n-Pentenyl Mannoside Precursors for Synthesis of the Nonamannan Component of High Mannose Glycoproteins

J. Robert Merritt, Elizabeth Naisang,† and Bert Fraser-Reid*

Department of Chemistry, Paul M. Gross Chemical Laboratory, Duke University, Durham, North Carolina 27708

Received February 17, 1994®

The high-mannose oligosaccharide **1** is present on the conserved V3 loop of the viral coat of HIV1 known as GP-120. The mannan portion of this molecule has been prepared by utilization of halogen-promoted *n*-pentenyl glycoside (NPG) coupling. Two advantageous properties of NPG's facilitated construction of **1**, one being the ability to activate the donor, even when C2 esterified (i.e., "disarmed"), with NIS/Et_3SiOTf, under which all reactions are complete within the time required to take a TLC sample. The second advantage was the "side-tracking" strategy which allowed the pentenyl group of a glycosyl acceptor to be rendered temporarily inactive by conversion to the dibromide. After coupling, the "side-tracked" NPG could be reactivated by reductive elimination to serve as the glycosyl donor in a subsequent step. With the appropriately protected monosaccharide precursors in hand, the nonamannan could be assembled by a virtually iterative protocol involving deprotection–coupling–deprotection–coupling...etc. as the only synthetic manipulations.

Spectacular advances in isolation methods and structure assignment[1] have helped to confirm the critical role that the oligosaccharide components of glycoconjugates had hitherto been suspected to play in biological regulation.[2] The complexity and diversity of oligosaccharides, structurally and conformationally, suggest that they may perform multiple functions. Indeed their roles thus far identified include protein masking sites for approaching microorganisms and macromolecules and mediation of a number of cell surface interactions.[3] Growing interest in the functions of oligosaccharides has heightened the need for ready access to materials for structure–activity, or "lock-and-key,"[4] investigations.

In this context the interations of mannose-containing oligosaccharides with lectins are of historical significance,[5] being the prototype for the broad area of chemistry now known as molecular recognition. The triantenary glycoprotein **1**, although well known as one of several high-mannose glycoproteins occurring in animals and plants,[6,7] now attracts special attention because of its presence on the conserved V3 loop of the viral coat of HIV1, known as GP-120.[8] In this paper we describe the preparation of the mannan portion of this glycoprotein based on the novel chemistry of NPG's.

Since their discovery in the late 1980's,[9] the unique properties of NPG's[10] have allowed preparation of several challenging oligosaccharides.[11] The pentenyl moiety may be installed early in the synthesis and can survive many types of protecting group manipulations. The combination of *N*-iodosuccinimide and triethylsilyl triflate (NIS/Et_3SiOTf)[12] as the coupling promoter provides a potent source of I^+ which enables a disarmed glycosyl donor to react within the time required to take a TLC sample. Lastly, unlike other glycosyl donors in which anomeric activation is a single step **4** → **10** (Scheme 2), NPG activation occurs in two stages, **4** → **5** → **6**, the second of which can be averted by the use of excess nucleophile to give **9**. An NPG (**4**, X = *O*-pentenyl) can therefore be prepared in bulk and divided into portions which can serve immediately as glycosyl donors (**4** → **5** → **6** → **7**) or be sidetracked by dibromination to **9** (Nu = E = Br) to serve as a glycosyl acceptor and, subsequently, after reductive elimination to regenerate the pentenyl group, as a glycosyl donor.[13] The sidetracking strategy has

† Undergraduate research participant.

® Abstract published in *Advance ACS Abstracts,* July 15, 1994.

(1) Dell, A. *Adv. Carbohyd. Chem. Biochem.* **1987**, *45*, 21. Vliegenthart, J. F. G.; Doorland, L., van Halbeek, H. *Adv. Carbohydr. Chem. Biochem.* **1983**, *41*, 209. Everett, J. R.; Readshaw, S. A. *Annu. Rep. Prog. Chem. Sect. B.* **1991**, *86*, 3.

(2) Ferguson, M. A. J. *Curr. Biol.* **1991**, *1*, 522. Robinson, P. J. *Immunol. Today* **1991**, *12*, 35. Findley, J. *Chem. Brit.* **1991**, 724. von Boehmer, H.; Kisielow, P. *Sci. Am.* **1991**, 74. Springer, T. A.; Lasky, L. A. *Nature* **1991**, *349*, 196. Springer, T. A. *Nature* **1990**, *346*, 425. Phillips, M. L. *Science* **1990**, *250*, 1130. Osborn, L. *Cell* **1990**, *62*, 3. Drickhammer, K. *J. Biol. Chem.* **1988**, *263*, 9557.

(3) For an excellent review of oligosaccharide function see: Varki, A. *Glycobiology* **1993**, *3*, 97.

(4) Fischer, E. *Ber.* **1894**, *27*, 2985 (at page 2993).

(5) Gottschalk, A., Ed. *Glycoprotein*; Elsevier: Amsterdam, 1972. Montreuil, J. *Adv. Carbohydr. Chem. Biochem.* **1980**, *37*, 157. Sharon, N.; Lis, H. *Chem. Eng. News* **1981**, *58*, 21. A review of glycoproteins: Montreuil, J. In *Comprehensive Biochemistry*; Elsevier: Amsterdam, 1982; Vol. 1911, p 1. Kobata, A. In *Biology of Carbohydrates*; V., Ginsburg, Ed.; Wiley: New York, 1984.

(6) Lis, H.; Sharon, N. *J. Biol. Chem.* **1978**, *253*, 3468. Li, E.; Kornfeld, S. *J. Biol. Chem.* **1979**, *254*, 1600. Dorland, L.; Van Halbeek, H.; Vliegenthart, J. F. G.; Lis, H.; Sharon, N. *J. Biol. Chem.* **1981**, *256*, 7708.

(7) For synthesis of major segments of high-mannose glycoproteins see: Ogawa, T.; Sugimoto, M.; Kitajima, T.; Sadozai, K. K.; Nukada, T. *Tetrahedron Lett.* **1986**, *27*, 5739. Ogawa, T.; Nukada, T. *Carbohydr. Res.* **1985**, *136*, 135. Ogawa, T.; Yamamoto, H.; Nukada, T.; Kitajima, T.; Sugimoto, M. *Pure Appl. Chem.* **1984**, *56*, 779. Ogawa, T.; Nukada, T.; Kitajima, T. *Carbohydr. Res.* **1983**, *123*, C12. Ogawa, T.; Kitajima, T.; Nukada, T. *Carbohydr. Res.* **1983**, *123*, C8. Paulsen, H. *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 823. Kung, H. *Angew Chem. Int. Ed. Engl.* **1987**, *26*, 294.

(8) LaRosa, G. J.; Davide, J. P.; Weinhold, K.; Waterbury, J. A.; Profy, A. T.; Lewis, J. A.; Langlois, A. J.; Dreesman, G. R.; Boswell, R. N.; Shadduck, P.; Holley, L. H.; Karplus, M.; Bolognesi, D. P.; Matthews, T. J.; Emini, E. A.; Putney, S. D. *Science* **1990**, *249*, 932. Leonard, C. K.; Spellman, M. W.; Riddle, L.; Harris, R. J.; Thomas, J. N.; Gregory, T. J. *J. Biol. Chem.* **1990**, *265*, 10373. Larkin, M.; Childs, R. A.; Matthews, T. J.; Thiel, S.; Mizuochi, T.; Lawson, A. M.; Svill, J. S.; Haslett, C.; Diaz, R.; Feizi, T. *AIDS* **1989**, *3*, 793. Geyer, H.; Holschbach, C.; Hunsmann, G.; Schneider, J. *J. Biol. Chem.* **1988**, *263*, 11760. Mizuochi, T.; Spellman, M. W.; Larkin, M.; Solomon, J.; Basa, L. J.; Feizi, T. *Biochem. J.* **1988**, *254*, 599.

(9) Mootoo, D. R.; Konradsson, P.; Udodong, U.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1988**, *110*, 5583.

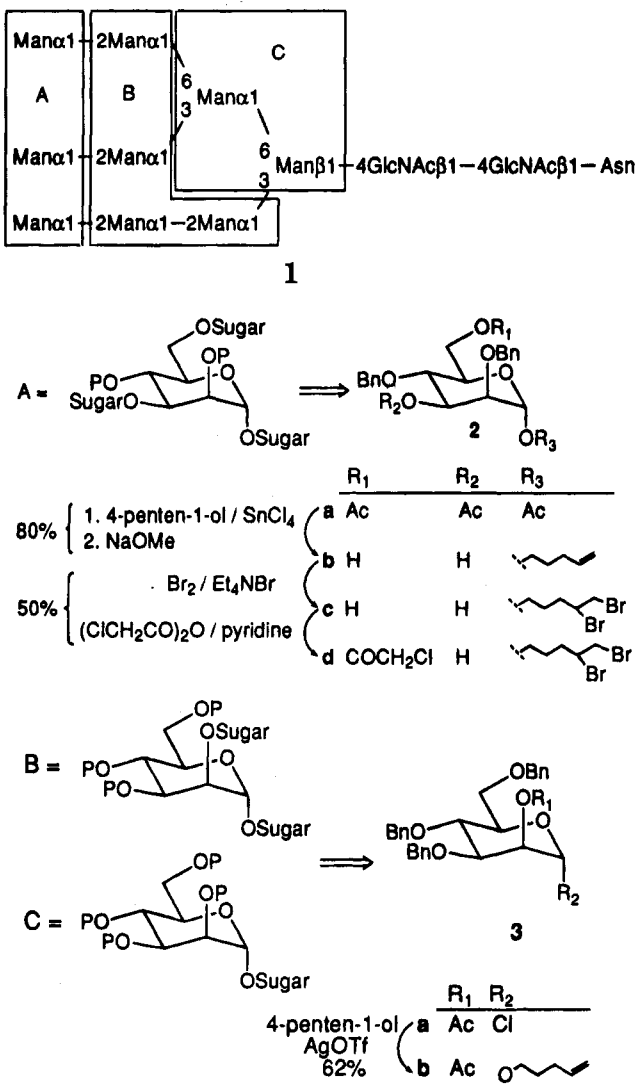
(10) For an excellent review of NPG methodology see: Fraser-Reid, B.; Udodong, U.; Wu, Z.; Ottosson, H.; Merritt, J. R.; Rao, C. S.; Roberts, C.; Madsen, R. *Synlett* **1992**, 927–942.

(11) Udodong, U. E.; Madsen, R.; Roberts, C.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1993**, *115*, 7886–7887.

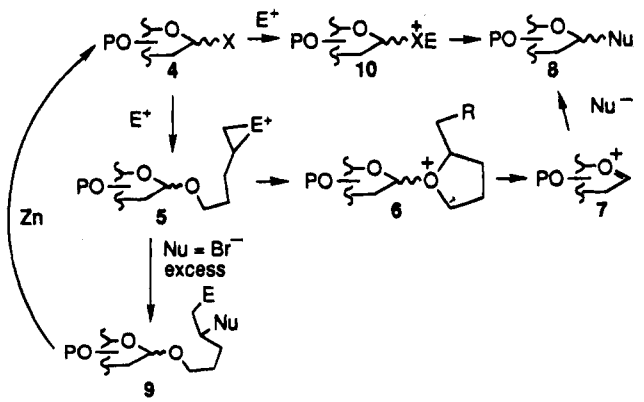
(12) Konradsson, P.; Mootoo, D. R.; McDevitt, R. E.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1990**, 270.

0022-3263/94/1959-4443$04.50/0

Scheme 1



Scheme 2

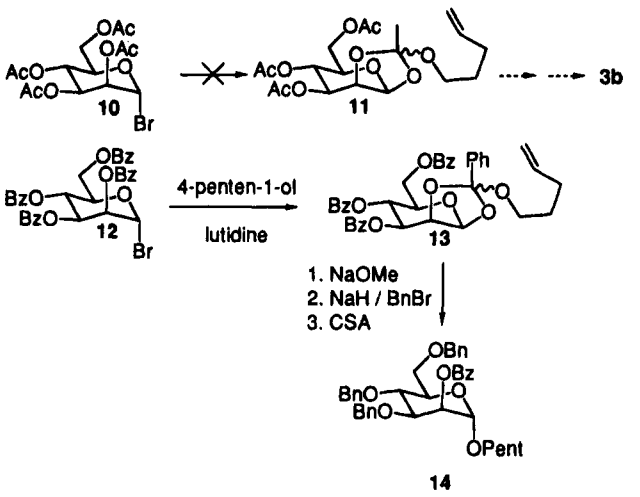


facilitated the construction of the high-mannose nonasaccharide portion of glycoprotein **1**.

Discussion

The mannan moiety of **1** can be dissected into three zones (Scheme 1) whose components carry three, two, and one sugar units **A**, **B**, and **C**, respectively. Further retroanalysis of **A** leads to the retron **2** with permanent protecting groups at O2 and O4 and a temporary protecting group at O6. Retrons **B** and **C** lead to the same synthon **3** where a C2 ester (R = Ac) serves for temporary protection required in B or permanent protection as required in C. Thus, the nonasaccharide component of **1** could conceivably be constructed from only only two mannopyranose precursors, **2** and **3**.

Scheme 3



Being regular *O*-glycosides, the pentenyl mannosides **2d** and **3b** were prepared by adapting literature procedures for the corresponding methyl[14] and acetyl analogs.[15] The triacetate **2a** was converted to a pentenyl glycoside, deacetylated, **2b**, and "side-tracked" to the dibromide **2c**. The primary hydroxyl of **2c** was selectively protected as the chloroacetyl ester **2d**.

For precursor **3b** we had originally hoped to adapt a procedure developed in our laboratory whereby a pentenyl ortho ester such as **11** could be opened to afford the pentenyl glycoside **3b**. The pentenyl ortho ester **13** is prepared easily from the benzoate **12** by treatment with pentenyl alcohol and lutidine, and the product has been transformed into **14**.[11] However, this method was unsuccessful when O2 of the starting material was protected as the acetate **10**. Because our synthetic approach requires the use of the acetate, both (a) for its ease of removal using mild conditions and (b) to facilitate identification in ^{1}H NMR analysis of coupling products, a standard procedure was adapted.[14] Thus, the glycosyl chloride **3a** was converted to the pentenyl glycoside **3b** upon treatment with 4-pentenyl alcohol and silver triflate.

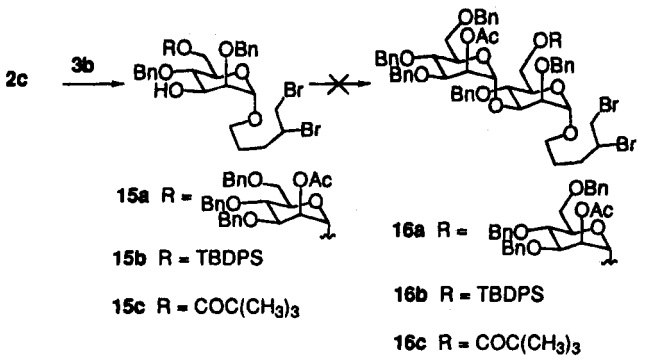
Initially preparation of the trisaccharide **16a** was attempted as a one-pot, double glycosidation by treating the diol **2c** with 2.5 equiv of the donor **3b** in the presence of NIS/Et_3SiOTf. This procedure yielded only disaccharide **15a**. Additional attempts to couple another unit of **3b** to the dissaccharide **15a** using NIS/Et_3SiOTf were unsuccessful leading only to the recovered acceptor **15a**. We postulated that bulky substituents at C6, as in the monosaccharide **15a**, somehow blocked approach of the NPG donor to the C3 position. Indeed, the corresponding silylated and pivaloylated acceptors, **16b** and **16c**, respectively, also failed to undergo NPG coupling at the C3-OH. This difficulty was overcome through the use of

(13) Fraser-Reid, B.; Wu, Z.; Udodong, U. E.; Ottosson, H. *J. Org. Chem.* **1990**, *55*, 6068–6070.

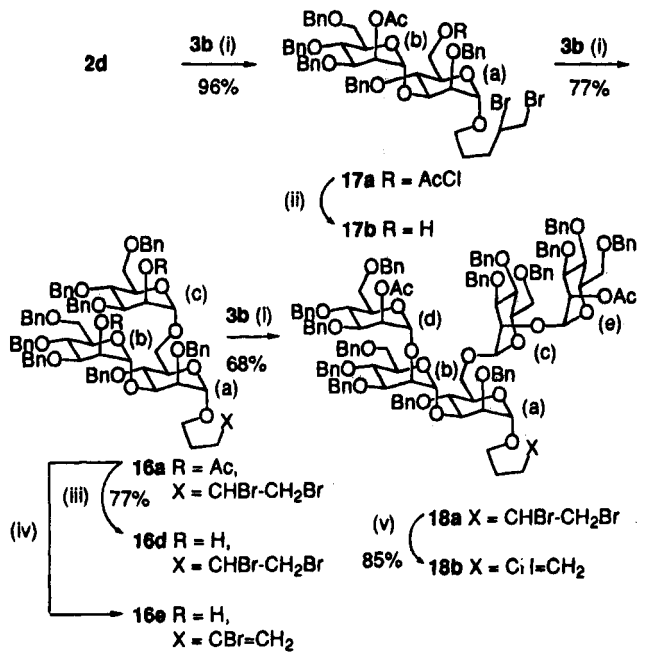
(14) Garegg, P. et al. *Acta Chem. Scand.* **1973**, *27*, 2639. Franks, N.; Montgomery, R. *Carbohydr. Res.* **1968**, *6*, 286.

(15) Ogawa, T.; Katano, K.; Sasajima, K.; Matsui, M. *Tetrahedron Lett.* **1981**, *37*, 2779.

Scheme 4



Scheme 5[a]



[a] (i) NIS/Et_3SiOTf; (ii) thiourea, $NaHCO_3$; (iii) NH_3/MeOH; (iv) K_2CO_3 or NaOMe; (v) Zn/Bu_4NBr.

chloroacetyl at C6, **2d**, this group having been chosen because it is less bulky as well as for easy removal in a subsequent step to allow coupling at C6.

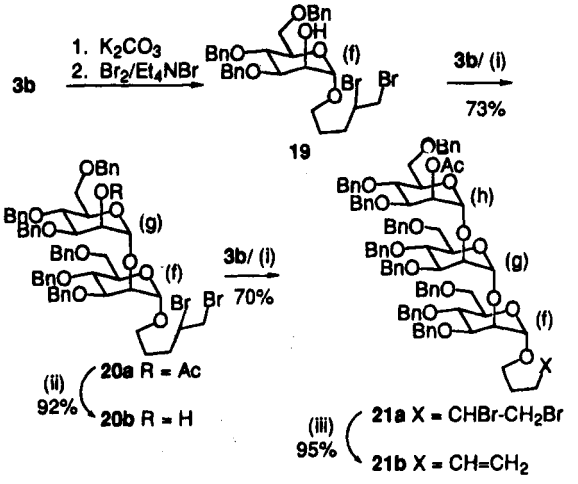
Under the agency of NIS/Et_3SiOTf, the disarmed glycosyl donor **3b** reacted with **2d** instantly, smoothly, and *via* neighboring group participation to afford, after deprotection, **17b** in virtually quantitative yield (Scheme 5). Coupling of acceptor **17b** with another unit of **3b** gave the trisaccharide **16a** which was deacetylated to the diol **16d** with ammonia in methanol. The pentasaccharide **18a** was obtained by double glycosylation of **16d** with the donor **3b**.

It should be noted that deacetylation of **16a** using stronger bases such as sodium methoxide or potassium carbonate resulted in elimination of bromine to give **16e**.[16] The elimination product **16e** was evident by the ^{1}H-NMR spectrum which showed the terminal hydrogens of the bromopentenyl group at shifts of 5.39 and 5.50 ppm. The deacetylation product **16d**, obtained by treatment of **16a** with ammonia in methanol, showed no such evidence of elimination.

The analysis in Scheme 1 shows that the lowest antenna of **1** is comprised of B (=C) components, and by

(16) Sahlberg, C. *Tetrahedron Lett.* **1992**, *33*, 679–682.

Scheme 6[a]



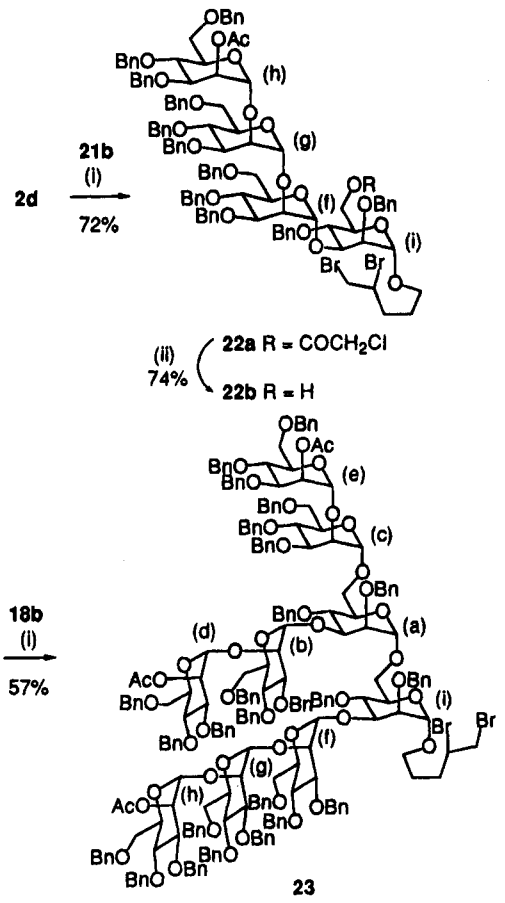
[a] (i) NIS/Et_3SiOTf; (ii) NH_3/MeOH; (iii) Zn/Bu_4NI.

employing the sidetracking strategy, compound **3b** could be made to serve both as the glycosyl donor and, after dibromination and deacylation to **19**, as the glycosyl acceptor, thereby permitting rapid assembly of the trisaccharide segment. Thus, coupling of **3b** and **19** afforded disaccharide **20a** in a 73% yield, and deacetylation then gave the disaccharide acceptor **20b** (Scheme 6). Further coupling of **20b** to the donor **3b** led to the trisaccharide **21a**. According to our retrosynthetic plan, the building blocks **18a** and **21a** would now become glycosyl donors in the upcoming steps. Reductive elimination, carried out most efficiently by sonication overnight with zinc in the presence of tetra-*N*-butylammonium iodide, gave **18b** and **21b**, respectively. Coupling of the latter with **2d** gave the tetrasaccharide **22a** (Scheme 7), which after deacylation to acceptor **22b** was ready for coupling with the pentasaccharide **18b** to give the protected nonasaccharide **23**.

From Schemes 4–7, it is apparent that once the properly-designed monosaccharide precursors are in hand, subsequent synthetic manipulations are confined to liberation of (a) an hydroxyl group or (b) the pentenyl double bond. With NIS/Et_3SiOTf as promoter, coupling is immediate, a circumstance which makes for rapid assembly, and the fact that these alterations do not tamper with the anomeric center greatly facilitates the use of ^{1}H NMR to monitor the progress. Thus, the progress of each successive coupling was easily determined by ^{1}H NMR. In all cases, the glycosyl donor and the glycosyl acceptor each had unique protecting groups that simplified identification of the product which now contained both sets of protecting groups. For example, in the coupling of **2d** and **21b** the donor, **21b**, contained an acetate while the acceptor, **2d**, contained a dibromopentanyl group. The ^{1}H NMR spectrum of the product **22a** showed chemical shifts of 2.19 ppm for the acetate protons and 3.39 ppm for one of the dibromopentanyl protons. The product of each coupling reaction also exhibited a new anomeric peak between 4.9 and 5.5 ppm which was visible just downfield from the benzyl CH_2 shifts. As successive couplings were carried out the anomeric protons retained their relative chemical shifts. In the final product **23** each of the nine anomeric peaks could be assigned by inspection of the 300-MHz spectrum in $CDCl_3$.

The *N*-acetylglucosamine portion of **1** (right half) has also been prepared in our laboratory from NPG's.[17]

Scheme 7[a]



[a] (i) NIS/Et_3SiOTf; (ii) thiourea, $NaHCO_3$.

Efforts are now being directed toward preparation of the β-mannose linkage between the two "halves" of **1**, and progress will be reported in due course.

Experimental Section

General Procedures. All NMR spectra were recorded in a 7.0-T, 300-MHz magnet and were referenced to $CHCl_3$. NMR spectral assignments were made with the aid of spin–spin decoupling, COSY, DEPT, and heteronuclear correlation experiments. Fast atom bombardment (FAB) mass spectra were conducted using a dithiothreitol/dithioerythritol matrix with xenon as the fast atom. Elemental analyses were performed by Atlantic Microlab, Inc. All reactions were conducted under inert argon atmosphere. TLC plates were Kieselgel 60 F_{254} (Merck Art. 5554). Carbohydrate compounds were visualized on the TLC plate by charring with H_2SO_4/EtOH/H_2O (1:10:10). Flash column chromatography was done with silica gel 60 (230–400 mesh, Merck). Dichloromethane was distilled from P_2O_5. Acetonitrile was distilled from CaH_2. Tetrahydrofuran and diethyl ether were distilled from sodium benzophenone ketyl. *N*-Iodosuccinimide (NIS) was crystallized from hot dioxane/CCl_4. Solutions of compounds in organic solvents were dried over sodium sulfate prior to rotary evaporation.

Standard Coupling Procedure. The glycosyl donor and acceptor, respectively, were taken up in a small quantity of toluene and placed under high vacuum overnight. The glycosyl acceptor (1.0 equiv) was dissolved in dry CH_2Cl_2 to give a 0.1 M solution. To the solution was added NIS (1.3 equiv) and triethylsilyl trifluoromethanesulfonate Et_3SiOTf (0.3 equiv) with stirring. The glycosyl donor (1.3 equiv) was dissolved in CH_2Cl_2 to give a 0.4 M solution which was added dropwise to the glycosyl acceptor solution. Once all of the NIS had dissolved (approximately 3 min), the reaction mixture was quenched with 10% aqueous sodium thiosulfate and saturated aqueous sodium bicarbonate. The organic layer was separated and dried, and the solvent was removed by rotary evaporation. The crude residue was then purified by column chromatography on silica gel.

Standard Deprotection of the Chloroacetate Ester. The starting material was dissolved in ethanol and a minimal amount of ethyl acetate to affect solubility. To the solution was added thiourea (1.2 equiv) and sodium bicarbonate (2 equiv). The mixture was refluxed for 2 h. The solvent was removed by rotary evaporation. The residue was taken up in CH_2Cl_2 and washed with water. The organic phase was separated, and the solvent was removed by rotary evaporation. The residue was purified by column chromatography on silica gel.

Standard Dibromination. The pentenyl mannoside and tetraethylammonium bromide (0.5 equiv) were dissolved in CH_2Cl_2 at 0 °C. Bromine (1 equiv) was added dropwise, allowing the solution to decolorize between each drop. When the brown color persisted, the reaction was quenched with 10% sodium thiosulfate. The organic phase was dried, and the solvent was removed by rotary evaporation. The residue was purified by column chromatography on silica gel.

Standard Deprotection of Acetate Esters in the Presence of a Vicinal Dibromide. The starting material was dissolved in methanol, and a minimal amount of acetone was added to affect solubility. The solution was cooled to 0 °C. Ammonia was bubbled through the solution for 10 min. The reaction mixture was allowed to stand for 4 days. The solvent was removed by rotary evaporation. The residue was purified by column chromatography on silica gel.

Reductive Elimination of Dibromide. The starting material was dissolved in ethanol and a minimal amount of ethyl acetate to effect solubility. To the solution was added Zn (5 equiv) and tetrabutylammonium iodide (1 equiv). The mixture was sonicated overnight and then filtered through Celite and evaporated to dryness. The residue was purified by column chromatography on silica gel.

Pentenyl 2,4-Di-*O*-benzyl-α-D-mannopyranoside (2b). The triacetate **2a**[15] (5.38 g, 11.4 mmol) was dissolved in CH_2Cl_2 (30 mL). Pentenyl alcohol (5 mL, 45 mmol) was added, followed by $SnCl_4$ (1.4 mL, 11.4 mmol). The reaction mixture was stirred overnight. Water and $NaHCO_3$ were added to the reaction mixture. The aqueous layer was extracted with CH_2Cl_2. The combined organic phases were dried, and the solvent was removed by rotary evaporation. The residue was passed through a short column (30% EtOAc/petroleum ether). The product was dissolved in MeOH (20 mL). A small chip of sodium was added, and the mixture was stirred for 2 h. The solvent was removed by rotary evaporation. The residue was taken up in 50% EtOAc/petroleum ether and passed though a short column of silica gel (3.902 g, 9.106 mmol, 80% yield): R_f 0.38 (30% EtOAc/petroleum ether); $[\alpha]^{22}_D$ = +28.5° (*c* = 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.25–7.41 (m, 10H, Ph), 5.74–5.78 (m, 1H, $OCH_2CH_2CH_2CH{=}CH_2$), 4.98–5.05 (m, 2H, $OCH_2CH_2CH_2CH{=}CH_2$), 4.90–4.95 (m, 1H, CH_2Ph), 4.85 (s, 1H, H-1), 4.60–4.75 (m, 3H, CH_2Ph), 3.99–4.05 (dd, 1H, *J* = 3.7, 8.8 Hz, H-5), 3.59–3.88 (m, 6H), 3.34–3.41 (m, 1H, $OCH_2CH_2CH_2CH{=}CH_2$), 2.06–2.20 (m, 2H,$OCH_2CH_2CH_2CH{=}CH_2$), 1.60–1.70 (m, 2H, $OCH_2CH_2CH_2CH{=}CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.8 ($OCH_2CH_2CH_2CH{=}CH_2$), 115.1 ($OCH_2CH_2CH_2CH{=}CH_2$), 97.1 (C-1, J_{CH} = 171.4Hz).

Dibromopentanyl 2,4-Di-*O*-benzyl-6-*O*-(chloroacetyl)-α-D-mannopyranoside (2d). The diol **2b** was subjected to standard dibromination procedures then purified by column chromatography. The dibromide (4.37 g, 7.43 mmol) was dissolved in CH_2Cl_2 (20 mL). To the solution was added chloroacetic anhydride (1.27 g, 7.43 mmol) with stirring, and pyridine (0.75 mL) was added in three aliquots over 30 min. The solvent was removed by rotary evaporation, and the residue was purified by column chromatography (10→30% EtOAc/petroleum ether) (2.301 g, 3.65 mmol, 50% yield): R_f 0.17 (20% EtOAc/petroleum ether); $[\alpha]^{22}_D$ = +24.8° (*c* = 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.25–7.42 (m, 10H, Ph), 4.56–4.96 (m, 4H, CH_2Ph), 4.88 (s, 1H, H-1), 4.45–4.51 (dd,

(17) Handlon, A. L.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1993**, *115*, 3796.

1H, J = 2.0, 11.7 Hz), 4.34–4.41 (dd, 1H, J = 5.2, 11.7 Hz), 3.99–4.07 (m, 3H, H-3, $OCOCH_2Cl$), 3.84–3.90 (dd, 1H, J = 10.5 Hz, H-5), 3.69–3.83 (m, 3H), 3.56–3.68 (m, 3H), 2.20–2.32 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 1.60–1.80 (m, 3H, $OCH_2CH_2CH_2CHBrCH_2Br$); ^{13}C NMR (75 MHz, $CDCl_3$); δ 167.11 ($COCH_2Cl$), 137.99, 137.50, 128.65, 128.53, 128.19, 127.96, 127.89, 96.72 (C-1), 78.35, 77.38, 75.94, 75.91, 74.89, 72.95, 71.91, 69.08, 66.68, 66.65, 65.08, 52.30, 52.26, 40.79, 36.00, 32.89, 26.68, 26.64. Anal. Calcd for $C_{27}H_{33}O_7Br_2Cl$; C, 48.78; H, 5.00. Found: C, 48.89; H, 5.06.

Pentenyl 2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (3b). The glycosyl chloride **3a**[14] (0.97 g, 1.90 mmol) was dissolved in CH_2Cl_2 (20 mL). Pentenyl alcohol (1.4 mL, 17.1 mmol) was added with stirring over molecular sieves (4 Å) for 15 min under Ar. To the mixture was added AgOTf (2.49 g, 17.1 mmol). The mixture was stirred for 2 h. Since the product could not be distinguished from starting material by TLC, the reaction was monitored by ^1H-NMR of crude aliquots of the reaction mixture until complete disappearance of the starting material. Water was added to the reaction mixture which was extracted with CH_2Cl_2 three times. The organic phases were combined and dried. The solvent was removed by rotary evaporation. The residue was purified by column chromatography (10%→20% EtOAc/petroleum ether) (682.8 mg, 1.22 mmol, 62% yield): R_f 0.47 (30% EtOAc/petroleum ether); $[\alpha]^{22}_D$ = +23.2° (c = 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.15–7.39 (m, 15H, Ph), 5.78 (m, 1H, $OCH_2CH_2CH_2CH{=}CH_2$), 5.34 (m, 1H, H-2), 4.97 (m, 2H, $OCH_2CH_2CH_2CH{=}CH_2$), 4.82 (s, 1H, H-1), 4.40-4.87 (m, 6H, CH_2Ph), 3.97 (dd, 1H, J = 9.3, 3.4 Hz, H-3), 3.86 (t, 1H, J = 9.3 Hz, H-4), 3.79 (m, 1H, H-5), 3.78 (m, 1H, H-6'), 3.68 (m, 1H, H-6), 3.67 (m, 1H, $OCH_2CH_2CH_2CH{=}CH_2$), 3.40 (m, 1H, $OCH_2CH_2CH_2CH{=}CH_2$), 2.14 (s, 3H, $OCOCH_3$), 2.07 (m, 2H, $OCH_2CH_2CH_2CH{=}CH_2$), 1.65 (m, 2H, $OCH_2CH_2CH_2CH{=}CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.53 ($COCH_3$), 138.34, 138.21, 137.94, 137.89 ($OCH_2CH_2CH_2CH{=}CH_2$), 128.36, 128.30, 128.28, 128.06, 127.90, 127.75, 127.71, 127.61, 127.55, 114.96 ($OCH_2CH_2CH_2CH{=}CH_2$), 97.74 (C-1), 78.21, 75.19, 74.35, 73.41, 71.78, 71.34, 68.85, 67.21, 30.20 ($OCH_2CH_2CH_2CH{=}CH_2$), 28.54 ($OCH_2CH_2CH_2CH{=}CH_2$), 21.14 ($COCH_3$); CI-MS m/z 578 (M + NH_4). Anal. Calcd for $C_{34}H_{40}O_7$: C, 72.83; H, 7.19. Found: C, 72.83; H, 7.20.

Dibromopentanyl *O*-(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→3)-2,4-di-*O*-benzyl-α-D-mannopyranoside (17b). The glycosyl acceptor **2d** (200 mg, 0.317 mmol) was coupled to the glycosyl donor **3b** (231 mg, 0.412 mmol) by standard coupling procedures. The crude residue was dechloroacetylated by standard procedures to give the alcohol **17b** (321.9 mg, 0.303 mmol, 96% yield): R_f 0.21 (30% EtOAc/petroleum ether); $[\alpha]^{22}_D$ = +42.5° (c = 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.16–7.40 (m, 25H, Ph), 5.50 (m, 1H, H-2_b), 5.23 (d, 1H, J = 2 Hz, H-1_b), 4.75 (d, 1H, J = 2 Hz, H-1_a), 4.59–4.94 (m, 9H), 4.45–4.52 (m, 3H), 4.12–4.19 (m, 2H), 3.29–3.39 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 2.20–2.32 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 2.11 (s, 3H, $COCH_3$), 1.60–1.69 (m, 3H, $OCH_2CH_2CH_2CHBrCH_2Br$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.14 ($COCH_3$), 138.61, 138.26, 138.08, 137.89, 137.80, 129.06, 128.48, 128.39, 128.29, 128.25, 128.14, 128.04, 127.88, 127.76, 127.69, 127.55, 127.52, 125.32, 99.7 (C-1_b), 97.6 (C-1_a), 77.91, 77.26, 75.23, 74.94, 74.30, 73.48, 72.56, 72.40, 72.26, 71.79, 69.05, 68.78, 66.68, 66.64, 62.10, 52.40, 36.09, 32.85, 26.70, 21.06 ($COCH_3$). Anal. Calcd for $C_{54}H_{62}O_{11}Br_2$: C, 61.95; H, 5.97. Found: C, 62.07; H, 6.02.

Dibromopentanyl *O*-(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→3)-*O*-[(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)]-2,4-di-*O*-benzyl-α-D-mannopyranoside (16a). The disaccharide **17b** (1.4139g, 1.35 mmol) was coupled to the glycosyl donor **3b** (986.8 mg. 1.76 mmol) by standard coupling procedures to give the trisaccharide **16a** (1.5729g, 1.034 mmol, 77%): R_f 0.34 (30% EtOAc/petroleum ether); $[\alpha]^{22}_D$ = +35.1° (c = 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.24–7.80 (m, 40H, Ph), 5.51 (m, 1H, H-2_c), 5.49 (m, 1H, H-2_b), 5.21 (d, 1H, J = 2 Hz, H-1_b), 4.98 (d, 1H, J = 2 Hz, H-1_c), 4.78 (d, 1H, J = 2 Hz, H-1_a), 4.42–4.68 (m, 16H, CH_2-Ph), 4.22–4.38 (m, 3H), 3.54–3.96 (m, 14H), 3.32 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 2.16 (s, 3H, $COCH_3$), 2.09 (s, 3H, $COCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$); δ 170.35 ($COCH_3$), 170.18 ($COCH_3$), 138.71, 138.59, 138.36, 138.30, 138.21, 137.92, 129.11, 128.71, 128.64, 128.51, 128.47, 128.43, 128.31, 128.15, 128.02, 127.89, 127.82, 127.69, 127.62, 127.54, 127.47, 127.36, 127.33, 125.38, 99.8 (C-1_b), 98.1 (C-1_c), 97.1 (C-1_a), 78.18, 77.74, 77.45, 76.85, 76.55, 75.18, 74.98, 74.88, 74.35, 74.22, 73.53, 73.43, 72.34, 72.26, 71.87, 71.55, 71.43, 71.31, 69.10, 68.82, 68.76, 68.69, 68.48, 68.40, 66.61, 66.52, 66.43, 52.54, 36.18, 36.14, 32.99, 32.92, 26.74, 21.24 ($COCH_3$), 21.09 ($COCH_3$). Anal. Calcd for $C_{83}H_{92}O_{17}Br_2{\cdot}H_2O$: C, 64.09; H, 6.09. Found: C, 64.10; H, 6.03.

Dibromopentanyl *O*-(3,4,6-Tri-*O*-benzyl-α-D-mannopyranosyl)-(1→3)-*O*-[(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)]-2,4-di-*O*-benzyl-α-D-mannopyranoside (16d). The trisaccharide **16a** (171 mg, 0.243 mmol) was deacetylated by the standard procedure to give the diol **16d** (124 mg, 0.0853 mmol, 77%): R_f 0.13 (30% EtOAc/petroleum ether); $[\alpha]^{22}_D$ = +44.3° (c = 1.3, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.24–7.78 (m, 40H, Ph), 5.26 (d, 1H, J = 2 Hz, H-1_b), 5.10 (d, 1H, J = 2 Hz, H-1c), 4.78 (d, 1H, J = 2Hz, H-1_a), 4.46–4.88 (m, 16H, CH_2Ph), 3.55–4.17 (m, 19H), 3.35 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.56, 138.45, 138.31, 138.27, 138.07, 137.90, 128.52, 128.43, 128.34, 128.30, 128.17, 128.09, 127.96, 127.92, 127.85, 127.80, 127.73, 127.64, 127.60, 127.48, 101.5 (C-1_b), 99.7 (C-1_c), 97.1 (C-1_a), 80.11, 79.72, 77.85, 75.12, 75.07, 74.91, 74.84, 74.39, 74.25, 73.53, 73.41, 72.31, 72.02, 71.98, 71.74, 71.52, 71.16, 69.24, 68.83, 68.70, 68.04, 66.63, 66.45, 66.06, 60.44, 53.82, 52.48, 36.16, 32.95, 32.86, 31.78, 29.31, 26.70. Anal. Calcd for $C_{79}H_{88}O_{16}Br_2{\cdot}H_2O$: C, 64.49; H, 6.16. Found: C, 64.69; H, 6.19.

Dibromopentanyl *O*-(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→3)-*O*-[(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)]-2,4-di-*O*-benzyl-α-D-mannopyranoside (18a). The diol **16d** (979.5 mg, 0.674 mmol) was coupled to the glycosyl donor **3b** (2.5 equiv 1.685 mmol, 944.8 mg) by standard coupling procedures using NIS (2.5 equiv) and Et_3SiOTf (0.6 equiv) to give the pentasaccharide **18a** (1.0967 g, 0.456 mmol, 68%): R_f 0.41 in 30% EtOAc/petroleum ether; $[\alpha]^{22}_D$ = +32.3° (c = 1.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.13–7.40 (m, 70H, Ph), 5.30 (m, 2H, H-2_{dore}), 5.23 (d, 1H, J = 2 Hz, H-1_b), 5.10 (d, 1H, J = 2 Hz, H-1_c), 4.98 (d, 1H, J = 2 Hz, H-1_{dore}), 4.37–4.89 (m, 28H, CH_2Ph), 3.48–4.19 (m, 29H), 3.35 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 2.00 (s, 6H, 2 × $COCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.92 ($COCH_3$), 169.87 ($COCH_3$), 138.68, 138.60, 138.54, 138.23, 138.17, 138.10, 137.88, 128.53, 128.45, 128.38, 128.33, 128.25, 128.07, 128.00, 127.91, 127.78, 127.67, 127.59, 127.42, 127.33, 127.27, 127.21, 127.13, 127.06, 101.46 (C-1_b), 99.60 (C-1_c), 99.46 (C-1_{dore}), 99.42 (C-1_{dore}), 96.86 (C-1_a), 79.91, 79.55, 78.13, 77.63, 77.39, 77.30, 76.96, 76.28, 75.81, 75.71, 75.35, 75.25, 75.07, 74.90, 74.53, 74.44, 74.29, 74.24, 73.58, 73.53, 73.45, 73.37, 73.31, 73.15, 73.10, 73.05, 72.82, 72.78, 72.63, 72.53, 72.45, 72.36, 72.12, 71.97, 71.51, 70.24, 70.00, 69.78, 69.09, 66.75, 66.56, 66.49, 63.63, 63.48, 52.48, 36.20, 32.85, 32.79, 26.76, 21.13, 21.04, 20.94 ($COCH_3$), 20.90 ($COCH_3$). Anal. Calcd for $C_{137}H_{148}O_{28}Br_2$: C, 68.49; H, 6.21. Found: C, 68.33; H, 6.28.

Pentenyl *O*-(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→3)-*O*-[(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1 → 2)-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1 → 6)]-2,4-di-*O*-benzyl-α-D-mannopyranoside (18b). The dibromide **18a** (610 mg, 0.2539 mmol) was subjected to standard reductive elimination procedures to afford the pentenyl pentasaccharide **18b** (484 mg, 0.2258 mmol, 85%): R_f 0.41 (30% EtOAc/petroleum ether); $[\alpha]^{22}_D$ = +33.9° (c = 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 2.00 (6 H, s, OAc × 2), 3.35 (1 H, m, $OCH_2CH_2CH_2CH{=}CH_2$), 4.75 (1 H, d, J = 2 Hz, H-1a), 4.92 (1 H, d, J = 2 Hz, H-1d or e), 5.00 (1 H, d, J = 2 Hz, H-1d or e) 5.09 (1 H, d, J = 2 Hz, H-1c), 5.20 (1 H, d, J = 2 Hz, H-1b), 5.52 (2 H, m, H-2d and e), 5.75 (1 H, m, $OCH_2CH_2CH_2CH{=}CH_2$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 96.9 (C-1a), 99.4 (C-1d or e), 99.5 (C-1d or e) 99.6 (C-1c), 101.5 (C-1b). Anal. Calcd for $C_{137}H_{148}O_{28}$: C, 73.37; H, 6.65. Found: C, 73.16; H, 6.67.

Dibromopentanyl 3,4,6-Tri-*O*-benzyl-α-D-mannopyranoside (19). The pentenyl glycoside **3b** (1.0000 g, 1.78 mmol) was dissolved in MeOH (50 mL). To the solution was added K_2CO_3 (100 mg) with stirring for 1.5 h. The reaction mixture was filtered, and the solvent was removed by rotary evaporation. The residue was purified by column chromatography (30% EtOAc/petroleum ether). The residue was subjected to the standard dibromination procedure, and column chromatography (30% EtOAc in petroleum ether) afforded the glycosyl acceptor **19** (849.7 mg, 1.25 mm, 70%): R_f 0.25 (30% EtOAc/petroleum ether); $[\alpha]^{22}_D = +41.4°$ (c = 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.15−7.44 (m, 15H, 3 × Ph), 4.92 (d, 1H, J = 2 Hz, H-1), 4.51−4.88 (m, 6H, 2 × OCH_2Ph), 4.18 (m, 1H), 4.04 (s, 1H), 3.72−3.94 (m, 8H), 3.62 (m, 1H), 2.20−2.32 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 1.59−1.95 (m, 3H, $OCH_2CH_2CH_2CHBrCH_2Br$); ^{13}C NMR (75 MHz, $CDCl_3$); δ 138.31, 138.27, 137.98, 128.61, 128.55, 128.42, 128.31, 128.21, 128.17, 128.14, 128.03, 127.94, 127.78, 127.66, 99.31 (C-1), 80.15, 75.23, 74.37, 73.52, 72.04, 71.26, 69.02, 68.45, 66.65, 52.58, 52.52, 36.25, 32.97, 26.86, 26.82. Anal. Calcd for $C_{32}H_{38}O_6Br_2$: C, 56.63; H, 5.64. Found: C, 56.50; H, 5.68.

Dibromopentanyl *O*-(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (20a). The glycosyl acceptor **19** (1.79 g, 2.63 mmol) was coupled to the glycosyl donor **3b** (1.92 g, 3.43 mmol) by standard coupling procedures. The residue was purified by column chromatography (15% → 20% EtOAc/petroleum ether) (2.73 g, 2.37 mmol, 90% yield): R_f 0.56 (30% EtOAc/petroleum ether); $[\alpha]^{22}_D = +17.2°$ (c = 1.9, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.14−7.40 (m, 30H, Ph), 5.55 (m, 1H, H-2_g), 5.08 (d, 1H, J = 2Hz, H-1_g), 4.89 (d, 1H, J = 2Hz, H-1_f), 4.44−4.73 (m, 12H, CH_2Ph), 3.56−4.05 (m, 12H), 3.29 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 2.20−2.32 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 2.17 (s, 3H, $COCH_3$) 1.59−1.95 (m, 3H, $OCH_2CH_2CH_2CHBrCH_2Br$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.13 ($COCH_3$), 138.58, 138.51, 138.46, 138.91, 138.37, 138.20, 138.01, 128.45, 128.34, 128.31, 128.21, 128.15, 128.08, 127.99, 127.93, 127.82, 127.59, 127.53, 127.45, 99.6 (C-1_g), 98.6 (C-1_f), 96.16, 79.56, 78.15, 77.28, 75.11, 75.01, 74.97, 74.76, 74.68, 74.62, 74.60, 74.40, 73.45, 73.34, 72.11, 71.94, 71.81, 69.30, 69.20, 68.74, 66.57, 66.50, 60.41, 52.52, 52.45, 36.11, 32.91, 26.80, 21.19 ($COCH_3$). Anal. Calcd for $C_{61}H_{68}O_{12}Br_2 \cdot 3H_2O$: C, 60.70; H, 6.18. Found: C, 59.59; H, 5.98.

Dibromopentanyl *O*-(3,4,6-Tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (20b). The pure residue **20a** (0.9231 g, 0.8006 mmol) was deacetylated by standard procedures (0.8187 g, 0.737 mmol, 92%): R_f 0.34 (30% EtOAc/petroleum ether); $[\alpha]^{22}_D = +30.6°$ (c = 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.22−7.48 (m, 30H, Ph), 5.22 (d, 1H, J = 2Hz, H-1_g), 5.04 (d, 1H, J = 2 Hz, H-1_f), 4.59−4.99 (m, 12H, CH_2Ph), 3.62−4.25 (m, 13H), 3.32 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 2.20−2.32 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 1.59−1.95 (m, 3H, $OCH_2CH_2CH_2CHBrCH_2Br$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.69, 138.55, 138.46, 138.37, 138.33, 138.08, 137.90, 129.14, 129.01, 128.58, 128.42, 128.34, 128.16, 128.05, 127.97, 127.91, 127.85, 127.73, 127.70, 127.64, 127.56, 127.50, 125.91, 125.42, 101.29 (C-1_g), 98.92 (C-1_f) 96.25, 80.12, 79.69, 79.66, 77.61, 77.19, 76.76, 75.29, 75.14, 74.86, 74.55, 73.53, 73.42, 72.38, 72.22, 72.12, 71.65, 69.44, 68.62, 66.67, 66.59, 52.62, 52.57, 36.22, 36.19, 32.98, 26.90, 21.60 ($COCH_3$). Anal. Calcd for $C_{59}H_{66}O_{11}Br_2$: C, 63.79; H, 5.99. Found: C, 64.40; H, 6.20.

Dibromopentanyl *O*-(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (21a). The glycosyl acceptor **20b** (791.6 mg, 0.713 mmol) was coupled to the glycosyl donor **3b** (519.4 mg, 0.926 mmol) by standard coupling procedures. The residue was purified by column chromatography (15% → 20% EtOAc/petroleum ether) (795.0 mg, 0.501 mmol, 70%): R_f 0.54 (30% EtOAc/petroleum ether); $[\alpha]^{22}_D = +20.0°$ (c = 1.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.16−7.43 (m, 45H, Ph), 5.55 (m, 1H, H-2_h), 5.21 (d, 1H, J = 2 Hz, H-1_g), 5.10 (d, 1H, J = 2 Hz, H-1_h), 4.90 (d, 1H, J = 2 Hz, H-1_f), 4.35−5.02 (m, 18H, CH_2Ph), 3.58−4.10 (m, 18H), 3.27 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 2.20−2.32 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 2.18 (s, 3H, $COCH_3$), 1.59−1.95 (m, 3H, $OCH_2CH_2CH_2CHBrCH_2Br$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.14 ($COCH_3$), 138.63, 138.49, 138.45, 138.36, 138.26, 138.11, 138.07, 138.04, 137.88, 135.12, 131.12, 129.62, 129.34, 129.29, 129.12, 129.03, 128.98, 128.93, 128.88, 128.82, 128.75, 128.65, 128.51, 128.41, 128.31, 128.27, 128.19, 128.13, 128.07, 128.00, 127.91, 127.83, 127.71, 127.65, 127.58, 127.51, 127.43, 127.01, 125.89, 125.40, 100.78 (C-1_g), 99.67 (C-1_h), 98.81 (C-1_f), 96.22, 79.58, 79.37, 79.26, 78.40, 78.36, 78.20, 77.58, 77.42, 77.35, 77.16, 76.73, 76.54, 75.13, 75.09, 74.87, 74.83, 74.74, 74.68, 74.46, 74.40, 74.31, 73.50, 73.39, 72.38, 72.18, 71.95, 71.87, 71.70, 69.76, 69.69, 69.55, 69.41, 69.36, 69.32, 69.26, 68.97, 68.79, 66.64, 66.54, 36.11, 32.91, 26.80, 21.23 ($COCH_3$). Anal. Calcd for $C_{88}H_{96}O_{17}Br_2$: C, 66.67; H, 6.10. Found: C, 66.40; H, 6.12.

Pentenyl *O*-(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (21b). The dibromide **21a** (285.6, 0.180 mmol) was subjected to standard reductive elimination procedures to afford the pentenyl trisaccharide **21b** (231.7 mg, 0.1625 mmol, 95%): R_f 0.54 (30% EtOAc/petroleum ether); $[\alpha]^{22}_D = +21.2°$ (c = 1.1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.13−7.43 (m, 45H, Ph), 5.77 (m, 1H, $OCH_2CH_2CH_2CH{=}CH_2$), 5.55 (m, 1H, H-2_h), 5.19 (d, 1H, J = 2 Hz, H-1_g), 5.09 (d, 1H, J = 2 Hz, H-1_h), 4.90 (d, 1H, J = 2 Hz, H-1_f), 4.34-5.02 (m, 18H, CH_2Ph), 3.50−4.19 (m, 18H), 3.27 (m, 1H, $OCH_2CH_2CH_2CH{=}CH_2$), 2.14 (s, 3H, $COCH_3$), 2.06−2.20 (m, 2H, $OCH_2CH_2CH_2CH{=}CH_2$), 1.60−1.70 (m, 2H, $OCH_2CH_2CH_2CH{=}CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.14 ($COCH_3$), 138.67, 138.63, 138.58, 138.51, 138.44, 138.39, 138.23, 138.20, 138.09, 138.05, 138.02, 137.94, 128.96, 128.90, 128.86, 128.66, 128.45, 128.38, 128.34, 128.24, 128.16, 128.02, 127.94, 127.83, 127.70, 127.59, 127.54, 127.47, 127.35, 127.23, 115.13, 114.98 ($OCH_2CH_2CH_2CH{=}CH_2$), 99.63 (C-1_g), 99.43 (C-1_h), 98.79 (C-1_f), 79.76, 79.43, 79.39, 78.38, 78.30, 78.20, 77.33, 75.63, 75.21, 75.11, 75.04, 74.92, 74.78. 74.69, 74.40, 74.29, 73.34, 72.31, 72.10, 71.92, 71.83, 71.76, 71.70, 71.44, 69.70, 69.58, 69.35, 69.28, 69.09, 69.05, 68.90, 68.77, 67.27, 67.01, 60.42, 30.33 ($OCH_2CH_2CH_2CH{=}CH_2$), 28.72, 28.67, 28.63 ($OCH_2CH_2CH_2CH{=}CH_2$), 21.23 ($COCH_3$). Anal. Calcd for $C_{88}H_{96}O_{17}$: C, 74.14; H, 6.79. Found: C, 73.87; H, 6.84.

Dibromopentanyl *O*-(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→3)-6-*O*-(chloroacetyl)-2,4-di-*O*-benzyl-α-D-mannopyranoside (22a). The glycosyl acceptor **2d** (1 equiv, 125 mg, 0.1976 mmol) was coupled to the glycosyl donor **21b** (1.3 equiv, 366.3 mg, 0.2569 mm) with NIS (1.3 equiv, 58 mg, 0.2569 mmol) and Et_3SiOTf (0.3 equiv, 13 μL, 0.0593 mmol) by standard coupling procedures. The product was purified by column chromatography (15% → 30% EtOAc/petroleum ether), 281 mg, 0.1413 mmol, 72%: R_f 0.38 (30% EtOAc/petroleum ether); $[\alpha]^{22}_D = +29.4°$ (c = 0.9, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.13−7.50 (m, 55H, Ph), 5.60 (d, 1H, J = 2 Hz, H-2_h), 5.27 (d, 1H, J = 2 Hz, H-1_f), 5.15 (d, 1H, J = 2 Hz, H-1_g), 5.13 (d, 1H, J = 2 Hz, H-1_h), 4.38−5.01 (m, 23H, CH_2Ph, H-1_i), 3.50−4.36 (m, 24H), 3.39 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 2.20−2.32 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 2.19 (s, 3H, $COCH_3$), 1.59−1.95 (m, 3H, $OCH_2CH_2CH_2CHBrCH_2Br$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.16 ($COCH_3$), 167.00 ($COCH_2Cl$), 138.67, 138.63, 138.59, 138.50, 138.45, 138.33, 138.26, 138.16, 138.08, 137.94, 137.84, 130.37, 129.93, 129.87, 129.78, 129.71, 129.66, 129.61, 129.55, 129.53, 129.43, 129.38, 129.34, 129.27, 129.20, 129.11, 128.97, 128.67, 128.59, 128.38, 128.32, 128.25, 128.17, 128.09, 127.94, 127.86, 127.79, 127.71, 127.66, 127.55, 127.42, 125.39, 101.17 (C-1_f), 99.60 (C-1_g), 99.44 (C-1_h), 96.20 (C-1_i), 79.96, 79.46, 78.28, 78.15, 77.36, 75.24, 75.06, 74.94, 74.85, 74.72, 74.64, 74.30, 74.18, 74.14, 74.08, 74.00, 73.48, 73.42, 73.32, 73.16, 72.79, 72.50, 72.24, 72.09, 71.94, 70.04, 69.70, 69.64, 69.16, 68.72, 68.66, 68.55, 64.92, 52.33, 40.78, 36.09, 32.92, 32.79, 32.74, 26.68, 21.25 ($COCH_3$). Anal. Calcd for $C_{110}H_{119}O_{23}Br_2Cl \cdot 2H_2O$: C, 64.75; H, 6.08. Found: C, 64.74; H, 6.00.

Pentenyl *O*-(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→3)-2,4-di-*O*-benzyl-α-D-mannopyranoside (22b). The tetra-

saccharide **22a** (144.0 mg, 0.0724 mmol) was dechloroacetylated by standard procedures to give the alcohol (102.0 mg, 0.0534 mmol, 74%): R_f 0.18 (30% EtOAc/petroleum ether); $[\alpha]^{22}_D = +25.6°$ (c = 1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.10–7.46 (m, 55H, Ph), 5.55 (m, 1H, H-2_h), 5.21 (m, 2H, H-1_{fandg}), 5.09 (d, 1H, J = 2Hz, H-1_h), 4.75 (d, 1H, J = 2Hz, H-1_i), 4.40–4.95 (m, 22H, CH_2Ph), 3.42–4.18 (m, 24H), 3.28 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 2.20–2.32 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 2.11 (s, 3H, $COCH_3$), 1.59–1.95 (m, 3H, $OCH_2CH_2CH_2CHBrCH_2Br$); ^{13}C NMR (75 MHz, $CDCl_3$); δ 170.16 ($COCH_3$), 138.67, 138.63, 138.59, 138.50, 138.45, 138.33, 138.26, 138.16, 138.08, 137.94, 137.84, 130.37, 129.93, 129.87, 129.78, 129.71, 129.66, 129.61, 129.55, 129.53, 129.43, 129.38, 129.34, 129.27, 129.20, 129.11, 128.97, 128.67, 128.59, 128.38, 128.32, 128.25, 128.17, 128.09, 127.94, 127.86, 127.79, 127.71, 127.66, 127.55, 127.42, 125.39, 101.2 (C-1_f), 101.0 (C-1_g), 99.3 (C-1_h), 97.8 (C-1_i), 79.96, 79.46, 78.28, 78.15, 77.36, 75.24, 75.06, 74.94, 74.85, 74.72, 74.64, 74.30, 74.18, 74.14, 74.08, 74.00, 73.48, 73.42, 73.32, 73.16, 72.79, 72.50, 72.24, 72.09, 71.94, 70.04, 69.70, 69.64, 69.16, 68.72, 68.66, 68.55, 64.92, 52.33, 40.78, 36.09, 32.92, 32.79, 32.74, 26.68, 21.25 ($COCH_3$); FAB mass spectrum M + NH_4^+ = 1947, M + 1 = 1929.

Dibromopentanyl *O*-(2-*O*-Acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→3)-[(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→3)-*O*-[(2-*O*-acetyl-3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→2)-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-(1→6)]-(2,4-di-*O*-benzyl-α-D-mannopyranosyl)]-(1→6)-2,4-di-*O*-benzyl-α-D-mannopyranoside (23). The tetrasaccharide acceptor **22b** (177.6 mg, 0.0921 mmol) was coupled to the pentasaccharide donor **18b** (271 mg, 0.121 mmol) by standard coupling procedures using NIS (27.2 mg, 0.121 mmol) and Et_3SiOTf (6 μL, 0.028 mmol). The product **23** was isolated by HPLC (214 mg, 0.0524 mmol, 57%): R_f 0.36 (30% EtOAc/petroleum ether); $[\alpha]^{22}_D = +35.2°$ (c = 1.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.01–7.38 (m, 125H, Ph), 5.54 (m, 3H, H-$2_{e,d,andh}$), 5.20 (m, 2H, H-1_{fandb}), 5.11 (d, 1H, J = 2Hz, H-1_a), 5.09 (d, 1H, J = 2Hz, H-1_c), 5.05 (d, 1H, J = 2Hz, H-1_g), 5.00 (d, 1H, J = 2Hz, H-1_d), 4.92 (d, 1H, J = 2Hz, H-1_e), 4.91 (d, 1H, J = 2Hz, H-1_h), 4.76 (d, 1H, J = 2Hz, H-1_i), 4.36–4.90 (m, 50H, CH_2Ph), 3.45–4.16 (m, 51H), 3.25 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 2.20–2.32 (m, 1H, $OCH_2CH_2CH_2CHBrCH_2Br$), 2.15 (m, 9H, 3 × $COCH_3$), 1.59–1.95 (m, 3H, $OCH_2CH_2CH_2CHBrCH_2Br$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.98 ($COCH_3$), 169.91 ($COCH_3$), 169.89 ($COCH_3$), 128.30, 128.28, 128.24, 128.19, 128.16, 128.12, 128.05, 127.93, 127.85, 127.73, 127.71, 127.66, 127.64, 127.60, 127.53, 127.50, 127.46, 127.42, 127.35, 127.27, 127.19, 101.29, 100.82, 99.50, 99.49, 99.05–99.20, 99.33, 97.01, 78.17, 78.12, 78.07, 77.99, 77.86, 75.04, 74.96, 74.92, 74.80, 74.74, 74.54, 74.32, 74.20, 74.05, 73.30, 73.24, 73.07, 72.98, 72.70, 72.11, 71.96, 71.86, 71.77, 71.68, 71.25, 71.19, 68.98, 68.81, 68.70, 68.62, 68.49, 66.32, 66.22, 60.25, 52.54, 52.51, 38.67, 36.22, 36.19, 36.12, 36.06, 32.91, 32.84, 32.76, 30.30, 29.59, 28.84, 26.45, 23.69, 22.89, 21.05, 20.93, 20.89, 20.79, 14.12, 13.97, 10.90.

Acknowledgment. This work was supported by grants from the NIH (AI 31862) and NSF (CHE 9311356).