7, 169.5, 166.3, 155.8, 143.6, 143.5, 141.3, 127.8, 127.1, 125.0, 120.0, 98.8, 68.3, 67.9, 67.6, 66.4, 65.8, 54.0, 47.0, 20.8, 20.7, 20.6; HRMS (ESI) [M + H]$^+$ calcd 752.1761, obsd 752.1736.

Solid Support 17. Aminomethyl polystyrene that was employed as a solid support was first acylated with a Fmoc-protected SCAL linker[16] using standard HATU activation.[17] Accordingly, 150 mg of the solid support was suspended in 1 mL of DMF, Fmoc-SCAL (2 molar equiv, 19.3 mg in 0.5 mL of DMF), HATU (3 molar equiv, 17.1 mg in 0.5 mL of DMF), and diisopropylethylamine (DIPEA, 4 molar equiv, 10.5 μL) were added, and the mixture was shaken for 3 h at room temperature. The support was filtered and washed with DMF, DCM, and MeOH, and finally dried under reduced pressure. The nonreacted amino groups were capped with Ac_2O in THF containing *N*-methylimidazole and lutidine. The Fmoc groups were removed with 25% piperidine in DMF (15 min at room temperature). According to UV spectroscopic quantification of piperidinyl benzofulvene released, the loading was 120 μmol g^{-1}. The exposed amino function of the SCAL linker was then acylated with *N*-Fmoc-glycine by adding *N*-Fmoc-glysine (5 molar equiv, 30 mg in 0.5 mL of DMF), HATU (5 molar equiv, 38 mg in 0.5 mL of DMF), and DIPEA (10 molar equiv, 35 μL) to a suspension of the support in DMF (1 mL), and shaking the mixture for 1 h at room temperature. The solid support was filtered, washed with DMF, DCM, and MeOH, and dried under reduced pressure to afford support **17**.

(20) For previous synthesis of **15**, see: Kragol, G.; Otvos, L, Jr. *Tetrahedron* **2001**, *57*, 957.

Synthesis of Glycoclusters 21−24. The Fmoc group was removed from support **17**, as described above. The support was washed with DCM and MeOH and dried under reduced pressure. The support (50 to 150 mg) was then suspended in 1 mL of DMF, and the branching building block **1** (3 molar equiv in 0.5 mL) was added together with HATU (3 molar equiv in 0.5 mL) and DIPEA (6 molar equiv). The mixture was shaken for 2 h at room temperature, then the support was filtered, washed with DMF, DCM, and MeOH, and dried under reduced pressure. The Fmoc group was removed, and the support was again washed with DCM and MeOH and dried under reduced pressure. The first *O*-(glycosyl)-*N*-Fmoc-L-Ser-OPfp building block (3 molar equiv in 0.5 mL of DMF) and HOBt (7.5 molar equiv in 0.5 mL of DMF) were added onto the support suspended in 1 mL of DMF. After 3 h of shaking at room temperature, the support was filtered, washed with DMF, DCM, and MeOH, and dried under reduced pressure. The Boc group was removed from the branching unit with 25% TFA in DCM (1 h at room temperature), and the filtered support was washed with 10% pyridine in DCM and then consecutively with DMF, DCM, and MeOH and dried under reduced pressure. The support was suspended in 1 mL of DMF, and the second glycosylated *N*-Fmoc-L-Ser-OPfp building block (4 molar equiv in 0.5 mL of DMF) and HOBt (10.0 molar equiv in 0.5 mL of DMF) were added. After 3 h of shaking at room temperature, the support was filtered, washed with DMF, DCM, and MeOH, and dried under reduced pressure. Finally, the Alloc group was removed via a palladium-catalyzed hydrostannolysis by Bu_3SnH.[18] Accordingly, a mixture of $Pd(OAc)_2$ (2 molar equiv) and PPh_3 (12 molar equiv) in DMF (1 to1.5 mL) and AcOH (12 molar equiv) was added onto the support (50−150 mg). After this, Bu_3SnH (12 molar equiv) was added to the reaction mixture. The mixture was shaken at room temperature for 15 min. The resin was filtered, washed with 10% pyridine in DCM and then with DMF, DCM, and MeOH, and dried under reduced pressure. The last glycosylated Fmoc-Ser-OPfp building block (7 molar equiv in 0.5 mL of DMF) and HOBt (17.5 molar equiv in 0.5 mL of DMF) were added onto the support suspended in 1 mL of DMF. The mixture was shaken for 5 h at room temperature. The support was filtered, washed with DMF, DCM, and MeOH, and dried under reduced pressure. After each coupling step, the product was released from an aliquot of the solid support and analyzed by HPLC. Only minor impurities gradually appeared. The coupling efficiency of the synthesis was 80−90%.

Cleavage from Solid Support. The solid support (50 to150 mg) was first swollen with a small amount of DCM and then 1 mL of 0.1% HBr in AcOH was added. The mixture was shaken for 2 h at room temperature. The support was filtered, washed with DCM and MeOH, and dried under reduced pressure. The support was suspended in a mixture of TFA and DCM (1 mL, 1:1, v/v). After 2 h of shaking at room temperature, the solution was collected by filtration and evaporated under reduced pressure. After HPLC purification, the authenticity of **21**−**24** was verified by HPLC/ESI-MS (Table 1). In addition, glycocluster **21** prepared in a larger quantity was characterized by HRMS and ^{1}H and ^{13}C NMR spectroscopy (including PDQF and HMBC spectra).

Glycocluster 21. Starting from 150 mg of solid support, the overall isolated yield was 3.8 mg (10%). ^{1}H NMR (DMSO-d_6, 90 °C, 500 MHz) δ 7.82 (d, 6H, J = 7.6 Hz), 7.63 (t, 6H, J = 7.2 Hz), 7.38 (t, 6H, J = 7.3 Hz), 7.30 (t, 6H, J = 7.3 Hz), 5.25 (d, 2H, J = 3.0 Hz), 5.18 (t, 1H, J = 9.0 Hz), 5.09 (dd, 2H, J = 10.5 and 3.5 Hz), 4.88−4.95 (m, 4H), 4.71−4.79 (m, 3H), 4.64 (d, 2H, J = 7.3 Hz), 4.18−4.30 (m, 14H), 4.15 (m, 1H), 4.09 (t, 2H, J = 6.8 Hz), 4.01−4.04 (m, 6H), 3.78−3.90 (m, 8H), 3.72 (dd, 1H, J = 13.0 and 5.3 Hz), 3.62 (dd, 1H, J = 16.1 and 5.3 Hz), 1.98, 1.96, 1.92, 1.91, 1.89 (5s, 36H); ^{13}C NMR (DMSO-d_6, 90 °C, 100 MHz) δ 171.4, 171.2, 169.6, 169.5, 169.4, 169.3, 168.9, 168.8, 168.6, 168.5, 168.4, 143.5, 143.4, 140.3, 140.2, 127.1, 126.6, 124.7, 124.6, 119.5, 99.6, 99.2, 72.0, 70.6, 70.5, 70.0, 69.8, 68.3, 68.2, 68.1, 67.0, 65.8, 61.4, 60.7, 54.8, 54.7,

51.8, 46.6, 19.9, 19.8, 19.7, 19.4; HRMS (FAB) $[M + H]^+$ calcd 2121.7316, obsd 2121.7314.

Acknowledgment. The authors wish to thank Mr. Jari Sinkkonen, M.Sc., for performing ^1H and ^{13}C NMR analysis on a JEOL JNM-A 500 NMR spectrometer.

Supporting Information Available: Experimental details and spectral data for the compounds **1**, **5**, **6**, **8**−**12**, **14**, **16**, and **21**, and HPLC analytical data and ESI-MS spectra for the glycoclusters **22**−**24**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO026053B