J|A|C|S
ARTICLES
Published on Web 04/23/2003

Chemoselective Ligation Applied to the Synthesis of a Biantennary *N*-Linked Glycoform of CD52

Matthew R. Pratt[‡] and Carolyn R. Bertozzi*[,†,‡,§,||,⊥]

Contribution from the Center for New Directions in Organic Synthesis, Departments of Chemistry and Molecular and Cell Biology, and Howard Hughes Medical Institute, University of California, and Materials Sciences Division, Lawrence Berkeley National Laboratory, Berkeley, California 94720

Received November 14, 2002; E-mail: bertozzi@cchem.berkeley.edu

Abstract: We report here a strategy for the synthesis of *N*-linked glycopeptide analogues that replace the glycosidic linkages extending from the core pentasaccharide with thioethers amenable to construction by chemoselective ligation. The key building block, a pentasaccharide-Asn analogue containing two thiol residues, was incorporated into CD52 by 9-fluorenylmethoxycarbonyl (Fmoc)-based solid-phase peptide synthesis. An undecasaccharide mimetic was then readily generated by alkylation of this glycopeptide with an *N*-bromoacetamido trisaccharide. The rapid assembly of a complex type *N*-linked glycopeptide mimetic was accomplished using this technique.

Introduction

Continuing research into the biological roles of glycoproteins has highlighted their importance in a variety of processes including cell−cell adhesion, immune system modulation, and signaling.[1] However, as a result of their complex biosynthesis,[2] glycoproteins exist as heterogeneous mixtures of glycoforms (i.e., proteins that differ only in the structure and abundance of the pendant glycans). Therefore, homogeneous glycoproteins for biological investigations are difficult to obtain using recombinant expression methods. Understandably then, glycoprotein synthesis has gained considerable attention in the field of organic synthesis.[3] Although many large carbohydrate structures have been synthesized,[4] the extension of these methodologies to glycans appended to glycoproteins or glycopeptides still remains a daunting task.

N-Linked glycoproteins, possessing one of the most prevalent forms of glycosylation in vertebrates, have proven particularly difficult targets for chemical synthesis. Their generally large size, branching, and the presence of the synthetically difficult β-mannoside linkage within their conserved pentasaccharide core (**1**, Figure 1) have frustrated efforts to construct important biological targets. Thus, glycoproteins bearing biantennary *N*-linked glycans such as structure **1** have not as yet been prepared chemically.

In previous work, we have applied the chemoselective ligation technique[5] to achieve the synthesis of *O*-linked glycopeptide mimetics bearing complex branches that are difficult to generate in their native forms.[6,7] Branched glycosidic linkages within *O*-linked glycans were substituted with alternative linkages, either oximes or thioethers, that can be formed convergently among unprotected fragments in an aqueous milieu. Use of the chemoselective ligation technique provided access to numerous glycoforms in a divergent fashion. In this report, we apply the chemoselective ligation approach to the synthesis of analogues of the *N*-linked glycopeptide CD52.

CD52 is a glycoprotein expressed on human lymphocytes and sperm cells.[8] CD52 possesses a single large *N*-linked glycan,

[†] Center for New Directions in Organic Synthesis, University of California.
[‡] Department of Chemistry, University of California.
[§] Department of Molecular and Cell Biology, University of California.
[||] Howard Hughes Medical Institute.
[⊥] Lawrence Berkeley National Laboratory.

(1) (a) Varki, A. *Glycobiology* **1993**, *3*, 97−130. (b) Dwek, R. A. *Chem. Rev.* **1996**, *96*, 683−720.
(2) (a) Bill, R. M.; Revers, L.; Wilson, I. B. H. *Protein Glycosylation*; Kluwer Academic Publishers: Massachusetts, 1998. (b) Helenius, A.; Aebi, M. *Science* **2001**, *291*, 2364−2369.
(3) Herzner, H.; Reipen, T.; Schultz, M.; Kunz, H. *Chem. Rev.* **2000**, *100*, 4495−4537.
(4) (a) Prahl, I.; Unverzagt, C. *Tetrahedron Lett.* **2000**, *41*, 10189−10193. (b) Seifert, J.; Unverzagt, C. *Tetrahedron Lett.* **1996**, *37*, 6527−6530. (c) Seifert, J.; Unverzagt, C. *Tetrahedron Lett.* **1997**, *38*, 7857−7860. (d) Unverzagt, C. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1102−1104. (e) Unverzagt, C. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2350−2353. (f) Unverzagt, C. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1989−1992. (g) Unverzagt, C. *Carbohydr. Res.* **1997**, *305*, 423−431. (h) Unverzagt, C. *Tetrahedron Lett.* **1997**, *38*, 5627−5630. (i) Danishefsky, S. J.; Hu, S.; Cirillo, P. F.; Eckhardt, M.; Seeberger, P. H. *Chem.—Eur. J.* **1997**, *3*, 1617−1628. (j) Wang, Z. G.; Zhang, X. F.; Live, D.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2000**, *39*, 3652−3656. (k) Wang, Z.-G.; Zhang, X.; Visser, M.; Live, D.; Zatorski, A.; Iserloh, U.; Lloyd, K. O.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 1728−1732. (l) Seifert, J.; Lergenmuller, M.; Ito, Y. *Angew. Chem., Int. Ed.* **2000**, *39*, 531−534.
(5) Hang, H. C.; Bertozzi, C. R. *Acc. Chem. Res.* **2001**, *34*, 727−736.
(6) (a) Rodriguez, E. C.; Winans, K. A.; King, D. S.; Bertozzi, C. R. *J. Am. Chem. Soc.* **1997**, *119*, 9905−9906. (b) Marcaurelle, L. A.; Rodriguez, E. C.; Bertozzi, C. R. *Tetrahedron Lett.* **1998**, *39*, 8417−8420.
(7) Marcaurelle, L. A.; Bertozzi, C. R. *J. Am. Chem. Soc.* **2001**, *123*, 1587−1595.
(8) (a) Treumann, A.; Lifely, M. R.; Schneider, P.; Ferguson, M. A. J. *J. Biol. Chem.* **1995**, *270*, 6088−6099. (b) Focarelli, R.; Francavilla, S.; Francavilla, F.; Della Giovampaola, C.; Santucci, A.; Rosati, F. *Hum. Reprod.* **1999**, *5*, 46−51. (c) Schröter, S.; Derr, P.; Conradt, H. S.; Nimtz, M.; Hale, G.; Kirchhoff, C. *J. Biol. Chem.* **1999**, *274*, 29862−29873. (d) Focarelli, R.; Della Giovampaola, C.; Seraglia, R.; Brettoni, C.; Sabatini, L.; Pescaglini, M.; Rosati, F. *Biochem. Biophys. Res. Commun.* **1999**, *258*, 639−643.

10.1021/ja029346v CCC: $25.00

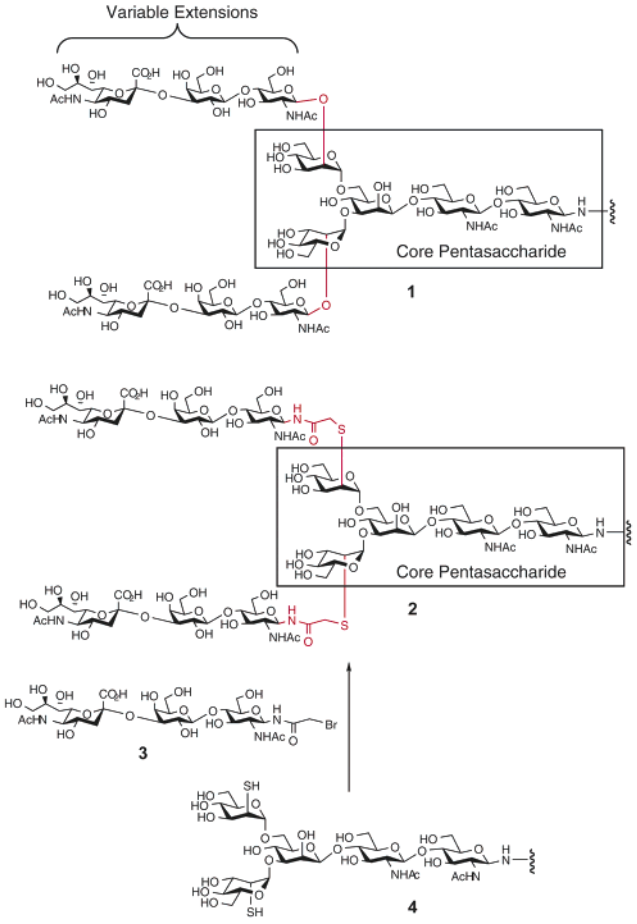
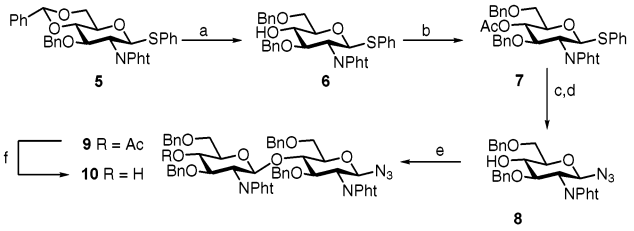


Figure 1. Chemoselective ligation applied to *N*-linked glycoproteins.

but its peptide backbone comprises only 12 amino acids, making it a fairly simple candidate for demonstration of the chemoselective ligation approach. In fact, the synthesis of CD52 containing the conserved *N*-linked pentasaccharide core was completed by Ogawa and co-workers.[9] However, further elaboration of the glycan has not yet been achieved.

All *N*-linked glycans possess the conserved pentasaccharide core shown in structure **1** (Figure 1). Their diversity is engendered within the variable extensions joined to the conserved core at the α-mannosyl residues. We chose to replace the glycosidic bonds that initiate these variable extensions with thioether linkages (**2**). These would be readily formed from a pentasaccharide containing 2-thiomannose residues (**4**) that can undergo condensation with *N*-bromoacetamido oligosaccharides (**3**). Thus, solid-phase peptide synthesis (SPPS) with a building block bearing glycan **4** would produce a core glycopeptide for divergent elaboration with any terminal glycan structure of interest. The thiols can be selectively alkylated in the presence of all naturally occurring amino acid functionalities with the exception of the sulfhydryl group of cysteine. The product (**2**) contains unnatural linkages at C-2 of the α-mannose residues but retains the structure of the conserved pentasaccharide core. This is a key feature of the approach, since the core region has been shown to influence the structure of the underlying

Scheme 1 [a]



[a] Reagents: (a) Triethylsilane, TFA, TFAA, CH_2Cl_2, 0 °C, 5 h, 85%; (b) Ac_2O, pyridine, 95%; (c) $TMSN_3$, NIS, TfOH, CH_2Cl_2, 4-Å MS, −40 °C, 20 min, 97%; (d) NaOMe, CH_2Cl_2/MeOH, 3 h, 96%; (e) **7**, NIS, TfOH, CH_2Cl_2, 4-Å MS, −20 °C, 20 min, 94%; (f) NaOMe, THF/MeOH, 20 min, 93%.

polypeptide.[10,11] By contrast, NMR structures of *N*-linked glycoproteins have shown the branch points to be quite flexible.[10] Furthermore, most carbohydrate receptors only recognize epitopes near the termini of large glycans of this type.[1b]

Results and Discussion

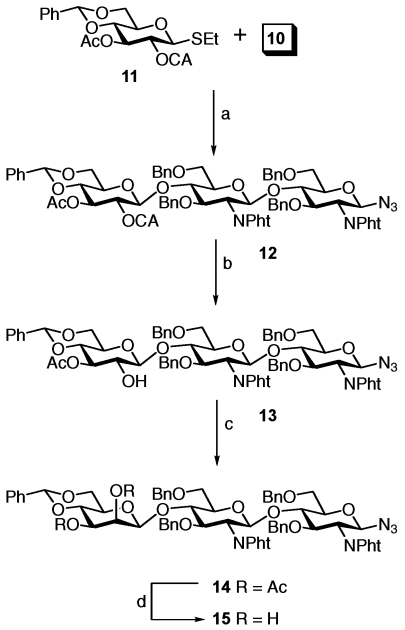
Toward the synthesis of pentasaccharide **4**, the benzylidene acetal of known monosaccharide **5**[12] was reductively opened with triethylsilane to give alcohol **6** (Scheme 1).[13] The unmasked hydroxyl group was acetylated to afford ester **7**. Compound **7** was reacted with trimethylsilyl azide, and the acetyl group was removed from the intermediate to give monosaccharide acceptor **8**. Glycosylation of **8**, using glycosyl donor **7** under the agency of NIS/TfOH,[14] then gave disaccharide **9** in excellent yield (94%), which was subsequently deactylated to provide **10**. Treatment of **10** with the known thioglycoside **11**,[14,15] containing an α-chloroacetyl group at the 2-position, yielded trisaccharide **12** (Scheme 2). The α-chloroacetyl ester of **12** was removed selectively using hydrazinedithiocarbonate,[16] and the unmasked hydroxyl group of **13** was inverted in a two-step procedure to afford the desired β-mannoside **14**.[17] The two acetyl groups on the 2- and 3-positions of the terminal mannose residue were removed to give the selectively protected trisaccharide **15**.

To install the 2-thiol functionality necessary for the chemoselective ligation, we took advantage of a rearrangement developed by Nicolaou and co-workers.[18] 3,4,6-Tri-*O*-benzylglucal (**16**) was oxidized with dimethyldioxirane (DMDO), and the resulting epoxide was opened with benzyl mercaptan to give thioglycoside **17** (Scheme 3). Treatment of **17** with (diethylamino)sulfur trifluoride (DAST) produced compound **18**.

Selective glycosylation of **15** at the 3-position with donor **18**, using $SnCl_2$/AgOTf as a catalyst, produced the tetrasaccharide **19** as the sole product in 80% yield (Scheme 4). The remaining hydroxyl group was then protected as the acetyl ester (**20**), and the benzylidene group was hydrolyzed with TFA.

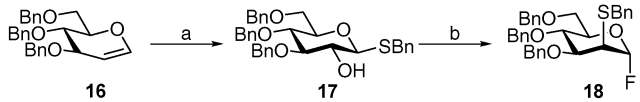
(9) (a) Guo, Z. W.; Nakahara, Y.; Ogawa, T. *Bioorg. Med. Chem.* **1997**, *5*, 1917−1924. (b) Guo, Z. W.; Nakahara, Y.; Ogawa, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1464−1466.
(10) Wyss, D. F.; Choi, J. S.; Li, J.; Knoppers, M. H.; Willis, K. J.; Arulanandam, A. R.; Smolyar, A.; Reinherz, E. L.; Wagner, G. *Science* **1995**, *269*, 1273−1278.
(11) Imperiali, B.; O'Connor, S. E. *Curr. Opin. Chem. Biol.* **1999**, *3*, 643−649.
(12) Gunther, W.; Kunz, H. *Carbohydr. Res.* **1992**, *228*, 217−241.
(13) Deninno, M. P.; Etienne, J. B.; Duplantier, K. C. *Tetrahedron Lett.* **1995**, *36*, 669−672.
(14) Matsuo, I.; Isomura, M.; Walton, R.; Ajisaka, K. *Tetrahedron Lett.* **1996**, *37*, 8795−8798.
(15) (a) Gridley, J. J.; Hacking, A. J.; Osborn, H. M. I.; Spackman, D. G. *Synlett* **1997**, 1397−1399. (b) Gridley, J. J.; Hacking, A. J.; Osborn, H. M. I.; Spackman, D. G. *Tetrahedron* **1998**, *54*, 14925−14946.
(16) van Boeckel, C. A. A.; Beetz, T. *Tetrahedron Lett.* **1983**, *24*, 3775−3778.
(17) Furstner, A.; Konetzki, I. *Tetrahedron Lett.* **1998**, *39*, 5721−5724.
(18) Nicolaou, K. C.; Ladduwahetty, J. L. R.; Chucholowski, A. *J. Am. Chem. Soc.* **1986**, *108*, 2466−2467.

Scheme 2 [a]



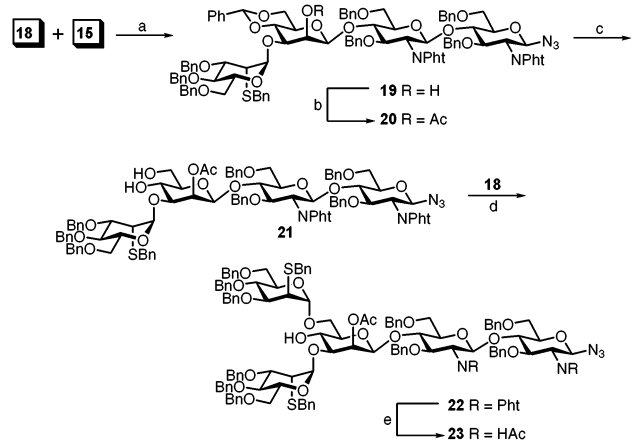
[a] Reagents: (a) NIS, TfOH, CH_2Cl_2, 4-Å MS, 20 min, 74%; (b) Hydrazinedithiocarbonate, lutidine, AcOH, 15 min, 95%; (c) (i) Tf_2O, pyridine, CH_2Cl_2, −15 °C, 3 h; (ii) Bu_4NOAc, toluene, 16 h, sonication, 95%; (d) NaOMe, CH_2Cl_2/MeOH, 1 h, 95%.

Scheme 3 [a]



[a] Reagents: (a) (i) DMDO, CH_2Cl_2, 0 °C, 1 h; (ii) BnSH, TFAA, CH_2Cl_2, 16 h, 90%; (b) DAST, CH_2Cl_2, 0 °C, 10 min, 92%.

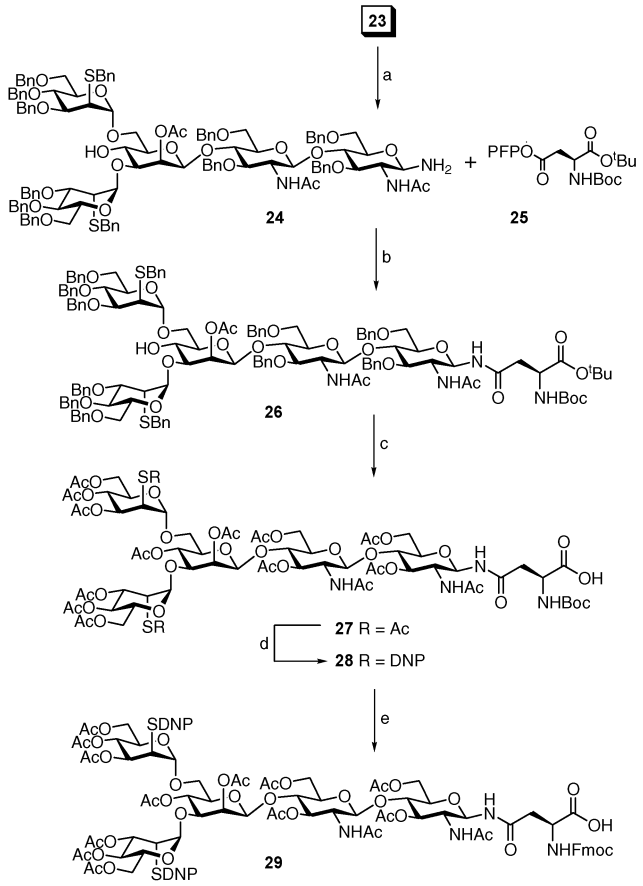
Scheme 4 [a]



[a] Reagents: (a) AgOTf, $SnCl_2$, CH_2Cl_2, 4-Å MS, 0 °C to rt, 16 h, 80%; (b) Ac_2O, pyridine, 16 h, 95%; (c) 5% TFA/CH_2Cl_2, 0 °C, 20 min, 65%; (d) **18**, AgOTf, $SnCl_2$, CH_2Cl_2, 4-Å MS, 0 °C to rt, 16 h, 85%; (e) (i) ethylenediamine, BuOH, 90 °C, 12 h; (ii) Ac_2O, pyridine, 16 h, 97%.

Unfortunately, hydrolysis of the 2-thio-mannose residue was facile under a range of acidic conditions and gave the demannosylated trisaccharide (**15**) as a side product (∼30%). This side product could be recycled, however, by reglycosylation with **18**, improving the overall yield of **21** above 90%. The 6″-position of oligosaccharide **21** was selectively glycosylated with **18**, under identical conditions as **15**, to give pentasaccharide **22**. The *N*-phthalimido groups of **22** were then removed with ethylenediamine, and the 2-amino functionalities were acetylated to give pentasaccharide **23**.

Scheme 5 [a]



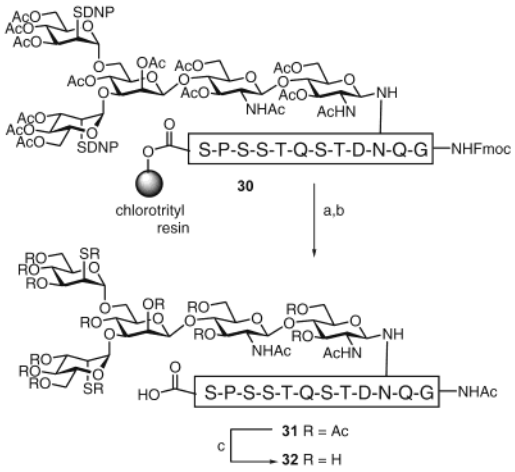
[a] Reagents: (a) propanedithiol, DIEA, MeOH, 4 h; (b) HOBt, DIEA, NMP, 16 h, 80%; (c) (i) Li^0, NH_3/THF, 1h; (ii) Ac_2O, pyridine, 16 h; (d) (i) NaSMe, MeOH, 3 h; (ii) DNPF, DIEA, CH_2Cl_2, 16 h, 77% over two steps; (e) (i) 95% TFA, 10 min; Fmoc-OSu, DIEA, CH_2Cl_2, 2 h, 92%.

Next, the glycosyl azide of **23** was reduced to give, with complete retention of stereochemistry as confirmed by NMR, the β-glycosylamine **24**, which was immediately coupled to the side chain pentafluorophenyl ester of protected aspartic acid derivative **25** (Scheme 5). Subjection of **26** to Li^0 in liquid NH_3 removed all benzyl ethers and unmasked the carboxylic acid functionality of the amino acid.[19] Concentration of the reaction mixture, followed by acetylation, gave **27** as the only product. Selective transthioesterification of **27** followed by selective protection of the resulting thiols as the 2,4-dinitrophenyl (DNP) thioethers gave **28**.[7] Finally, removal of the Boc group of **28** (95% TFA) and subsequent reprotection with Fmoc-*O*-succinimide (Fmoc-OSu) gave the glycosyl amino acid building block **29** ready for SPPS.

Peptide synthesis was carried out on Fmoc-Ser-(^{t}Bu)-chlorotrityl resin employing HBTU-DCC coupling conditions. All amino acids were used in 10-fold excess except **29**, of which only 1.5 equiv were used, affording **30**. The *N*-terminus of the protected CD52 analogue (**30**) was liberated followed by removal of the DNP groups by transthioetherification with DTT,[7] followed by on-resin acetylation (Scheme 6). Cleavage and deprotection of the peptide side chains were achieved by

(19) Frick, W.; Bauer, A.; Bauer, J.; Wied, S.; Müller, G. *Biochemistry* **1998**, *37*, 13421−13436.

Scheme 6 [a]



[a] Reagants: (a) (i) 20% piperidene, NMP, 2 h; (ii) DTT, DMF, 1 h; (iii) Ac_2O, pyridine, 16 h; (b) Reagent K, 5 h; (c) 10% hydrazine, H_2O, 20 min.

incubation of **30** with Reagent K[20] for 5 h to give glycopeptide **31**. The crude glycopeptide was then concentrated and subjected to 10% hydrazine hydrate in H_2O to remove all acetyl esters. The CD52 analogue **32** was purified by RP-HPLC, and its identity was confirmed by ESIMS.

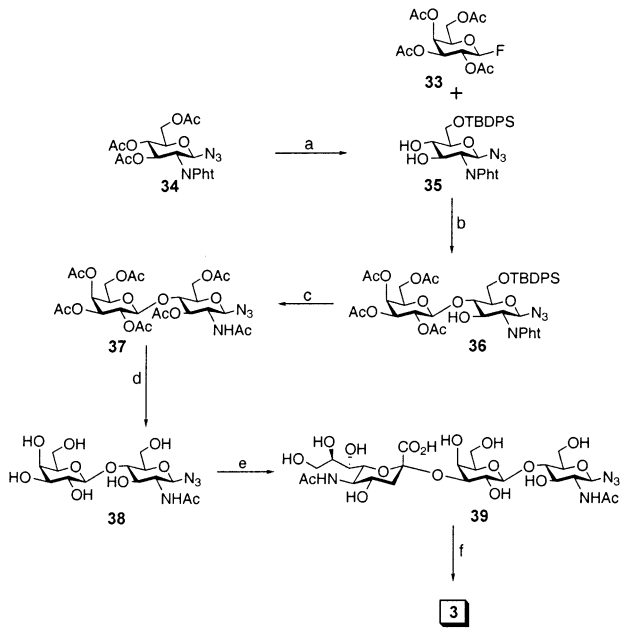
We selected the α-2,3-sialyl-*N*-acetyllactosamine trisaccharide for the variable, extensions as these epitopes are found on natural CD52 glycoforms.[8] For the preparation of an *N*-bromoacetamido oligosaccharide, we first generated the corresponding glycosyl azide (Scheme 7). Toward this goal, known fluoride donor **33**[21] was used to glycosylate acceptor **35**, available from glycosyl azide **34**,[22] to give disaccharide **36** with complete regioselectivity. The silyl ether of **36** was then removed, and the phthalimido group was cleaved by treatment with ethylenediamine. The resulting free amine was acetylated to afford a fully protected glycosyl azide intermediate **37**. Compound **37** was subsequently treated with NaOMe in MeOH to remove the acetyl esters yielding **38**. An α-2,3-sialyltransferase was utilized to transform **38** to trisaccharide **39** using CMP-*β*-D-sialic acid as a donor.[23] The glycosyl azide of **39** was reduced by hydrogenation and immediately reacted with bromoacetic anhydride to give the *N*-bromoacetamido trisaccharide **3**.

Chemoselective ligation of glycopeptide **32** with an excess of **3** at 37 °C for 16 h gave the desired biantennary glycopeptide **40**, which was isolated by RP-HPLC and characterized using ESIMS (Scheme 8).

Summary

In summary, the synthesis of CD52 containing a biantennary *N*-linked glycan highlights the utility of the chemoselective thioalkylation approach. To date, no glycoprotein containing a fully extended *N*-linked glycan has been synthesized by traditional chemical means (although smaller glycopeptides have). Furthermore, the need to synthesize very complex glycosyl amino acids is circumvented, allowing for a wider range

Scheme 7 [a]



[a] Reagents: (a) (i) NaOMe, MeOH, 16 h; (ii) TBDPSCl, DIEA, DMAP, CH_2Cl_2, 16 h, 98%; (b) AgOTf, $SnCl_2$, CH_2Cl_2, 4-Å MS, 0 °C to rt, 16 h, 84%; (c) (i) TBAF, AcOH, THF, 0 °C to rt, 16 h; (ii) ethylenediamine, BuOH, 90 °C, 16 h; (iii) Ac_2O, pyridine, 16 h, 80%; (d) NaOMe, MeOH, 16 h, 98%; (e) CMP-*β*-D-sialic acid, α-2,3-sialyltransferase, alkaline phosphatase, 5 d, 99%; (f) (i) Pd/C, H_2, H_2O, 20 min; (ii) bromoacetic anhydride, H_2O, 30 min, 56%.

of glycoforms to be synthesized from a common glycopeptide intermediate. When combined with protein synthesis methods such as native chemical ligation and expressed protein ligation, the chemoselective approach should provide access to *N*-linked glycoproteins with a high level of complexity.

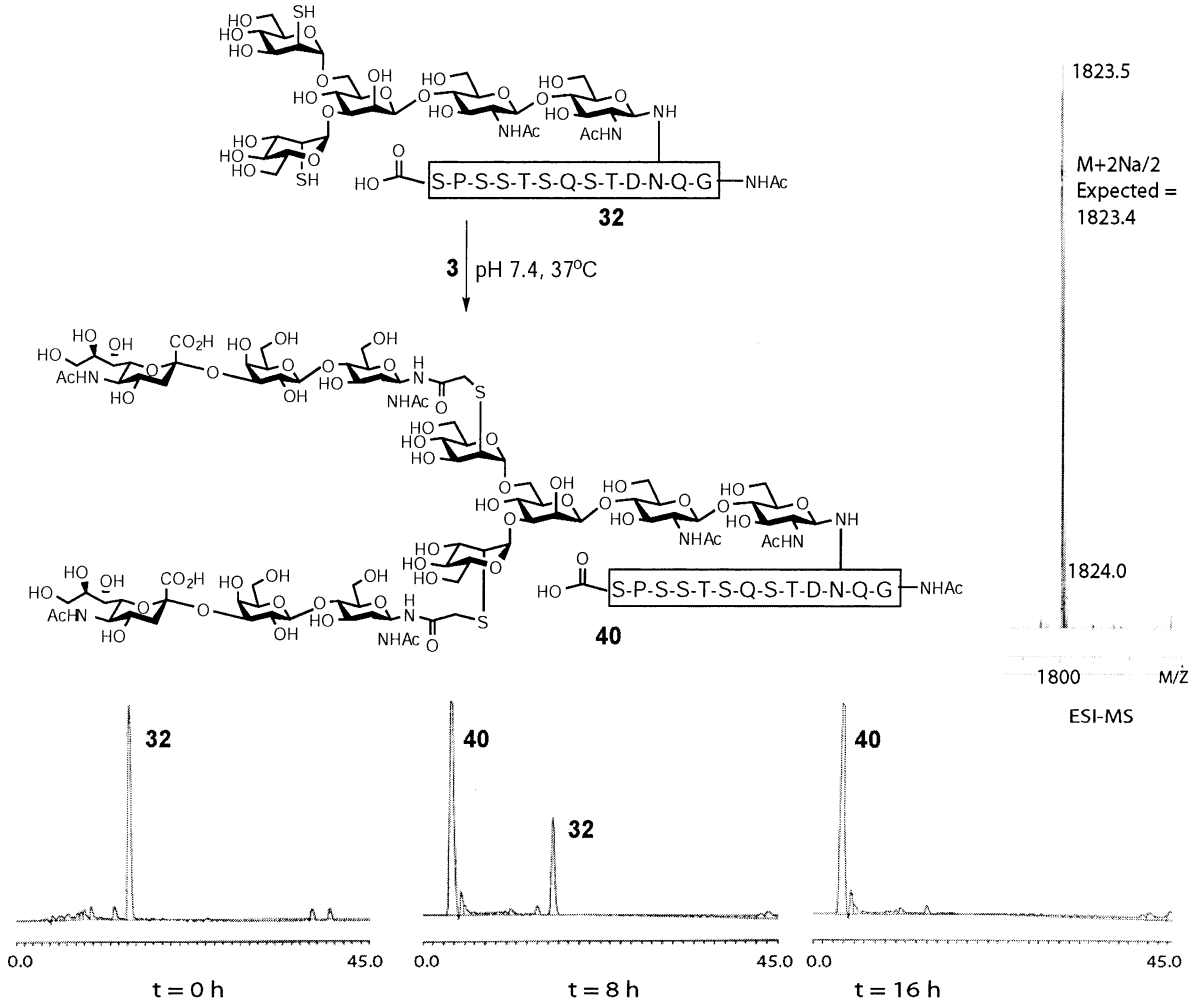
Experimental Section

General Methods. All chemical reagents were purchased from Sigma or Aldrich and used without further purification. All reaction solvents were distilled under a nitrogen atmosphere. THF was dried and degassed over benzophenone and Na^0. CH_2Cl_2, toluene, and pyridine were dried over CaH_2, and CH_3OH was dried over Mg^0. Thin-layer chromatography was carred out using Analtech Uniplate silica gel plates. Flash chromatography was performed using Merck 60-Å 230−400 mesh silica gel. All solvents were concentrated using rotary evaporation. All ^1H and ^{13}C NMR spectra were acquired on Bruker AM-400 or DRX-500 spectrometers as noted. All ^1H chemical shifts are reported in δ referenced to solvent. Coupling constants (J) are reported in Hz. Fast atom bombardment (FAB+) and electrospray (ESI±) spectra were obtained at the UC Berkeley Mass Spectrometry Laboratory. IR spectra were from thin film on NaCl disks and were acquired on a Perkin-Elmer series 1600 Fourier transform infrared spectrometer. Melting points (mp) were taken on a Thomas-Hoover Uni-Melt capillary melting point apparatus.

Phenyl 3,6-Di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-*β*-D-glucopyranoside (6). To a solution of **5** (2.34 g, 4.00 mmol) in freshly distilled CH_2Cl_2 (9 mL) at 0 °C was added trifluoroacetic anhydride (1.70 mL, 12.1 mmol) and triethylsilane (3.22 mL, 20.2 mmol). The reaction mixture was allowed to stir at 0 °C for 5 min, and then TFA (1.55 mL, 20.2 mmol) was added dropwise over a 2-min period. The reaction was allowed to warm to rt and was stirred for an additional 2 h. The reaction was diluted with ethyl acetate (150 mL), and the solution was washed with aqueous $NaHCO_3$, H_2O, and a brine solution. The organic layer was then dried over Na_2SO_4, filtered, and concentrated to an oil. Silica gel chromatography (40% ethyl acetate in hexanes)

(20) King, D. S.; Fields, C. G.; Fields, G. B. *Int. J. Pept. Protein Res.* **1990**, *36*, 255−266.
(21) Jain, R. K.; Huang, B. G.; Chandrasekaran, E. V.; Matta, K. L. *Chem. Commun.* **1997**, 23−24.
(22) Szilagyi, L.; Gyorgydeak, Z. *Carbohydr. Res.* **1985**, *143*, 21−41.
(23) Bowman, K. G.; Cook, B. N.; de Graffenried, C. L.; Bertozzi, C. R. *Biochemistry* **2001**, *40*, 5382−5391.

Scheme 8 [a]



[a] Ligation of glycopeptide with bromoacetamido sugars. Details of the reaction are provided in the Experimental Section.

yielded 2.00 g (85%) of **6** as a slightly colored oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87−7.68 (m, 4 H), 7.42−7.17 (m, 10 H), 7.06−6.92 (m, 5 H), 5.55 (d, 1 H, J = 10.2 Hz), 4.73 (d, 1 H, J = 12.2 Hz), 4.65−4.52 (m, 3 H), 4.33−4.24 (m, 3 H), 3.89−3.79 (m, 3 H), 3.72 (app q, 1 H, J = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.76, 167.55, 137.89, 137.56, 133.75, 132.36, 132.10, 128.71, 128.40, 128.08, 127.84, 127.78, 127.71, 127.69, 127.45, 123.39, 123.23, 83.57, 79.60, 77.69, 74.44, 74.02, 73.69, 70.61, 54.33; FAB−HRMS calcd for $C_{34}H_{31}NO_6S$ (M + Li^+) 588.2032, found 588.2043; IR (thin film) cm^{-1} 2924.4, 1774.2, 1712.7, 1386.1, 1079.9, 874.1, 720.0; $[\alpha]_D^{25^\circ} = +64.8^\circ$ (*c* 1.0, $CHCl_3$).

Phenyl 4-*O*-Acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (7). To a solution of **6** (2.0 g, 3.4 mmol) in pyridine (50 mL) was added Ac_2O (0.52 mL), and the reaction was stirred at rt for 16 h. The reaction mixture was then concentrated to yield 2.0 g (95%) of **7** as an off-white foam. The product was used in subsequent reactions without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82−7.68 (m, 4 H), 7.40−7.16 (m, 10 H), 7.00−6.89 (m, 5 H), 5.55 (d, 1 H, J = 10.5 Hz), 5.13 (app t, 1 H, J = 9.0 Hz), 4.6 (d, 1 H, J = 12.0 Hz), 4.55 (s, 1 H), 4.46 (app t, 1 H, J = 9.0 Hz), 4.33 (app t, 1 H, J = 10.2 Hz), 4.32 (d, 1 H, J = 10.7 Hz), 3.84−3.80 (m, 2 H), 3.64−3.65 (m, 2 H), 1.97 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.64, 168.17, 167.00, 138.02, 137.53, 134.19, 134.03, 132.21, 132.16, 129.05, 128.95, 128.87, 128.54, 128.45, 128.36, 128.33, 128.24, 128.11, 128.04, 127.92, 127.91, 127.87, 127.73, 127.62, 127.52, 127.47, 123.51, 123.41, 83.66, 77.10, 74.26, 73.49, 72.25, 69.62, 54.62, 20.81; FAB−HRMS calcd for $C_{36}H_{33}NO_7S$ (M + Li^+) 630.2138, found 630.2144; IR (thin film) cm^{-1} 1745.7, 1713.0, 1385.9, 1226.1, 1059.1, 719.9; $[\alpha]_D^{25^\circ} = +92.8^\circ$ (*c* 1.1, $CHCl_3$).

4-*O*-Acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl Azide. To a solution of **7** (1.0 g, 1.7 mmol) and 4-Å molecular sieves in freshly distilled CH_2Cl_2 (20 mL) under an Ar atmosphere was added $TMSN_3$ (0.24 mL, 1.8 mmol). The reaction was cooled to −40 °C, and NIS (930 mg, 4.1 mmol) was added. Tf_2O (140 μL, 0.85 mmol) was then added dropwise at −40 °C, and the reaction was stirred at this temperature for 20 min. The reaction mixture was then filtered through a bed of Celite and washed with aqueous NaS_2O_3, aqueous $NaHCO_3$, and H_2O. The organic layer was dried over Na_2SO_4, filtered, and concentrated to an oil. Silica gel chromatography (35% ethyl acetate in hexanes) yielded 934 mg (97%) of 4-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl azide as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90−7.65 (m, 4 H), 7.37−7.27 (m, 5 H), 7.0−6.9 (m, 5 H), 5.37 (d, 1 H, J = 9.4 Hz), 5.17 (app t, 1 H, J = 9.1 Hz), 4.61 (d, 1 H, J = 12.1 Hz), 4.58 (s, 2 H), 4.47 (app t, 1 H, J = 9 Hz), 4.31 (d, 1 H, J = 12.1 Hz), 4.18 (app t, 1 H, J = 9.5 Hz), 3.85 (m, 1 H), 3.62 (d, 2 H, J = 4.4 Hz), 1.96 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.42, 168.36, 137.68, 137.45, 134.07, 131.34, 128.39, 128.00, 127.82, 127.73, 127.63, 127.43, 127.40, 110.54, 85.55, 76.72, 75.73, 74.01, 73.65, 71.92, 69.13, 54.89, 20.72; FAB−HRMS calcd for $C_{30}H_{28}N_4O_7$ (M + Li^+) 563.2118, found 563.2123; IR (thin film) cm^{-1} 2116.1, 1713.6, 1386.9, 1226.0, 1077.5, 720.4; $[\alpha]_D^{25^\circ} = +54.0^\circ$ (*c* 1.3, $CHCl_3$).

3,6-Di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl Azide (8). To a solution of 4-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-

β-D-glucopyranosyl azide (1.2 g, 2.2 mmol) in CH_2Cl_2 (20 mL) was added MeOH (10 mL) and a 0.5 M solution of NaOMe in MeOH until a pH of 10 was reached. The reaction was stirred at rt for 2 h. Amberlite IRC-50 resin was added until a pH of approximately 5 was obtained. The reaction mixture was then filtered, and the solution was concentrated to give a clear oil. Silica gel chromatography (50% ethyl acetate in hexanes) yielded 1.06 g (96%) of **8** as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82−7.71 (m, 4 H), 7.41−7.33 (m, 5 H), 7.06−6.95 (m, 5 H), 5.37 (d, 1 H, J = 9.4 Hz), 4.75 (d, 1 H, J = 12.2 Hz), 4.67 (d, 1 H, J = 12.0 Hz), 4.61 (d, 1 H, J = 12.0 Hz), 4.53 (d, 1 H, J = 12.2 Hz), 4.28 (app t, 1 H, 8.5 Hz), 4.1 (app t, 1 H, J = 9.4 Hz), 3.89−3.73 (m, 3 H), 2.89 (d, 2 H, 2.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.12, 167.33, 137.94, 137.51, 134.08, 131.45, 128.57, 128.33, 128.14, 127.99, 127.84, 127.77, 127.75, 127.43, 123.41, 110.23, 85.67, 78.43, 77.38, 76.32, 74.57, 73.74, 73.43, 69.89, 54.93; FAB−HRMS calcd for $C_{28}H_{26}N_4O_6$ (M + Li^+) 521.2012, found 521.2023; IR (thin film) cm^{-1} 2871.7, 2112.7, 1766.4, 1714.8, 1390.6, 1066.3, 874.8; $[\alpha]_D^{25°}$ = +12.6° (*c* 1.0, $CHCl_3$).

***O*-(4-*O*-Acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-β-D-glucopyranosyl Azide (9).** To a solution of **7** (522 mg, 1.02 mmol) and **8** (575 mg, 0.922 mmol) in freshly distilled CH_2Cl_2 (50 mL) under an Ar atmosphere was added 500 mg of activated 4-Å molecular sieves. The reaction was cooled to −20 °C, and NIS (520 mg, 2.31 mmol) was added. TfOH (41 μL, 0.46 mmol) was then added dropwise over a 5-min period. The reaction mixture was stirred for 20 min. The reaction mixture was then filtered through Celite, and the filtrate was washed with aqueous $NaHCO_3$, aqueous $Na_2S_2O_3$, and a brine solution. The organic layer was dried over Na_2SO_4, filtered, and concentrated to give a yellow oil. Silica gel chromatography (35% ethyl acetate in hexanes) yielded 806 mg (94%) of **9** as a clear oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91−7.53 (m, 8 H), 7.38−7.27 (m, 10 H), 7.01−6.83 (m, 10 H), 5.34 (d, 1 H, J = 8.4 Hz), 5.17 (app t, 1 H, J = 9.1 Hz), 5.17 (d, 1 H, J = 9.4 Hz), 4.84 (d, 1 H, J = 12.5 Hz), 4.63−4.44 (m, 7 H), 4.32 (d, 1 H, J = 12.4 Hz), 4.29−4.18 (m, 3 H), 4.07−4.04 (m, 1 H), 3.60−3.57 (m, 3 H), 3.55 (app quin, 1 H, J = 3.5 Hz), 3.49−3.42 (m, 2 H), 1.61 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.59, 168.24, 167.92, 167.53, 167.24, 138.11, 138.06, 137.94, 137.63, 137.54, 134.03, 133.88, 131.46, 128.54, 128.39, 128.26, 128.11, 128.03, 127.90, 127.83, 127.75, 127.73, 127.61, 127.58, 127.43, 127.40, 127.38, 127.30, 127.00, 123.29, 97.01, 85.44, 76.78, 76.39, 75.54, 74.53, 74.53, 73.90, 73.48, 73.40, 72.72, 72.57, 69.28, 60.29, 56.16, 55.11, 29.60, 20.95, 20.81, 14.13; FAB−HRMS calcd for $C_{58}H_{53}N_5O_{13}$ (M + Li^+) 1034.3800, found 1034.3775; IR (thin film) cm^{-1} 2115.4, 1713.1, 1386.2, 1074.9, 720.9; $[\alpha]_D^{25°}$ = +29.1° (*c* 1.3, $CHCl_3$).

***O*-(3,6-Di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-β-D-glucopyranosyl Azide (10).** To a solution of **9** (50 mg, 0.049 mmol) in 1:1 THF/MeOH (3 mL) was added a 0.5 M solution of NaOMe in MeOH until a pH of 10 was reached. The reaction was stirred for 20 min at rt, and Amberlite IRC-50 resin was added until a pH of approximately 5 was obtained. The reaction mixture was filtered, and the filtrate was concentrated to a white solid. Silica gel chromatography (40% ethyl acetate in hexanes) yielded 44.5 mg (93%) of **10** as a white foam. Mp 69−70 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91−7.52 (m, 8 H), 7.38−7.26 (m, 10 H), 7.05−6.80 (m, 10 H), 5.31 (d, 1 H, J = 8.3 Hz), 5.16 (d, 1 H, J = 9.4 Hz), 4.78 (d, 2 H, J = 12.3 Hz), 4.58−4.45 (m, 6 H), 4.28−4.13 (m, 4 H), 4.03 (app t, 1 H, J = 10.1 Hz), 3.82 (app t, 1 H, J = 9.5 Hz), 3.71 (app quin, 1 H, J = 4.4 Hz), 3.58−3.53 (m, 2 H), 3.45−3.39 (m, 3 H), 3.10 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.59, 168.23, 167.52, 167.21, 138.36, 138.27, 138.13, 137.54, 133.84, 131.42, 128.53, 128.24, 127.87, 127.77, 127.74, 127.65, 127.42, 127.37, 127.28, 126.94, 123.64, 123.38, 110.40, 96.95, 85.54, 78.38, 77.27, 76.38, 75.19, 75.05, 74.33, 73.62, 73.07, 72.71, 80.70, 67.63, 56.02, 55.13; FAB−HRMS calcd for $C_{56}H_{51}N_5O_{12}$ (M + Li^+) 992.3694, found 992.3699; IR (thin film) cm^{-1} 2922.4, 2116.0, 1775.3, 1712.4, 1388.6, 1075.3, 721.0; $[\alpha]_D^{25°}$ = +9.2° (*c* 1.0, $CHCl_3$).

***O*-(3-*O*-Acetyl-4,6-*O*-benzylidene-2-chloroacetyl-β-D-glucopyranosyl)-(1→4)-*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-β-D-glucopyranosyl Azide (12).** Compounds **10** (707 mg, 0.717 mmol) and **11** (281 mg, 0.652 mmol) were combined and concentrated from toluene (25 mL) 3 times. After the mixture was placed under high vacuum for 1 h, freshly distilled CH_2Cl_2 (20 mL) was added followed by the addition of freshly activated 4-Å molecular sieves. NIS (734 mg, 3.26 mmol) and TfOH (57.0 μL, 0.652 mmol) were then added, and the reaction was stirred for 20 min. The reaction contents were then filtered through a pad of Celite. The filtrate was washed with $NaHCO_3$, NaS_2O_3, and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated to a yellow oil. Silica gel chromatography (10:1 toluene/ethyl acetate) yielded 647 mg (74%) of **12** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86−7.56 (m, 8 H), 7.42−7.24 (m, 15 H), 7.17 (app t, 1 H, J = 6.8 Hz), 7.02−6.90 (m, 7 H), 6.81−6.77 (m, 2 H), 5.38 (s, 1 H), 5.27 (d, 1 H, J = 8.2 Hz), 5.18 (app t, 1 H, J = 10.3 Hz), 5.16 (d, 1 H, J = 9.6 Hz), 4.97 (app t, 1 H, J = 8.1 Hz), 4.87 (d, 1 H, J = 12.8 Hz), 4.75 (app dd, 2 H, J = 12.4, 15.4 Hz), 4.65 (d, 1 H, J = 12.1 Hz), 4.56−4.45 (m, 4 H), 4.39 (d, 1 H, J = 12.3 Hz), 4.28−4.12 (m, 5 H), 4.05 (app t, 1 H, J = 9.6 Hz), 3.91 (app dd, 2 H, J = 14.8, 24.2 Hz), 3.64 (d, 1 H, J = 10.8 Hz), 3.59−3.55 (m, 3 H), 3.44−3.39 (m, 3 H), 3.25−3.20 (m, 3 H), 2.04 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.92, 168.57, 138.52, 138.43, 138.25, 138.07, 137.81, 128.67, 128.33, 128.22, 128.19, 128.06, 127.94, 127.81, 127.78, 127.69, 127.54, 127.42, 127.31, 127.21, 127.00, 126.23, 101.8, 99.87, 85.56, 74.52, 71.82, 70.15, 69.87, 69.10, 67.54, 56.23, 54.92, 40.49, 20.67; FAB−HRMS calcd for $C_{73}H_{68}ClN_5O_{19}$ (M + Li^+) 1360.4357, found 1360.4357; IR (thin film) cm^{-1} 2922.2, 2861.1, 2116.3, 1748.3, 1715.7, 1389.6, 1075.9; $[\alpha]_D^{25°}$ = −16.9° (*c* 1.2, $CHCl_3$).

***O*-(3-*O*-Acetyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-(1→4)-*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-β-D-glucopyranosyl Azide (13).** To a solution of **12** (7.66 g, 5.66 mmol) in lutidine (40 mL) and acetic acid (14 mL) were added 45 mL of a 0.375 M solution of hydrazinedithiocarbonate in ethanol. The reaction was stirred for 15 min and then diluted with ethyl acetate (200 mL). The resulting mixture was washed twice with H_2O and then brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated. Silica gel chromatography (40% ethyl acetate in hexanes) yielded 6.87 g (95%) of **13** as a white foam. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85−7.56 (m, 8 H), 7.41−7.26 (m, 15 H), 7.02−6.89 (m, 7 H), 6.81−6.76 (m, 3 H), 5.38 (s, 1 H), 5.27 (d, 1 H, J = 8.4 Hz), 5.16 (d, 1 H, J = 9.4 Hz), 5.08 (app t, 1 H, J = 9.5 Hz), 4.85 (d, 1 H, J = 12.7 Hz), 4.79 (d, 1 H, J = 12.2 Hz), 4.69 (d, 1 H, J = 7.7 Hz), 4.61 (d, 1 H, J = 12.1 Hz), 4.56−4.49 (m, 4 H), 4.42−4.36 (m, 2 H), 4.30−4.04 (m, 6 H), 3.81 (app dd, 1 H, J = 2.7, 11.6 Hz), 3.65 (d, 1 H, J = 9.7 Hz), 3.51 (d, 1 H, J = 9.5 Hz), 3.49−3.41 (m, 3 H), 3.40−3.38 (m, 3 H), 3.32 (d, 1 H, J = 10.0 Hz), 3.23−3.20 (m, 1 H), 2.13 (s, 3 H);^{13}C NMR (125 MHz, $CDCl_3$) δ 168.92, 168.57, 138.52, 138.43, 138.25, 138.07, 137.81, 128.67, 128.33, 128.22, 128.19, 128.06, 127.94, 127.81, 127.78, 127.69, 127.54, 127.42, 127.31, 127.21, 127.00, 126.23, 101.8, 98.87, 85.57, 74.42, 70.67, 70.15, 70.09, 69.87, 69.10, 67.54, 56.23, 54.92, 20.67; FAB−HRMS calcd for $C_{71}H_{67}N_5O_{18}$ (M + Li^+) 1284.4641, found 1284.4640; IR (thin film) cm^{-1} 2924.3, 2116.4, 1698.6, 1650.7, 1557.8, 1078.7.

***O*-(2,3-Di-*O*-acetyl-4,6-*O*-benzylidene-β-D-mannopyranosyl)-(1→4)-*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-β-D-glucopyranosyl Azide (14).** Compound **13** (671 mg, 0.525 mmol) was concentrated from toluene (10 mL) 2 times. After it was placed under high vacuum for 1 h, freshly distilled CH_2Cl_2 (10 mL) was added. Strictly anhydrous pyridine (170 μL, 0.787 mmol) was subsequently added, and the reaction was cooled to −15 °C. Tf_2O (133 μL, 0.788 mmol) was then

added dropwise over 2 min, and the reaction mixture stirred for 3 h. At this time, the reaction was concentrated under high vacuum, and Bu_4NOAc (950 mg, 3.15 mmol) was added. The resulting syrup was concentrated from toluene (10 mL) 2 times and placed under high vacuum for 30 min. Freshly distilled toluene (10 mL) was then added, and the reaction was sonicated for 16 h. Ethyl acetate (50 mL) was then added, and the reaction mixture was subsequently washed with H_2O followed by brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated. Silica gel chromatography (10% ethyl acetate in hexanes) yielded 659 mg (95%) of **14** as a white foam. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87−7.67 (m, 8 H), 7.43−7.26 (m, 15 H), 7.05−7.01 (m, 2 H), 6.96−6.92 (m, 5 H), 6.80−6.75 (m, 3 H), 5.47 (d, 1 H, J = 3.2 Hz), 5.45 (s, 1 H), 5.26 (d, 1 H, J = 8.3 Hz), 5.16 (d, 1 H, J = 9.4), 4.97 (app dd, 1 H, J = 3.3, 10.3 Hz), 4.88−4.83 (m, 3 H), 4.61 (d, 1 H, J = 12.0 Hz), 4.53−4.49 (m, 4 H), 4.41 (d, 1 H, J = 12.0 Hz), 4.28−4.23 (m, 2 H), 4.21−4.13 (m, 4 H), 4.06 (app t, 1 H, J = 9.6 Hz), 3.87 (app t, 1 H, J = 9.8 Hz), 3.68 (d, 1 H, J = 10.9 Hz), 3.59−5.53 (m, 3 H), 3.43−3.39 (m, 2 H), 3.22−3.17 (m, 2 H), 2.19 (s, 3 H), 2.03 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.95, 169.43, 138.57, 138.42, 138.21, 138.00, 137.84, 128.66, 128.37, 128.23, 128.12, 128.00, 127.97, 127.83, 127.71, 127.61, 127.50, 127.44, 127.38, 127.27, 127.09, 126.24, 101.82, 98.23, 97.16, 85.15, 78.54, 77.32, 76.81, 75.01, 74.50, 73.27, 72.86, 70.16, 69.82, 69.13, 67.59, 56.26, 54.95, 20.94, 20.78; FAB−HRMS calcd for $C_{73}H_{69}N_5O_{19}$ (M + Li^+) 1326.4747, found 1326.4797; IR (thin film) cm^{-1} 2924.1, 1747.9, 1698.6, 1540.7, 1388.6, 1075.3; $[\alpha]_D^{25^\circ} = -0.4^\circ$ (*c* 1.1, $CHCl_3$).

***O*-(4,6-*O*-Benzylidene-*β*-D-mannopyranosyl)-(1→4)-*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-*β*-D-glucopyranosyl Azide (15).** Compound **14** (101 mg, 0.0770 mmol) was dissolved in CH_2Cl_2 (10 mL). A 1 M solution of NaOMe in MeOH was then added until a pH of 10 was reached. The reaction was stirred at rt for 1 h, at which point AcOH was added until a pH of 6 was obtained. The reaction mixture was then washed with $NaHCO_3$, H_2O, and finally brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated. Silica gel chromatography (50% ethyl acetate in hexanes) yielded 90 mg (95%) of **15** as a white foam. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87−7.51 (m, 8 H), 7.46−7.26 (m, 15 H), 7.02−7.01 (m, 2 H), 6.97−6.91 (m, 5 H), 6.81−6.76 (m, 3 H), 5.46 (s, 1 H), 5.29 (d, 1 H, J = 8.4 Hz), 5.16 (d, 1 H, J = 9.4 Hz), 4.87−4.82 (m, 2 H), 4.75 (s, 1 H), 4.61−4.53 (m, 3 H), 4.51−4.46 (m, 2 H), 4.43−4.38 (m, 3 H), 4.29 (app t, 1 H, J = 8.7 Hz), 4.23 (app dd, 1 H, J = 8.4, 10.7 Hz), 4.17−4.12 (m, 3 H), 4.06 (app t, 1 H, J = 9.4 Hz), 3.94 (d, 1 H, J = 3.4 Hz), 3.76 (app t, 1 H, J = 9.5 Hz), 3.67−3.58 (m, 5 H), 3.54 (app t, 1 H, J = 10.3 Hz), 3.43 (d, 1 H, J = 11.4 Hz), 3.39 (d, 1 H, J = 10.0 Hz), 3.32 (d, 1 H, J = 9.9 Hz), 3.15−3.12 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.90, 169.43, 138.57, 138.42, 138.21, 138.00, 137.84, 128.66, 128.37, 128.23, 128.12, 128.00, 127.97, 127.83, 127.71, 127.61, 127.50, 127.44, 127.38, 127.27, 127.09, 126.24, 101.51, 87.27, 78.39, 74.81, 72.21, 75.01, 70.16, 69.82, 69.13, 67.59, 56.26, 54.95, 20.95; FAB−HRMS calcd for $C_{69}H_{65}N_5O_{17}$ (M + Li^+) 1242.4536, found 1242.4538; IR (thin film) cm^{-1} 3100.0, 2924.8, 2116.0, 1827.7, 1698.8, 1540.2, 1077.5, 724.0. $[\alpha]_D^{25^\circ} = +11.1^\circ$ (*c* 1.10, $CHCl_3$).

Benzyl 3,4,6-Tri-*O*-benzyl-1-thio-*β*-D-glucopyranoside (17). 3,4,6-Tri-*O*-benzyl glucal (**16**) (2.9 g, 6.9 mmol) was dissolved in freshly distilled CH_2Cl_2 (50 mL) at 0 °C. A recently prepared and dried dimethyl dioxirane solution (250 mL, 0.03 M in acetone) was then added in a dropwise fashion. The reaction was stirred at 0 °C for 1 h and was then concentrated at 0 °C. Distilled CH_2Cl_2 (50 mL) was then added followed by addition of benzyl mercaptan (16 mL, 140 mmol) and trifluoroacetic anhydride (100 μL, 0.7 mmol). The reaction was stirred for 16 h and subsequently concentrated and purified by silica gel chromatography (20% ethyl acetate in hexanes) to yield 3.5 g (90%) of **17** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.19 (m, 20 H), 4.90 (d, 1 H, J = 11.3 Hz), 4.84 (d, 2 H, J = 10.0 Hz), 4.65 (d, 1 H, J = 12.2 Hz), 4.58 (d, 2 H, J = 12.6 Hz), 4.18 (d, 1 H, J = 9.7 Hz), 3.99 (d, 1 H, J = 13.1 Hz), 3.89 (d, 1 H, J = 13.1 Hz), 3.77−3.71 (m, 2 H), 3.66−3.58 (m, 2 H), 3.52 (app t, 1 H, J = 8.7 Hz), 3.46−4.43 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.53, 138.27, 138.00, 137.21, 129.13, 128.65, 128.54, 128.44, 128.37, 128.05, 127.96, 127.89, 127.72, 127.64, 127.52, 127.21, 86.27, 84.33, 79.21, 77.58, 75.23, 75.00, 73.49, 73.39, 69.05, 33.83; FAB−HRMS calcd for $C_{34}H_{36}O_5S$ (M + Li^+) 563.2443, found 563.2441; IR (thin film) cm^{-1} 1856.5, 1744.9, 1656.3, 1027.2.

3,4,6-Tri-*O*-benzyl-2-deoxy-2-thiobenzyl-α-D-mannopyranosyl Fluoride (18). To a solution of **17** (100 mg, 0.180 mmol) in freshly distilled CH_2Cl_2 (5 mL) at 0 °C was added DAST (71.0 μL, 0.530 mmol). The reaction was stirred for 10 min and then diluted with CH_2Cl_2 (20 mL) and washed with $NaHCO_3$, H_2O, and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated. Silica gel chromatography (10% ethyl acetate in hexanes) yielded 92 mg (92%) of **18** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.15 (m, 20 H), 5.62 (dd, 1 H, J = 1.6, 52.6 Hz), 4.86 (d, 1 H, J = 10.8 Hz), 4.68 (d, 1 H, J = 12.2 Hz), 4.52−4.48 (m, 4 H), 4.10−4.09 (m, 1 H), 4.08−3.74 (m, 5 H), 3.67 (app dd, 1 H, J = 1.3, 12.5 Hz), 3.24−3.23 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.17, 138.14, 137.92, 137.60, 129.16, 128.74, 128.52, 128.40, 128.01, 127.86, 127.78, 127.64, 127.48, 108.69 (d, J = 226.4 Hz), 77.69, 75.08, 74.52, 74.07, 73.47, 71.78, 68.45, 46.91, 46.63, 36.89; FAB−HRMS calcd for $C_{34}H_{35}FO_4S$ (M + Li^+) 565.2400, found 565.2400; IR (thin film) cm^{-1} 1856.7, 1743.9, 1654.7, 1029.3.

***O*-(3,4,6-Tri-*O*-benzyl-2-deoxy-2-thiobenzyl-α-D-mannopyranosyl)-(1→3)-*O*-(4,6-*O*-benzylidene-*β*-D-mannopyranosyl)-(1→4)-*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-*β*-D-glucopyranosyl Azide (19).** Compounds **15** (145 mg, 0.117 mmol) and **18** (85.0 mg, 0.152 mmol) were combined and concentrated from toluene (50 mL) 3 times. The resulting foam was then placed under high vacuum for 1 h. Freshly distilled CH_2Cl_2 (20 mL) was then added along with 4-Å molecular sieves. The reaction mixture was then cooled to 0 °C, and $SnCl_2$ (40.0 mg, 0.211 mmol) was added. After 15 min, AgOTf (44.0 mg, 0.211 mmol) was added, and the reaction was allowed to warm to rt over 16 h. The mixture was then filtered through a pad of Celite, and the filtrate was washed with $NaHCO_3$, H_2O, and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated. Silica gel chromatography (30% ethyl acetate in hexanes) yielded 165 mg (80%) of **19** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88−7.68 (m, 8 H), 7.43−7.22 (m, 30 H), 7.15−7.10 (m, 5 H), 7.06−7.04 (m, 1 H), 7.01 (d, 1 H, J = 6.4 Hz), 6.95−6.88 (m, 5 H), 6.79−6.73 (m, 3 H), 5.45 (s, 1 H), 5.28 (d, 1 H, J = 8.4 Hz), 5.22 (d, 1 H, J = 2.9 Hz), 5.16 (d, 1 H, J = 9.4 Hz), 4.85 (app dd, 2 H, J = 5.2, 12.8 Hz), 4.70 (d, 1 H, J = 11.0 Hz), 4.66 (s, 1 H), 4.61−4.56 (m, 3 H), 4.52−4.41 (m, 6 H), 4.28−4.20 (m, 3 H), 4.16−4.09 (m, 5 H), 4.07−4.02 (m, 3 H), 3.94 (app t, 1 H, J = 9.6 Hz), 3.68−3.63 (m, 6 H), 3.60−3.49 (m, 6 H), 3.43 (dd, 1 H, J = 3.5, 11.2 Hz), 3.39 (app d, 1 H, J = 10.6 Hz), 3.26 (app d, 1 H, J = 9.9 Hz), 3.19 (app t, 1 H, J = 3.2 Hz), 3.16−3.12 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.23, 170.61, 170.09, 169.44, 138.63, 138.37, 138.17, 138.10, 137.98, 137.97, 137.96, 137.84, 137.70, 137.33, 134.43, 133.27, 130.95, 129.72, 129.72, 129.23, 128.99, 128.97, 128.89, 128.60, 128.58, 128.47, 128.40, 128.33, 128.32, 128.30, 128.29, 128.28, 128.20, 128.18, 128.17, 128.11, 128.09, 128.05, 128.01, 127.90, 127.88, 127.85, 127.84, 127.83, 127.82, 127.74, 127.73, 127.70, 127.62, 127.57, 127.51, 127.48, 127.30, 127.20, 127.04, 126.97, 126.85, 126.27, 126.22, 123.70, 102.00, 100.67, 96.92, 85.53, 83.04, 78.83, 78.44, 77.24, 76.33, 75.88, 75.55, 75.08, 74.60, 74.54, 73.47, 73.16, 72.74, 71.84, 71.59, 71.37, 70.71, 68.69, 67.66, 66.85, 64.33, 60.36, 56.52, 55.17, 53.55, 47.02; FAB−HRMS calcd for $C_{103}H_{99}N_5O_{21}S$ (M + Na^+) 1796.6451, found 1796.6480; IR (thin film) cm^{-1} 3438.1, 2922.5, 2115.3, 1699.0, 1650.7, 1507.0, 1075.7, 723.0.

***O*-(3,4,6-Tri-*O*-benzyl-2-deoxy-2-thiobenzyl-α-D-mannopyranosyl)-(1→3)-*O*-(2-*O*-acetyl-4,6-*O*-benzylidene-*β*-D-mannopyranosyl)-(1→4)-*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyrano-**

syl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-*β*-D-glucopyranosyl Azide (20). Compound **19** (380 mg, 0.214 mmol) was dissolved in pyridine, and Ac_2O (40 μL, 0.428 mmol) was added. The reaction was stirred for 16 h and then concentrated under high vacuum. Silica gel chromatography (30% ethyl acetate in hexanes) yielded 377 mg (95%) of **20** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87−7.69 (m, 8 H), 7.47−7.46 (app d, 2 H, J = 6.5 Hz), 7.35−7.13 (m, 30 H), 7.03−6.97 (m, 10 H), 6.79−6.76 (m, 3 H), 5.49 (s, 1 H), 5.41 (d, 1 H, J = 2.8 Hz), 5.32 (s, 1 H), 5.26 (d, 1 H, J = 8.2 Hz), 5.16 (d, 1 H, J = 9.4 Hz), 4.87−4.80 (m, 3 H), 4.74 (s, 1 H), 4.65 (d, 1 H, J = 12.2 Hz), 4.58−4.38 (m, 9 H), 4.29−4.13 (m, 10 H), 4.05 (app t, 1 H, J = 9.6 Hz), 3.92−3.88 (m, 3 H), 3.82 (app t, 1 H, J = 9.3 Hz), 3.75−3.64 (m, 5 H), 3.58−3.52 (m, 3 H), 3.22 (app d, 1 H, J = 9.9 Hz), 3.11−3.09 (m, 2 H), 2.03 (s, 3 H);^{13}C NMR (125 MHz, $CDCl_3$) δ 171.23, 170.61, 170.09, 169.55, 169.44, 138.98, 138.60, 138.57, 138.48, 138.41, 138.35, 138.29, 138.20, 138.05, 138.01, 137.94, 137.86, 137.22, 133.79, 131.51, 129.41, 129.27, 129.11, 129.03, 128.65, 128.44, 128.39, 128.35, 128.25, 128.22, 128.16, 128.13, 128.09, 128.05, 128.01, 127.95, 127.88, 127.86, 127.78, 127.73, 127.70, 127.66, 127.63, 127.56, 127.43, 127.25, 127.02, 126.88, 126.31, 126.25, 123.30, 102.08, 101.41, 99.14, 96.95, 85.56, 78.74, 78.44, 77.72, 76.77, 76.46, 75.59, 75.14, 75.05, 74.60, 74.53, 74.44, 74.34, 73.40, 73.28, 73.08, 72.89, 72.78, 72.14, 71.04, 70.74, 69.15, 68.51, 67.69, 67.54, 66.59, 56.54, 55.19, 47.32, 20.87; FAB−HRMS calcd for $C_{105}H_{101}N_5O_{22}S$ (M + Na^+) 1838.6557, found 1838.6662; IR (thin film) cm^{-1} 2923.3, 2112.4, 1716.0, 1650.7, 1557.8.6, 1073.2, 728.0.

***O*-(3,4,6-Tri-*O*-benzyl-2-deoxy-2-thiobenzyl-α-D-mannopyranosyl)-(1→3)-*O*-(2-*O*-acetyl-*β*-D-mannopyranosyl)-(1→4)-*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-*β*-D-glucopyranosyl Azide (21).** Compound **20** (325 mg, 0.179 mmol) was placed in an ice bath, and a precooled solution (0 °C) of 5% TFA in CH_2Cl_2 (15 mL) was added. The reaction was stirred at 0 °C for 20 min, at which time the acid was quenched with addition of aqueous $NaHCO_3$. The resulting mixture was washed with H_2O and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated. Silica gel chromatography (40% ethyl acetate in hexanes) yielded 200 mg (65%) of **21** as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89−7.55 (m, 8 H), 7.38−7.15 (m, 25 H), 7.01−6.94 (m, 7 H), 6.77−6.73 (m, 3 H), 5.37 (d, 1 H, J = 3.1 Hz), 5.26 (d, 1 H, J = 8.1 Hz), 5.16 (d, 1 H, J = 9.4 Hz), 5.13 (d, 1 H, J = 4.0 Hz), 4.87 (d, 1 H, J = 12.0 Hz), 4.86 (d, 1 H, J = 12.9 Hz), 4.67−4.32 (m, 16 H), 4.26−4.03 (m, 8 H), 3.83−3.63 (m, 6 H), 3.57−4.48 (m, 5 H), 3.43−3.38 (m, 4 H), 3.22 (app d, 1 H, J = 9.8 Hz), 3.04 (app t, 2 H, J = 9.9 Hz), 2.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.23, 170.61, 170.09, 169.55, 169.53, 138.39, 138.36, 138.16, 138.14, 138.13, 138.09, 138.03, 137.85, 129.12, 128.58, 128.56, 128.37, 128.34, 128.32, 128.29, 128.21, 128.15, 128.08, 127.89, 127.86, 127.82, 127.81, 127.78, 127.74, 127.68, 127.65, 127.63, 127.58, 127.57, 127.34, 127.19, 126.96, 102.22, 98.23, 96.95, 85.51, 79.58, 78.32, 77.86, 77.29, 76.75, 76.68, 76.48, 75.36, 75.19, 75.14, 74.65, 74.44, 74.41, 73.30, 73.06, 72.88, 71.82, 71.21, 69.03, 67.65, 67.43, 64.35, 62.29, 56.45, 55.18, 47.85, 21.06; FAB−HRMS calcd for $C_{98}H_{97}N_5O_{22}S$ (M + Li^+) 1734.6506, found 1734.6483; IR (thin film) cm^{-1} 3339.8, 2923.5, 2115.2, 1715.9, 1657.7, 1557.8, 1073.3, 719.8.

***O*-(3,4,6-Tri-*O*-benzyl-2-deoxy-2-thiobenzyl-α-D-mannopyranosyl)-(1→3)-*O*-[(3,4,6-tri-*O*-benzyl-2-deoxy-2-thiobenzyl-α-D-mannopyranosyl)-(1→6)]-*O*-(2-*O*-acetyl-*β*-D-mannopyranosyl)-(1→4)-*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-*β*-D-glucopyranosyl Azide (22).** Compounds **21** (537 mg, 0.311 mmol) and **18** (191 mg, 0.342 mmol) were combined and evaportated from toluene (50 mL) 3 times. The mixture was placed under high vacuum for 1 h, and dry CH_2Cl_2 (20 mL) and freshly activated 4-Å molecular sieves were added. The reaction mixture was cooled to 0 °C, and $SnCl_2$ (106 mg, 0.560 mmol) was added. The reaction was stirred for 15 min, at which time AgOTf (144 mg, 0.560 mmol) was added. The reaction was allowed to warm to rt over 16 h. The mixture was then filtered through a pad of Celite, and the filtrate was washed with concentrated $NaHCO_3$, H_2O, and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated. Silica gel chromatography (30% ethyl acetate in hexanes) yielded 600 mg (85%) of **22** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83−7.57 (m, 8 H), 7.31−7.07 (m, 45 H), 6.94−6.92 (m, 5 H), 6.75−6.74 (m, 10 H), 5.39 (d, 1 H, J = 1.2 Hz), 5.26 (d, 1 H, J = 1.1 Hz), 5.22 (d, 1 H, J = 8.0 Hz), 5.14 (d, 1 H, J = 9.3 Hz), 4.87−4.83 (m, 3 H), 4.74−4.67 (m, 4 H), 4.65 (s, 1 H), 4.58−4.32 (m, 14 H), 4.26−4.11 (m, 6 H), 4.08−4.02 (m, 2 H), 3.90−3.88 (m, 5 H), 3.83−3.47 (m, 15 H), 3.36 (app d, 2 H, J = 9.3 Hz), 3.25−3.20 (m, 2 H), 3.06 (m, 2 H), 2.03 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.75, 169.53, 169.21, 167.56, 138.84, 138.54, 138.48, 138.42, 138.38, 138.28, 138.24, 138.21, 138.19, 138.18, 138.11, 138.08, 138.04, 138.03, 137.96, 137.94, 137.88, 133.80, 131.81, 131.54, 129.24, 129.19, 129.16, 129.08, 128.78, 128.60, 128.59, 128.58, 128.56, 128.53, 128.49, 128.48, 128.45, 128.40, 128.36, 128.34, 128.31, 128.30, 128.27, 128.25, 128.17, 128.03, 128.00, 127.94, 127.91, 127.89, 127.87, 127.81, 127.79, 127.76, 127.75, 127.74, 127.73, 127.69, 127.65, 127.61, 127.59, 127.56, 127.55, 127.52, 127.48, 127.20, 127.17, 127.12, 127.11, 127.01, 123.38, 102.46, 100.60, 99.20, 96.95, 85.54, 81.47, 78.82, 78.42, 77.42, 76.80, 75.63, 75.56, 75.22, 75.07, 74.87, 74.63, 74.52, 73.52, 73.40, 73.36, 73.30, 72.87, 71.99, 71.51, 71.33, 69.13, 55.23, 37.07, 36.72, 21.19; ESI−HRMS calcd for $C_{132}H_{131}N_5O_{26}S_2$ (M + 2Na^+/2) 1156.4170, found 1156.4198; IR (thin film) cm^{-1} 3340.8, 2924.3, 2115.3, 1725.9.3, 1650.7, 1553.8, 1072.3, 720.8.

***O*-(3,4,6-Tri-*O*-benzyl-2-deoxy-2-thiobenzyl-α-D-mannopyranosyl)-(1→3)-*O*-[(3,4,6-tri-*O*-benzyl-2-deoxy-2-thiobenzyl-α-D-mannopyranosyl)-(1→6)]-*O*-(2-*O*-acetyl-*β*-D-mannopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-benzyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2-acetamido-3,6-di-*O*-benzyl-2-deoxy-1-*β*-D-glucopyranosyl Azide (23).** Pentasaccharide **22** (130 mg, 0.06 mmol) was dissolved in *n*-BuOH (10 mL) and ethylenediamine (2.5 mL). The reaction mixture was then heated at 90 °C for 16 h. At this time, the reaction was concentrated under high vacuum and evaporated from toluene (20 mL) 2 times. A solution of pyridine/Ac_2O (2:1, 20 mL) was then added, and the reaction was stirred for 4 h. The solvent was removed under high vacuum, and the resulting oil was purified by silica gel chromatography (66% ethyl acetate in hexanes) to yield 115 mg (97%) of **23** as a colorless oil.^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31−7.21 (m, 55 H), 7.14−7.11 (m, 5 H), 6.15 (d, 1 H, J = 12 Hz), 5.35 (d, 1 H, J = 3.0 Hz), 5.12 (app t, 1 H, J = 9.8 Hz), 4.99 (d, 1 H, J = 3.7 Hz), 4.89 (d, 1 H, J = 1 Hz), 4.83−4.76 (m, 4 H), 4.70 (d, 1 H, J = 8.4 Hz), 4.67−4.58 (m, 7 H), 4.55−4.48 (m, 7 H), 4.43−4.32 (m, 8 H), 3.95 (app t, 1 H, J = 5.4 Hz), 3.84−3.81 (m, 6 H), 3.71−3.54 (m, 15 H), 3.49 (d, 1 H, J = 8.3 Hz), 3.45 (dd, 1 H, J = 10.8, 1.0 Hz), 3.39 (dd, 1 H, J = 7.8, 3.3 Hz), 3.20 (m, 2 H), 3.10 (dd, 1 H, J = 2.6, 1.4 Hz), 2.99 (dd, 1 H, J = 7.3, 3.6 Hz), 2.01 (s, 3 H), 1.85 (s, 3 H), 1.82 (s, 3 H), 1.65 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.42, 170.39, 169.84, 169.57, 138.62, 138.58, 138.39, 138.38, 138.35, 138.29, 138.26, 138.22, 138.19, 138.17, 137.99, 137.89, 129.15, 129.05, 128.58, 128.55, 128.50, 128.48, 128.36, 128.32, 128.31, 128.30, 128.29, 128.28, 128.24, 128.19, 128.04, 127.94, 127.92, 127.89, 127.86, 127.79, 127.73, 127.70, 127.68, 127.65, 127.63, 127.61, 127.55, 127.50, 127.48, 127.12, 127.04, 103.24, 100.34, 99.73, 98.03, 88.19, 79.11, 79.05, 78.19, 77.83, 76.43, 75.88, 75.47, 75.10, 74.78, 74.41, 73.80, 73.56, 73.40, 73.35, 73.29, 73.24, 73.21, 72.80, 72.73, 72.16, 72.10, 71.89, 71.56, 71.03, 69.08, 69.01, 68.84, 68.42, 67.00, 23.40, 23.10, 21.02, 20.96; FAB−HRMS calcd for $C_{122}H_{133}N_5O_{25}S_2$ (M + Na^+) 2154.8629, found 2154.8541; IR (thin film) cm^{-1} 2922.9, 2113.2, 1650.4, 1557.8, 1072.3, 719.5.

***N*$^{\alpha}$-(*tert*-Butoxycarbonyl)-N$^{\gamma}$-{*O*-(3,4,6-tri-*O*-benzyl-2-deoxy-2-thiobenzyl-α-D-mannopyranosyl)-(1→3)-*O*-[(3,4,6-tri-*O*-benzyl-2-deoxy-2-thiobenzyl-α-D-mannopyranosyl)-(1→6)]-*O*-(2-*O*-acetyl-*β*-D-mannopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-benzyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2-acetamido-3,6-di-*O*-benzyl-2-deoxy-1-*β*-D-glucopyranosyl}-L-asparagine *tert*-Butyl Ester 26.** Pentasaccharide

23 (260 mg, 0.12 mmol) was dissolved in MeOH (6 mL), and DIEA (213 μL, 1.22 mmol) was added. The reaction flask was then purged with Ar, and propanedithiol (612 μL, 6.10 mmol) was subsequently added. The reaction was allowed to stir for 4 h, at which time it was concentrated and the resulting glycosylamine **24** was placed under high vacuum for 1 h. A solution of pentafluorophenyl ester **25** (360 mg, 0.79 mmol), DIEA (210 μL, 1.22 mmol), and HOBt (91 mg, 0.67 mmol) in NMP (5 mL) was then added to **24**, and the mixture was stirred for 16 h. The reaction was then diluted with ethyl acetate (10 mL) and washed with concentrated $NaHCO_3$, H_2O, and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated. Silica gel chromatography (70% ethyl acetate in hexanes) yielded 224 mg (80%) of **26** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31−7.20 (m, 55 H), 7.13−7.12 (m, 5 H), 5.60 (d, 1 H, J = 10.5 Hz), 5.37 (d, 1 H, J = 3.0 Hz), 5.13 (app t, 1 H, J = 10.0 Hz), 4.98 (d, 1 H, J = 3.7 Hz), 4.86 (d, 1 H, J = 12.2 Hz), 4.76 (d, 1 H, J = 11.1 Hz), 4.69−4.50 (m, 12 H), 4.45−4.30 (m, 10 H), 3.86−3.82 (m, 8 H), 3.78−3.53 (m, 15 H), 3.44 (d, 2 H, J = 9.1 Hz), 3.36−3.33 (m, 5 H), 3.20−3.14 (m, 5 H), 3.07 (d, 1 H, J = 3.2 Hz), 2.99 (d, 1 H, J = 4.6 Hz), 2.04 (s, 3 H), 1.80 (s, 3 H), 1.74 (s, 3 H), 1.63 (s, 3 H), 1.41 (s, 18 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.43, 170.38, 170.28, 169.85, 169.84, 169.55, 138.62, 138.54, 138.39, 138.38, 138.32, 138.29, 138.25, 138.17, 138.15, 138.14, 137.91, 137.85, 129.12, 129.01, 128.58, 128.53, 128.51, 128.44, 128.38, 128.37, 128.32, 128.29, 128.23, 128.22, 128.21, 128.19, 128.03, 127.94, 127.92, 127.84, 127.77, 127.71, 127.69, 127.68, 127.66, 127.65, 127.61, 127.58, 127.57, 127.48, 127.45, 127.36, 127.08, 103.27, 100.38, 100.00, 99.73, 88.21, 79.10, 79.08, 78.17, 77.81, 76.43, 75.88, 75.47, 75.10, 74.78, 74.41, 73.80, 73.56, 73.38, 73.35, 73.26, 73.23, 73.21, 72.80, 72.73, 72.19, 72.14, 71.89, 71.56, 71.03, 69.08, 69.01, 68.84, 68.42, 67.00, 50.22, 36.07, 28.02, 27.52, 23.42, 23.09, 21.08, 20.99; ESI−HRMS calcd for $C_{135}H_{156}N_4O_{30}S_2$ (M + 2Na$^+$/2) 1212.0032, found 1212.0047; IR (thin film) cm^{-1} 2925.0, 2113.2, 1827.7, 1698.6, 1557.8, 1456.5, 1072.3, 719.5.

***N*$^\alpha$-(*tert*-Butoxycarbonyl)-*N*$^\gamma$-{*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-thioacetyl-α-D-mannopyransyl)-(1→3)-*O*-[(3,4,6-tri-*O*-acetyl-2-deoxy-2-thioacetyl-α-D-mannopyransyl)-(1→6)]-*O*-(2,4-di-*O*-acetyl-*β*-D-mannopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2-acetamido-3,6-di-*O*-acetyl-2-deoxy-1-*β*-D-glucopyranosyl}-L-asparagine 27.** NH_3 (10 mL) was collected at −78 °C. Li^0 (6.4 mg, 0.91 mmol) was added and stirred until a deep blue color was obtained. Glycosyl amino acid **26** (84 mg, 0.04 mmol) was subsequently added as a solution in THF (1 mL). The reaction was stirred at −78 °C for 1 h. At this time, NH_4Cl (55 mg, 1.0 mmol) was added, and the blue color disappeared. The reaction was then allowed to warm to rt, and Ar was blown over the solution until it reached dryness. Pyridine (20 mL), followed by Ac_2O (10 mL) and DMAP (1.3 mg, 0.01 mmol), was added, and the reaction was stirred for 16 h. The solvent was removed under high vacuum, and the resulting oil was purified by silica gel chromatography (5% MeOH in CH_2Cl_2) to yield 49 mg of **27** as a colorless oil, which was used in the next reaction without characterization.

***N*$^\alpha$-(*tert*-Butoxycarbonyl)-*N*$^\gamma$-{*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-(thio-2,4-di-nitrophenyl)-α-D-mannopyranosyl)-(1→3)-*O*-[(3,4,6-tri-*O*-acetyl-2-deoxy-2-(thio-2,4-di-nitrophenyl)-α-D-mannopyranosyl)-(1→6)]-*O*-(2,4-di-*O*-acetyl-*β*-D-mannopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2-acetamido-3,6-di-*O*-acetyl-2-deoxy-1-*β*-D-glucopyranosyl}-L-asparagine 28.** Glycosyl amino acid **27** (40 mg, 0.02 mmol) was dissolved in 1 mL of MeOH. A 1 M solution of NaSMe in MeOH (40 μL) was then added dropwise. After 5 h, the reaction was concentrated and placed under high vacuum for 30 min. The resulting off-white solid was then dissolved in 5:1 CH_2Cl_2/pyridine (5 mL) containing DIEA (12 μL, 0.06 mmol) and 2,4-dinitrophenyl fluoride (8.2 mg, 0.04 mmol). The reaction was allowed to stir for 16 h and was then concentrated. Silica gel chromatography (5% MeOH in CH_2Cl_2) yielded 36 mg (77% over two steps) of **28** as a yellow oil. ^{1}H NMR (500 MHz, MeOD) δ 8.98 (d, 1 H, J = 2.3 Hz), 8.95 (d, 1 H, J = 3.1 Hz), 8.48 (m, 2 H), 7.91 (d, 1 H, J = 8.9 Hz), 7.85 (d, 1 H, J = 9.0 Hz), 5.61 (app t, 1 H, J = 7.6 Hz), 5.57 (d, 1 H, J = 2.8 Hz), 5.43 (app t, 1 H, J = 7.1 Hz), 5.44−5.10 (m, 10 H), 4.65 (m, 2 H), 4.52−4.07 (m, 15 H), 3.90−3.65 (m, 10 H), 2.19−1.97 (m, 33 H), 1.93−1.80 (m, 10 H), 1.42 (s, 9 H); ^{13}C NMR (125 MHz, MeOD) δ 174.38, 173.67, 173.65, 173.02, 172.38, 172.26, 172.18, 172.00, 171.54, 171.04, 170.88, 170.68, 170.61, 170.54, 170.23, 169.99, 169.32, 146.40, 146.32, 144.51, 144.50, 143.52, 143.49, 128.07, 128.05, 126.83, 126.80, 121.60, 121.57, 103.27, 100.38, 100.10, 99.85, 88.40, 70.03, 69.85, 69.02, 68.88, 68.39, 67.72, 67.66, 67.04, 66.77, 66.76, 66.52, 66.41, 66.03, 65.86, 65.83, 65.44, 65.42, 64.30, 64.27, 64.15, 61.99, 61.87, 61.50, 60.83, 60.47, 48.39, 48.17, 48.00, 47.83, 47.03, 29.22, 27.27, 25.02, 21.98, 21.89, 21.05, 20.97, 20.87, 20.85, 20.76, 20.53, 20.14, 20.02, 19.93, 19.72, 19.32, 19.17; ESI−HRMS calcd For $C_{71}H_{98}N_4O_{42}S_2$ (M + 2Li + Na$^+$/2) 909.2470, found 909.2683; IR (thin film) cm^{-1} 2923.4, 2114.1, 1698.6, 1650.8, 1557.8, 1456.2, 1049.8.

***N*$^\alpha$-(9-Fluroenylmethoxycarbonyl)-*N*$^\gamma$-{*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-(thio-2,4-di-nitrophenyl)-α-D-mannopyranosyl)-(1→3)-*O*-[(3,4,6-tri-*O*-acetyl-2-deoxy-2-(thio-2,4-di-nitrophenyl)-α-D-mannopyranosyl)−(1→6)]-*O*-(2,4-di-*O*-acetyl-*β*-D-mannopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-*β*-D-glucopyranosyl)-(1→4)-2-acetamido-3,6-di-*O*-acetyl-2-deoxy-1-*β*-D-glucopyranosyl}-L-asparagine 29.** Glycosyl amino acid **28** (20 mg, 0.01 mmol) was dissolved in 95% TFA in H_2O (1 mL), and the reaction was stirred for 10 min. The mixture was then concentrated under high vacuum. CH_2Cl_2 (1 mL) was subsequently added followed by the addition of Fmoc-OSu (6.8 mg, 0.02 mmol) and DIEA (3.5 μL, 0.02 mmol). The reaction was allowed to stir for 2 h, after which time it was concentrated. Silica gel chromatography (2.5% MeOH in CH_2Cl_2) yielded 19 mg (92%) of **29** as a yellow oil. ^{1}H NMR (500 MHz, MeOD) δ 9.05 (d, 1 H, J = 2.7 Hz), 8.99 (d, 1 H, J = 2.9 Hz), 8.41 (m, 2 H), 7.76 (d, 1 H, J = 8.8 Hz), 7.74 (app d, 2 H, J = 7.0 Hz), 7.70 (d, 1 H, J = 9.1 Hz), 7.54 (bs, 2 H), 7.37 (app d, 2 H, J = 8.4 Hz), 7.06 (app d, 2 H, J = 8.2 Hz), 5.68 (app t, 1 H, J = 7.4 Hz), 5.56 (d, 1 H, J = 2.5 Hz), 5.43−4.93 (m, 15 H), 4.49−4.21 (m, 15 H), 3.74−3.47 (m, 14 H), 2.22−1.84 (m, 42 H); ^{13}C NMR (125 MHz, MeOD) δ 174.57, 173.47, 173.63, 172.48, 172.38, 172.28, 172.08, 172.00, 171.57, 171.10, 170.86, 170.71, 170.65, 170.52, 170.27, 170.01, 155.98, 146.40, 146.12, 144.54, 144.48, 143.59, 143.46, 143.52, 143.52, 141.11, 128.08, 128.04, 127.63, 127.13, 126.79, 126.78, 121.60, 121.57, 120.26, 119.89, 103.27, 100.38, 100.10, 99.86, 88.39, 70.04, 69.86, 69.04, 68.90, 68.41, 67.70, 67.68, 67.01, 66.99, 66.76, 66.74, 66.56, 66.43, 66.08, 65.83, 65.81, 65.45, 65.41, 64.31, 64.26, 64.12, 62.00, 61.84, 61.47, 60.84, 60.48, 48.41, 48.13, 48.00, 47.85, 47.01, 46.96, 29.23, 27.29, 25.03, 21.99, 21.84, 21.06, 20.99, 20.87, 20.85, 20.73, 20.53, 20.12, 20.00, 19.94, 19.30, 19.19; ESI−HRMS calcd For $C_{89}H_{102}N_8O_{48}S_2$ (M + 2Na$^+$/2) 1080.2512, found 1080.2535; IR (thin film) cm^{-1} 2922.5, 2115.3, 1698.8, 1650.6, 1557.4, 1456.2, 1048.8.

Glycopeptide 32. The synthesis of glycopeptide **32** was carried out on Fmoc-Ser(^{t}Bu) chlorotrityl resin (0.01 mmol scale). *N*$^\alpha$-Fmoc-protected amino acids were coupled manually using DCC/HOBt in NMP. A 10-fold excess of amino acid was used in each coupling step, except for glycosyl amino acid **29**, which was coupled using only 1.5 equiv. DNP cleavage was achieved by treatment of the resin-bound glycopeptide with DTT (16.0 equiv) and DBU/DIEA (4 equiv) in DMF for 30 min (2×). Following acetylation with Ac_2O/pyridine (1:2), the resin was washed thoroughly with DMF and CH_2Cl_2. Peptide cleavage/deprotection was accomplished by treatment with Reagent K[20] at rt for 5 h. The crude glycopeptide was concentrated and deacetylated with 10% aq $N_2H_4\cdot H_2O$ in the presence of DTT (excess) at rt for 30 min. It was then purified by reversed-phase HPLC with a gradient of 0−40% CH_3CN in water (0.1% TFA) over 30 min to give 8 mg (37%) of **32**: ESIMS (pos) calcd for (M + Na) = 2198.1, found 2198.6; ESIMS (neg) calcd for (M − H) = 2172.3, found 2172.1.

6-*O*-*tert*-Butyldiphenylsilyl-2-deoxy-2-phthalimido-*β*-D-glucopy-

ranosyl Azide (35). Glycosyl azide **34** (33.4 g, 72.6 mmol) was dissolved in MeOH (500 mL). A 0.5 M solution of NaOMe in MeOH was then added until a pH of 10 was obtained. After the reaction was stirred for 16 h, it was neutralized by addition of AcOH. The mixture was then concentrated and azeotroped with toluene before being placed under high vacuum for 1 h. The resulting white solid was dissolved in CH_2Cl_2 (250 mL) to which were added DIEA (25.3 mL, 145 mmol) and DMAP (890 mg, 7.3 mmol). TBDPSCl (20.8 mL, 79.9 mmol) was then added, and the reaction was stirred for 16 h. At this time, the mixture was washed with H_2O twice, followed by brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated. Silica gel chromatography (5% MeOH in CH_2Cl_2) yielded 41 g (98%) of **35** as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, 2 H, J = 2.6 Hz), 7.73−7.72 (m, 6 H), 7.49−7.42 (m, 6 H), 5.39 (d, 1 H, J = 9.3 Hz), 4.43 (app t, 1 H, J = 10.0 Hz), 4.08 (app t, 1 H, J = 10.7 Hz), 4.04−3.95 (m, 2 H), 3.77 (app t, 1 H, J = 8.3 Hz), 3.69−3.65 (m, 1 H), 1.09 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.38, 170.99, 168.26, 167.68, 135.60, 135.54, 134.23, 133.01, 132.91, 131.36, 129.82, 127.79, 127.77, 123.52, 85.35, 77.09, 76.77, 72.24, 71.28, 63.72, 55.94, 26.75, 19.21; FAB−HRMS calcd for $C_{30}H_{32}N_4O_6Si$ (M + Li^+) 579.2251, found 579.2242; IR (thin film) cm^{-1} 3431.9, 2930.8, 2116.2, 1775.5, 1713.3, 1641.5, 1388.6, 1111.3, 1070.9.

***O*-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-galactopyranosyl)-(1→4)-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl Azide (36).** To a mixture of **35** (2.0 g, 3.5 mmol), **33** (1.5 g, 4.2 mmol), $SnCl_2$ (1.2 g, 6.3 mmol), and 35 g of 4-Å molecular sieves was added a solution of 5:1 CH_2Cl_2/toluene (300 mL). The reaction was then cooled to −10 °C and stirred for 1 h. At this time, AgOTf (1.6 g, 6.3 mmol) was added, and the reaction was allowed to warm to rt over 16 h. The mixture was filtered through a plug of Celite and washed with concentrated $NaHCO_3$, H_2O, and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated. Silica gel chromatography (20% ethyl acetate in toluene) yielded 2.2 g (84%) of **36** as a white foam. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88−7.85 (m, 2 H), 7.77−7.72 (m, 4 H), 7.48−7.40 (m, 4 H), 7.26−7.24 (m, 2 H), 7.18−7.14 (m, 2 H), 5.44 (d, 1 H, J = 9.5 Hz), 5.36 (app d, 1 H, J = 3.4 Hz), 5.23 (dd, 1 H, J = 8.1, 10.4 Hz), 4.98 (dd, 1 H, J = 3.5, 10.4 Hz), 4.73 (d, 1 H, J = 8.1 Hz), 4.51 (dd, 1 H, J = 8.6, 10.6 Hz), 4.15−4.07 (m, 2 H), 4.03 (app d, 1 H, J = 10.1 Hz), 3.97−3.93 (m, 1 H), 3.87 (dd, 1 H, J = 3.0, 11.5 Hz), 3.67 (app d, 1 H, J = 8.5 Hz), 2.35 (s, 3 H), 2.13 (s, 3 H), 1.98 (s, 3 H), 1.74 (s, 3 H), 1.13 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.32, 169.96, 169.78, 168.99, 168.00, 167.56, 137.74, 135.81, 135.45, 134.14, 133.33, 132.26, 131.57, 129.91, 128.94, 128.12, 127.86, 127.74, 125.20, 101.12, 85.13, 80.27, 76.68, 71.26, 70.69, 69.00, 68.65, 66.76, 61.39, 61.15, 55.71, 26.79, 21.34, 20.48, 20.39, 20.29, 19.31; FAB−HRMS calcd for $C_{36}H_{46}N_3O_{13}Si$ (M + Li^+) 909.3202, found 909.3305; IR (thin film) cm^{-1} 3470.9, 2931.3, 2116.7, 1754.1, 1718.1, 1385.7, 1219.9, 1073.0.

***O*-(2,3,4,6-Tetra-*O*-acetyl-*β*-D-galactopyranosyl)-(1→4)-3,6-di-*O*-acetyl-2-acetamido-2-deoxy-*β*-D-glucopyranosyl Azide (37).** To a solution of **36** (1.0 g, 1.1 mmol) at 0 °C were added a 1 M solution of TBAF in THF (1.1 mL) and AcOH (100 μL). The reaction was allowed to warm to rt overnight. The mixture was subsequently concentrated to a yellow oil. This oil was dissolved in *n*-BuOH (20 mL), and ethylenediamine (5 mL) was added. The reaction was heated to 90 °C and stirred for 16 h. The mixture was then concentrated under high vacuum and dissolved in a solution of 2:1 pyridine/Ac_2O (100 mL), and the reaction was stirred for 8 h. The reaction was again concentrated to give a yellow oil which was purified by silica gel chromatography (2.5% MeOH in CH_2Cl_2) to yield 580 mg (80%) of **37** as a white foam. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.04 (d, 1 H, J = 9.5 Hz), 5.34 (app d, 1 H, J = 2.8 Hz), 5.07 (app t, 1 H, J = 8.6 Hz), 4.95 (dd, 1 H, J = 3.4, 10.5 Hz), 4.53−4.47 (m, 4 H), 4.14−4.03 (m, 4 H), 3.87 (app t, 1 H, J = 6.9 Hz), 3.80 (app t, 1 H, J = 9.1 Hz), 3.70−3.67 (m, 1 H), 2.13 (s, 3 H), 2.12 (s, 3 H), 2.08 (s, 3 H), 2.04 (s, 3 H), 2.03 (s, 3 H), 1.97 (s, 3 H), 1.95 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.91, 170.37, 170.34, 170.30, 170.04, 169.96, 169.24, 101.18, 88.38, 75.74, 74.57, 72.76, 70.75, 70.72, 69.02, 66.52, 61.85, 60.67, 53.05, 23.06, 20.80, 20.74, 20.58, 20.55, 20.52, 20.43; FAB−HRMS calcd for $C_{26}H_{36}N_4O_{16}$ (M + H^+) 661.2205, found 661.2208; IR (thin film) cm^{-1} 2917.0, 2117.9, 1748.1, 1664.6, 1370.6, 1229.1, 1061.0.

***O*-(*β*-D-Galactopyranosyl)-(1→4)-2-acetamido-2-deoxy-*β*-D-glucopyranosyl Azide (38).** Compound **37** (500 mg, 0.76 mmol) was dissolved in MeOH (50 mL). A 0.5 M solution of NaOMe in MeOH was then added until a pH of 10 was obtained. The reaction was stirred for 16 h, at which time the mixture was quenched by addition of AcOH. The solvent was then removed under vacuum, and purification by silica gel chromatography (20% MeOH in CH_2Cl_2) yielded 300 mg (98%) of **38** as a white foam. ^{1}H NMR (500 MHz, MeOD) δ 4.36 (d, 1 H, J = 7.8 Hz), 3.88 (dd, 1 H, J = 2.1, 12.4 Hz), 3.81 (d, 1 H, J = 3.3 Hz), 3.75 (dd, 1 H, J = 4.8, 12.4 Hz), 3.69−3.61 (m, 6 H), 3.58−3.52 (m, 3 H), 3.43 (dd, 1 H, J = 7.8, 9.9 Hz), 1.94 (s, 3 H); ^{13}C NMR (125 MHz, D_2O) δ 174.71, 102.77, 88.48, 77.78, 76.66, 75.27, 72.39, 72.19, 70.86, 68.46, 60.94, 59.77, 54.49, 22.02; FAB−HRMS calcd for $C_{14}H_{24}N_4O_{10}$ (M + H^+) 409.1571, found 409.1579; IR (thin film) cm^{-1} 3433.9, 2916.2, 1624.8.

***O*-(5-Acetamido-3,4-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylate)-(2→3)-*O*-(*β*-D-galactopyranosyl)-(1→4)-2-acetamido-2-deoxy-*β*-D-glucopyranosyl Azide (39).** Compound **38** (39 mg, 0.10 mmol), CMP-*β*-D-sialic acid (126 mg, 0.190 mmol), α-2,3-sialyltransferase (340 milliunits, Sigma), and alkaline phosphatase (40 units, Sigma) were dissolved in 50 mM sodium cacodylate (pH 7.4), 1% BSA, and 30 mM $MnCl_2$ (5 mL). The reaction was incubated at 37 °C for 2 d with gentle agitation. At this time, an additional 60 mg of CMP-*β*-D-sialic acid and 170 milliunits of α-2,3-(*N*)-sialyltransferase were added. The reaction was incubated for 3 additional d at 37 °C, after which time it was concentrated under vacuum. Silica gel chromatography (7:2:1 ethyl acetate/MeOH/H_2O) yielded 68 mg (99%) of **39** as a waxy solid. ^{1}H NMR (500 MHz, D_2O) δ 4.42 (d, 1 H, J = 7.9 Hz), 3.98 (dd, 1 H, J = 2.9, 9.9 Hz), 3.87 (app d, 1 H, J = 10.9 Hz), 3.82 (d, 1 H, J = 2.8 Hz), 3.78−3.72 (m, 4 H), 3.67−3.49 (m, 14 H), 2.62 (dd, 1 H, J = 4.6, 12.5 Hz), 1.92 (s, 3 H), 1.90 (s, 3 H), 1.68 (app t, 1 H, J = 11.2 Hz); ^{13}C NMR (125 MHz, D_2O) δ 174.94, 174.71, 102.47, 88.53, 77.65, 76.69, 75.39, 75.11, 72.81, 72.17, 71.69, 69.29, 68.27, 68.01, 67.39, 62.50, 62.40, 60.96, 59.77, 54.49, 51.60, 48.78, 39.55, 22.02, 21.95; FAB−HRMS calcd for $C_{25}H_{41}N_5O_{18}$ (M + Na^+) 722.2344, found 722.2360; IR (thin film) cm^{-1} 3440.9, 2916.2, 2117.8, 1786.5, 1624.8.

α-Bromoacetamido-*O*-(5-acetamido-3,4-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylate)-(2→3)-*O*-(*β*-D-galactopyranosyl)-(1→4)-2-acetamido-2-deoxy-*β*-D-glucopyranoside (3). Compound **39** (40 mg, 0.06 mmol) was dissolved in H_2O (3 mL) and stirred in the presence of 10% Pd/C (40 mg) at rt under an atmosphere of hydrogen. After 20 min, the reaction mixture was filtered through Celite, washed with H_2O (1 mL), and immediately treated with bromoacetic anhydride (78 mg, 0.30 mmol) in the presence of $NaHCO_3$ (150 mg). After 3 h the mixture was loaded onto a column of Bio-Gel P-2 and eluted with H_2O to give 27 mg (56%) of **3** as a white solid after lyophilization. ^{1}H NMR (500 MHz, D_2O) δ 4.41 (d, 1 H, J = 5.0 Hz), 3.95 (d, 1 H, J = 9.7 Hz), 3.84−3.66 (m, 9 H), 3.58−3.44 (m, 10 H), 3.20 (s, 2 H), 2.62 (dd, 1 H, J = 4.8, 12.5 Hz), 1.89 (s, 3 H), 1.88 (s, 3 H), 1.70 (app t, 1 H, J = 11.0 Hz); ^{13}C NMR (125 MHz, D_2O) δ 174.94, 173.80, 160.16, 102.48, 99.73, 90.45, 78.13, 75.39, 75.09, 72.79, 72.37, 71.70, 69.30, 69.15, 68.27, 68.02, 67.40, 62.50, 60.94, 59.75, 53.65, 51.61, 48.78, 39.55, 21.96, 21.80; FAB−HRMS calcd for $C_{27}H_{44}BrN_3O_{19}$ (M + Na^+) 816.1650, found 816.1653; IR (thin film) cm^{-1} 3441.9, 2117.8, 1865.7, 1786.5, 1624.8.

Glycopeptide 40. To glycopeptide **32** (1 mg, 0.4 mmol) in sodium phosphate buffer (0.1 M, pH 7.2) (100 μL) was added bromoacetamide **3** (5 mg, 6 mmol). The reaction mixture was incubated at 37 °C overnight, and the thioether-linked product **40** was isolated by reversed-phase HPLC using a gradient of 0−40% CH_3CN in water (0.1% TFA)

over 60 min. The products were lyophilized and analyzed by ESIMS ((pos) calcd for (M + 2Na/2) = 1823.4, found 1823.5). Yields for thiol alkylations appeared quantitative by HPLC and ESIMS analysis. During the course of the reaction (after 8 h), mass spectrometry analysis revealed the transient presence of the monoalkylated glycan. This compound had the same elution time as that of the fully alkylated product and was therefore indistinguishable by HPLC. After 16 h, no monoalkylated product was observed by mass spectrometry, and the reaction was deemed complete.

Acknowledgment. The Center for New Directions in Organic Synthesis is supported by Bristol−Myers Squibb as Sponsoring Member, and Novartis, as Supporting Member. This research was supported by grants to C.R.B. from the National Science Foundation (CHE-9734439) and the Director, Division of Materials Sciences and Engineering, and the Office of Energy Biosciences of the U.S. Department of Energy under Contract No. DE-AC03-76SF00098.

Supporting Information Available: Mass spectra and HPLC traces for glycopeptides **32** and **40**. This material is available free of charge via the Internet at http://pubs.acs.org.

JA029346V