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Synthesis of a fucosylated and a non-fucosylated core structure of xylose-containing carbohydrate chains from N-glycoproteins

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Abstract

The synthesis is reported of methyl 2-acetamido-4-*O*-[2-acetamido-2-deoxy-4-*O*-(3,6-di-*O*-α-D-mannopyranosyl-2-*O*-β-D-xylopyranosyl-β-D-mannopyranosyl)-β-D-glucopyranosyl]-2-deoxy-β-D-glucopyranoside (**4**) and methyl 2-acetamido-4-*O*-[2-acetamido-2-deoxy-4-*O*-(3,6-di-*O*-α-D-mannopyranosyl-2-*O*-β-D-xylopyranosyl-β-D-mannopyranosyl)-β-D-glucopyranosyl]-2-deoxy-6-*O*-α-L-fucopyranosyl-β-D-glucopyranoside (**5**), which represent the invariant hexasaccharide core structure of the xylose-containing glycans of N-glycoproteins and its 6-*O*-fucosylated derivative. Ethyl 4-*O*-[3-*O*-allyl-4-*O*-benzoyl-6-*O*-*tert*-butyldimethylsilyl-2-*O*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**9**) was coupled with methyl 3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**11**). Desilylation of the resulting tetrasaccharide derivative, followed by condensation with 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl trichloroacetimidate (**7**), gave methyl 4-*O*-{4-*O*-[3-*O*-allyl-4-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-2-*O*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl}-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**14**). Deallylation of **14**, followed by condensation with **7** and deprotection, gave hexasaccharide **4**. Ethyl 3,6-di-*O*-benzyl-2-deoxy-4-*O*-[4,6-di-*O*-acetyl-3-*O*-allyl-2-*O*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-2-phthalimido-1-thio-β-D-glucopyranoside (**17**) was coupled with methyl 3-*O*-benzyl-2-deoxy-6-*O*-(4-methoxybenzyl)-2-phthalimido-β-D-glucopyranoside. Demethoxybenzylation of the tetrasaccharide derivative thus obtained, followed by fucosylation using ethyl 2,3,4-tri-*O*-benzyl-1-thio-

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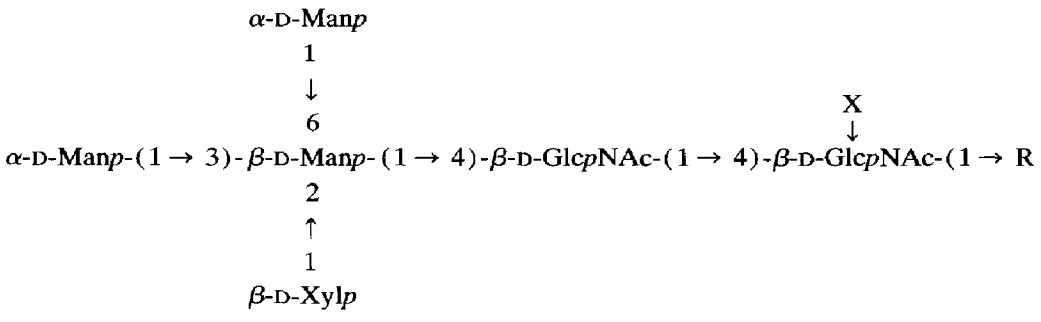
β-L-fucopyranoside, gave methyl 3-*O*-benzyl-2-deoxy-4-*O*-{3,6-di-*O*-benzyl-2-deoxy-4-*O*-[4,6-di-*O*-acetyl-3-*O*-allyl-2-*O*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-2-phthalimido-β-D-glucopyranosyl}-2-phthalimido-6-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside (**23**). *O*-Deacetylation followed by *tert*-butyldimethylsilylation, benzoylation, and desilylation gave methyl 4-*O*-{4-*O*-[3-*O*-allyl-4-*O*-benzoyl-2-*O*-(2,3,4-tri-*O*-benzoyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl}-3-*O*-benzyl-2-deoxy-2-phthalimido-6-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside (**24**). Mannosylation of **24** using **7**, followed by deallylation, further mannosylation with **7**, and deprotection, gave the heptasaccharide **5**.

Keywords: Hemocyanin; Lectin; Xylose-type N-glycan; Glycoprotein; Oligosaccharide synthesis

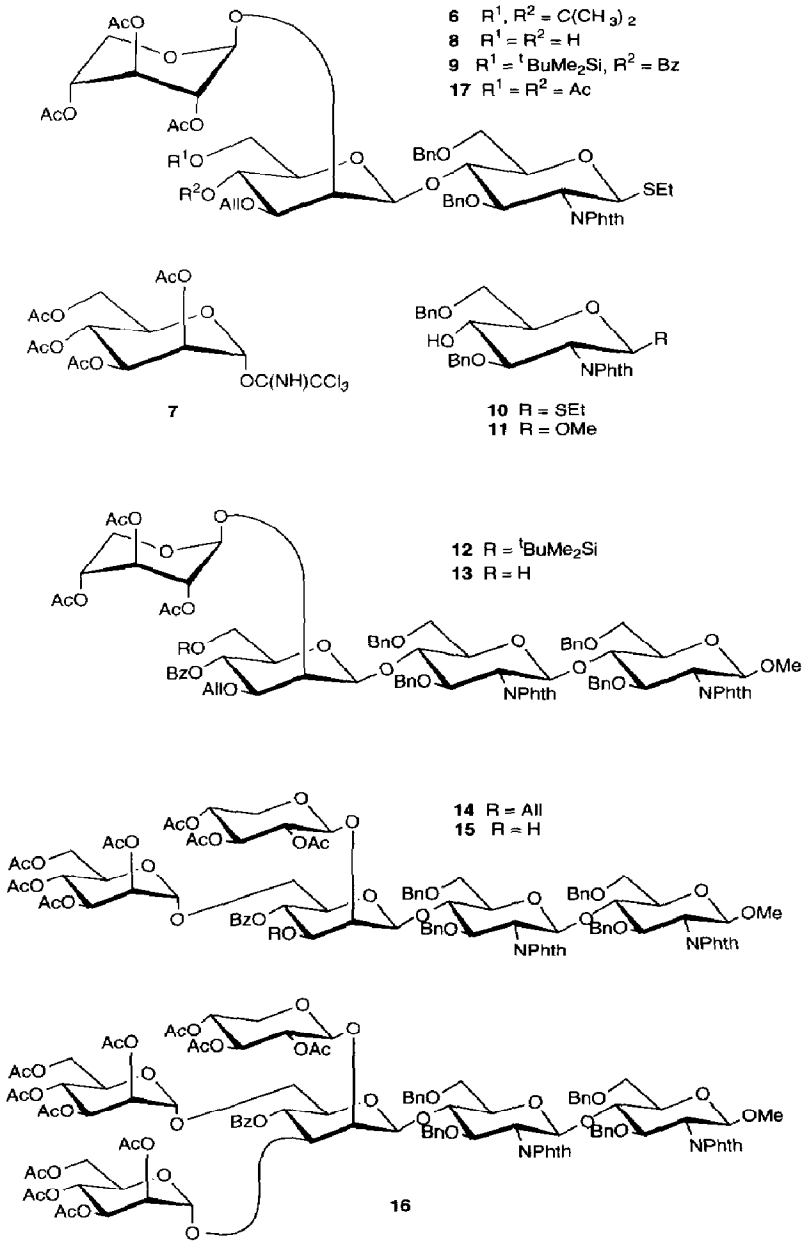
1. Introduction

Since their discovery in the late 70's, xylose-containing N-linked carbohydrate chains have become well established constituents of glycoproteins, mostly of plant but also of animal origin [1]. Because β-D-Xyl*p* is always (1→2)-linked to β-D-Man*p* of the usual $Man_3GlcNAc_2$ core structure, a new invariant hexasaccharide core structure (**1**) can be defined for the xylose-type N-linked glycans. Already many glycans based on this core structure have been isolated and characterized [1]. A striking difference in the xylose-containing N-glycans of plant and animal origin is found in the fucosylation (if present) of the innermost Glc*p*NAc residue of the core structure. In xylose-type glycans of animal origin, L-Fuc*p* is α-(1→6)-linked, as in the glycans derived from α-hemocyanin of *Helix pomatia* [2] (**2**), and in those of plant origin, such as a seed lectin obtained from *Sophora japonica* [3,4] (**3**), it is α-(1→3)-linked.



1 X = H, R = Asn
2 X = α-L-Fuc*p*-(1→6), R = Asn
3 X = α-L-Fuc*p*-(1→3), R = Asn
4 X = H, R = OMe
5 X = α-L-Fuc*p*-(1→6), R = OMe

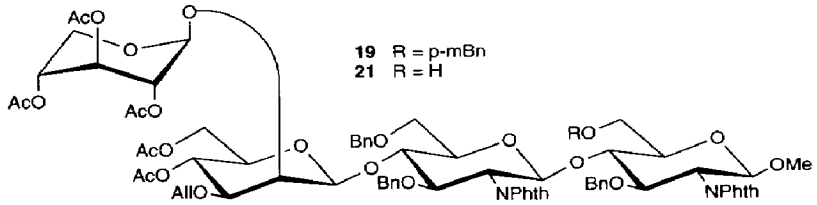
As part of our program focused on the structure elucidation [1], conformation analysis [5–7], organic synthesis, and biosynthesis [8] of xylose-containing glycans, the synthesis of structural elements, comprising only the branching point of the core structure, has been reported [9–11]. We now describe the synthesis of the hexasaccharide methyl β-glycoside



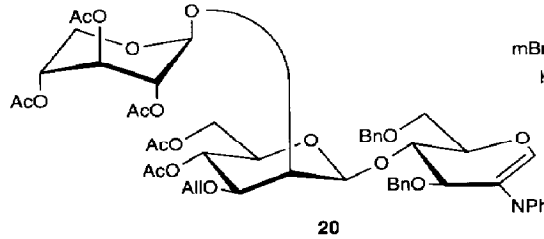
4, representing the complete invariant core structure, and the heptasaccharide methyl β-glycoside **5**, having a Fuc residue α-(1→6)-linked to the innermost GlcNAc residue.

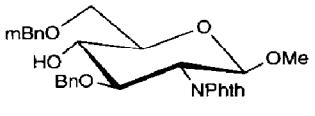
2. Results and discussion

Previously, the synthesis of the selectively protected trisaccharide ethyl 4-*O*-[3-*O*-allyl-4,6-*O*-isopropylidene-2-*O*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-β-D-mannopyrano-



19 R = p-mBn
21 R = H





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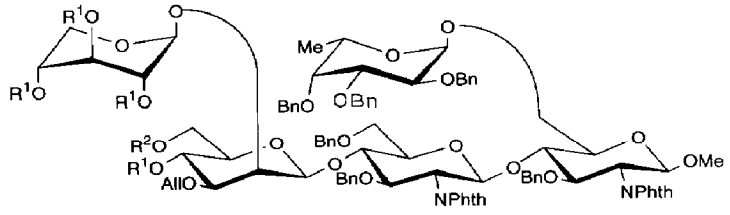

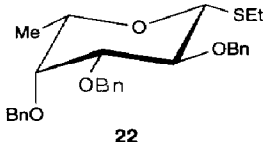

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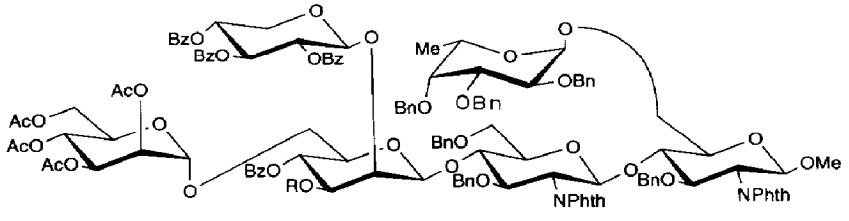
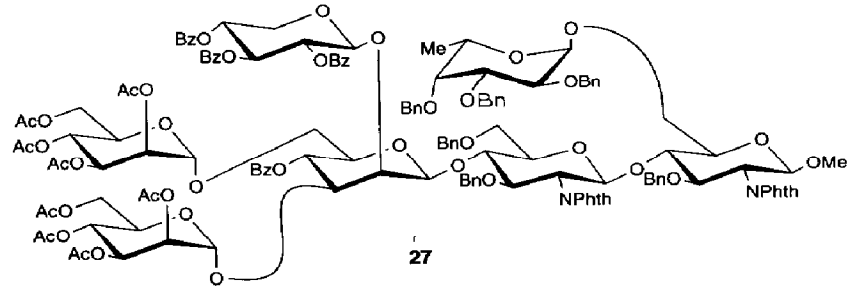
23 R^1 = R^2 = Ac
24 R^1 = Bz, R^2 = H



25 R = Allyl
26 R = H



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syl]-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside [10] (**6**) has been reported. This unit was chosen as the central building block for the synthesis of the glycans **4**–**5**. The presence of the isopropylidene acetal at HO-4′,6′ and the allyl group at HO-3′ gives the opportunity to carry out regioselective α-mannosylations at HO-6′ and/or HO-3′. Furthermore, by activating the thioethyl glycoside, this building block (or extended with α-D-Man*p* residues) can serve as a glycosyl donor. Coupling of this donor to two different acceptors, namely, derivatized glucosamine or α-(1→6)-fucosylated glucosamine, looks attractive for the synthesis of the two desired glycans.

However, the regioselective coupling of mannosyl donors, such as 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl trichloroacetimidate [9] (**7**) and 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide, with deisopropylidenated **6** (**8**) turned out to be extremely difficult. The main problem was the relative lability of the thioethyl group of the acceptor during coupling reactions, giving rise to degradation of the acceptor. Moreover, the transfer of the thioethyl group to the anomeric center of the donor (trans-glycosidation) was sometimes observed. As we had already noticed during the synthesis of **6** [10], it was only possible to carry out coupling reactions employing glycosyl bromides catalyzed by silver triflate in toluene–dichloromethane at −40°C/−60°C. Although some interesting protected tetra- and penta-saccharides [12] could be prepared using this glycosylation procedure, the yields were extremely low and undesired ortho-ester formation was also encountered. Thus, although the thioethyl glycoside behaved well during all kinds of protective group manipulation, for example, *O*-deacetylation, deisopropylidenation, oxidation–reduction, and deallylation [10], its behaviour in glycosylation reactions was not satisfactory. It must be noted that this behaviour might well be due to the use of a 2-deoxy-2-phthalimidothioglycoside, because many other thioglycosides have been described which were stable during coupling reactions [13,14].

To build up the oligosaccharides **4**–**5**, it was decided that it would be better to couple the trisaccharide donor first to an acceptor, and then to elongate the resulting structures in a stepwise manner with mannosyl donors at the non-reducing end. This is now described separately for the two target structures **4** and **5**, in both cases starting with compound **8**.

Synthesis of hexasaccharide **4**.—Ethyl 4-*O*-[3-*O*-allyl-2-*O*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside [10] (**8**) was silylated on HO-6′ with *tert*-butyldimethylsilyl chloride in pyridine for 16 h [15], and then benzoylated on HO-4′ with benzoyl chloride, to give the trisaccharide donor **9** (93%). The choice of the protective groups of HO-3′,4′,6′ allows the possibility to perform the planned regioselective α-mannosylations in a later stage. Ethyl 3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside [10] (**10**) was converted into the corresponding methyl glycoside **11** (66%) by treatment with methanol and methyl triflate in toluene. Coupling of **9** with **11**, using *N*-iodosuccinimide (NIS) and trifluoromethanesulfonic acid [14] (HOTf) as catalyst, gave the tetrasaccharide derivative **12** (52%). Removal of the *tert*-butyldimethylsilyl group, using *p*-toluenesulfonic acid in acetonitrile–water, gave the tetrasaccharide acceptor **13** (97%). Mannosylation of **13** with 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl trichloroacetimidate [9] (**7**) in dichloromethane at −20°C, using trimethylsilyl triflate as catalyst, gave **14** (71%). After deallylation of **14** using the Wilkinson catalyst in the presence of 1,4-diazabicyclo[2.2.2]octane [16]

followed by hydrolysis (→ **15**, 85%), mannosylation with **7**, as described for **13**, gave the hexasaccharide derivative **16** (59%). The chosen procedure for the deprotection of **16**, involving dephthaloylation/deacylation with methylamine in ethanol [17], re-*N*-acetylation with acetic anhydride in methanol, and then hydrogenolysis using palladium on activated carbon, was not completely successful. ^{1}H NMR analysis of the final product showed an incomplete dephthaloylation, and therefore the residue was treated with hydrazine acetate in boiling ethanol [18], followed by re-*N*-acetylation, column chromatography, and RP-HPLC, to give the hexasaccharide **4** (77%). For ^{1}H NMR data, see Table 1.

Synthesis of heptasaccharide **5**.—Ethyl 3,6-di-*O*-benzyl-2-deoxy-4-*O*-[4,6-di-*O*-acetyl-3-*O*-allyl-2-*O*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-2-phthalimido-1-thio-β-D-glucopyranoside (**17**) was prepared from **8** via acetylation with pyridine–acetic anhydride (99%). The choice of this trisaccharide donor also makes regioselective α-mannosylation possible in a later stage. Condensation of **17** with methyl 3-*O*-benzyl-2-deoxy-6-*O*-(4-methoxybenzyl)-2-phthalimido-β-D-glucopyranoside [18] (**18**), using NIS/HOTf, gave the tetrasaccharide derivative **19** (61%) and the trisaccharide derivative **20** as the major side-product [19,20] (20%). Demethoxybenzylation of **19**, using ceric(IV) ammonium nitrate in acetonitrile–water [21], yielded the tetrasaccharide acceptor **21** (86%), which was fucosylated with ethyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside [19] (**22**), in dichloroethane–ether using iodonium dicollidine perchlorate [14] as promoter, to give the pentasaccharide derivative **23** (49%) and an unknown compound **23-a**.

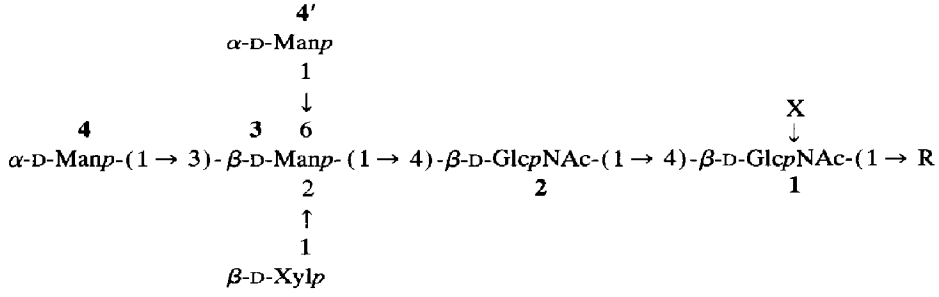
Zemplén deacetylation of **23**, followed by silylation of HO-6‴ with *tert*-butyldimethylsilyl chloride in pyridine [15], benzoylation of HO-4‴,2⁗,3⁗,4⁗ using benzoyl chloride, and removal of the silyl ether with *p*-toluenesulfonic acid in acetonitrile–water gave methyl 4-*O*-{4-*O*-[3-*O*-allyl-4-*O*-benzoyl-2-*O*-(2,3,4-tri-*O*-benzoyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl}-3-*O*-benzyl-2-deoxy-2-phthalimido-6-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside (**24**, 72%). Mannosylation of **24** with imidate **7** in dichloromethane at −20°C, using trimethylsilyl triflate as catalyst, gave the hexasaccharide derivative **25** (45%). Deallylation of **25** using the Wilkinson catalyst in the presence of 1,4-diazabicyclo[2.2.2]octane [16], followed by hydrolysis (→ **26**, 73%), and subsequent mannosylation, as described for **24**, gave the heptasaccharide derivative **27** (88%). The chosen procedure for the deprotection of **27**, involving dephthaloylation/deacylation using hydrazine acetate in boiling ethanol [18], followed by re-*N*,*O*-acetylation using pyridine–acetic anhydride, and finally hydrogenolysis using palladium on carbon, was not completely successful. Again, ^{1}H NMR analysis of the final product showed incomplete dephthaloylation, and it was therefore treated with methylamine in ethanol [17], followed by re-*N*-acetylation, column chromatography, and RP-HPLC, to afford the heptasaccharide **5** (83%). For ^{1}H NMR data, see Table 1.

As was observed during the preparation of smaller oligosaccharides [10,11], the ^{1}H NMR data of the compounds containing a β-D-xylopyranose residue showed that the ^3J-values of the skeleton protons of xylose vary to some extent. As has been discussed [10,11], this behaviour can be ascribed to the presence of a $^1C_4 \rightleftarrows {}^4C_1$ conformational equilibrium, but also distortions of the $^4C_1$ chair can lead to deviating J-values. At least for **9**, **12**, **13**, **17**, **19**, **20**, **21**, **23**, and **24**, the D-xylose residue does not seem to occur exclusively in the $^4C_1$ chair conformation ($^3J_{1,2} \leq 3.5$ Hz).

Table 1
500-MHz ^{1}H NMR data of hexasaccharide **4** and heptasaccharide **5**, and of relevant reference compounds

Residue	Reporter group (J)	δ (ppm)/J (Hz)					
		X = H			X = α-L-Fuc*p*-(1→6)		
		4	**1** [22]	Ref [23]	**5**	**2**	Ref [1]
		R = OMe	R = Asn	R = OH [a]	R = OMe	R = Asn	R = OH [a]
GlcNAc-**1**	H-1 ($J_{1,2}$)	4.432 (8.1)	5.048	5.189$^{\alpha}$ 4.703$^{\beta}$	4.429 (8.3)	5.088	5.181$^{\alpha}$ 4.694$^{\beta}$
	NAc	2.029	2.010	2.039	2.029	2.010	2.040
	OMe	3.495			3.487		
GlcNAc-**2**	H-1 ($J_{1,2}$)	4.597 (8.0)	4.608	4.615$^{\alpha}$ 4.607$^{\beta}$	4.670 (8.0)	4.686	4.666$^{\alpha}$ 4.673$^{\beta}$
	NAc	2.077	2.070	2.074	2.087	2.086	2.088$^{\alpha}$ 2.085$^{\beta}$
Man-**3**	H-1	4.869	4.869	4.875	4.871	4.872	4.873
	H-2 ($J_{2,3}$)	4.265 (3.1)	4.264	4.265	4.265 (3.2)	4.267	4.266
Man-**4**	H-1 ($J_{1,2}$)	5.121 (1.7)	5.121	5.122	5.122 (1.7)	5.122	5.123
	H-2	4.038	4.037	4.041	4.038	4.037	4.038
Man-**4′**	H-1 ($J_{1,2}$)	4.913 (1.8)	4.911	4.912	4.913 (1.8)	4.914	4.913
	H-2	3.982	3.981	3.982	3.980	3.979	3.981
Xyl	H-1 ($J_{1,2}$)	4.448 (7.7)	4.447	4.453	4.450 (7.7)	4.449	4.450
	H-2 ($J_{2,3}$)	3.374 (9.4)	3.373	3.375	3.374 (9.4)	3.377	3.375
	H-3 ($J_{3,4}$)	3.440 (9.3)	3.438	3.444	3.456 (9.3)	n.d.[b]	3.456
	H-5*ax* ($J_{4,5ax}$/ $J_{5ax,5eq}$)	3.248 (10.6/ −11.7)	3.248	3.253	3.252 (10.7/ −11.6)	3.252	3.253
Fuc	H-1 ($J_{1,2}$)				4.906 (4.5)	4.878	4.890$^{\alpha}$ 4.898$^{\beta}$
	H-5				4.134	n.d.[b]	4.100
	H-6 ($J_{5,6}$)				1.229 (6.7)	1.206	1.210$^{\alpha}$ 1.222$^{\beta}$

[a] Oligosaccharide occurs as an anomeric mixture; α and β refer to GlcNAc-**1**.
[b] n.d., Not determined.



3. Experimental

General methods.—The ^{1}H (300 and 500 MHz) and ^{13}C (APT, 50 and 75 MHz) NMR spectra were recorded at 25°C with a Bruker AC 300, AM 500, or WP 200 spectrometer.

Chemical shifts (δ) are given in ppm relative to the signal for internal Me_4Si ($CDCl_3$) or sodium 4,4-dimethyl-4-silapentane-1-sulfonate (D_2O; indirectly to internal acetone δ 2.225) for ^1H, and to the signal for internal Me_4Si ($CDCl_3$; indirectly to $CDCl_3$, δ 76.9) or external Me_4Si (D_2O; indirectly to internal acetone, δ 31.55) for ^{13}C. Column chromatography was performed on Kieselgel 60 (Merck, < 230 mesh) and fractions were monitored by TLC on Kieselgel 60 F_{254} (Merck) by detection with UV light and then charring with H_2SO_4. Preparative TLC was performed on Kieselgel 60 F_{254} (Merck, schichtdicke 0.5 mm). Optical rotations were measured for solutions in $CHCl_3$, unless otherwise stated, at 20°C with a Perkin–Elmer 241 polarimeter, using a 10-cm 1-mL cell. In the work-up procedures, washings were carried out three times with appropriate quantities of water or aq 5% $NaHCO_3$ unless indicated otherwise. Solvents were evaporated under reduced pressure at 40°C (bath). All solvents were distilled from the appropriate drying agents.

*Ethyl 4-O-[3-O-allyl-4-O-benzoyl-6-O-*tert*-butyldimethylsilyl-2-O-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-3,6-di-O-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside* (**9**).—A solution of ethyl 4-*O*-[3-*O*-allyl-2-*O*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside [10] (**8**; 954 mg, 0.96 mmol) and *tert*-butyldimethylsilyl chloride (434 mg, 2.88 mmol) in pyridine (15 mL) was stirred for 16 h. TLC (1:1 hexane–EtOAc) then showed the silylation to be complete (R_f 0.56), and benzoyl chloride (200 μL, 1.72 mmol) was added. After stirring for 16 h, the mixture was diluted with CH_2Cl_2 (500 mL), washed with aq 5% $NaHCO_3$ (2 × 50 mL) and water, dried ($MgSO_4$), filtered, and concentrated. Column chromatography (95:5 CH_2Cl_2–acetone) of the residue gave **9**, isolated as a white foam (1.1 g, 93%); $[\alpha]_D$ −30° (*c* 1); R_f 0.54. NMR data ($CDCl_3$): ^1H, δ 8.02–6.72 (m, 19 H, 3 Ph and Phth), 5.687 (m, 1 H, H_2C=C*H*CH_2O), 5.338 (t, 1 H, $J_{4',5'}$ 9.8 Hz, H-4'), 5.260 (d, 1 H, $J_{1,2}$ 10.4 Hz, H-1), 5.192 (d, 1 H, $J_{1'',2''}$ 1.8 Hz, H-1''), 5.125 and 5.028 (2 m, 2 H, H_2C=CHCH_2O), 4.976 and 4.401 (2 d, each 1 H, PhCH_2O), 4.774 and 4.552 (2 d, each 1 H, PhCH_2O), 4.753 (m, 1 H, H-4''), 4.678 (s, 1 H, H-1'), 4.618 (dd, 1 H, $J_{5''eq/ax,4''}$ 2.5, $J_{5''eq,5''ax}$ −13.1 Hz, H-5''*eq* or H-5''*ax*), 3.315 (dd, 1 H, $J_{3',2'}$ 3.0, $J_{3',4'}$ 9.9 Hz, H-3'), 2.646 (m, 2 H, CH_3CH_2S), 2.148 and 2.131 (2 s, 3 and 6 H, 3 Ac), 1.180 (t, 3 H, CH_3CH_2S), 0.718 [s, 9 H, $(CH_3)_3CSi$], −0.146 and −0.208 [2 s, each 3 H, $(CH_3)_2Si$]; ^{13}C, δ 169.5, 169.4, and 168.5 (3 $COCH_3$), 167.6 and 167.1 (*C*O Phth), 164.9 (*C*OPh), 138.7, 137.8, 134.1, 133.3, 132.7, 131.4, 131.3, 129.9, 129.3, 128.2–127.3, 126.4, and 122.9 ($C_6H_5CH_2O$, C_6H_5CO, H_2C=*C*HCH_2O, and Phth), 116.6 (H_2C=CHCH_2O), 101.1 and 97.5 (C-1',1''), 80.8, 79.9, 78.6, 78.4, 78.2, 75.2, 72.7, 69.2, 67.2, 67.0, and 66.1 (C-1,3,4,5,2',3',4',5',2'',3'',4''), 74.7, 73.3, 70.4, 68.9, 63.5, and 58.3 (C-6,6',5'', 2 PhCH_2O, and H_2C=CHCH_2O), 54.5 (C-2), 25.5 [$(CH_3)_3$CSi], 23.4 (CH_3CH_2S), 20.7 (2 C) and 20.5 (3 $COCH_3$), 17.9 [$(CH_3)_3$*C*Si], 14.6 (CH_3CH_2S), −5.9 [$(CH_3)_2$Si]. Anal. Calcd for $C_{63}H_{77}NO_{19}SiS$: C, 62.4; H, 6.4. Found: C, 62.0; H, 6.0.

Methyl 3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**11**).—A solution of ethyl 3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside [10] (**10**; 558 mg, 1.05 mmol) in toluene (10 mL) and MeOH (800 μL, 20 mmol) containing powdered 4A molecular sieves (2 g) was stirred for 30 min under N_2. Methyl triflate (553 μL, 5.04 mmol) was added at room temperature and the mixture was stirred for 16 h, when TLC (7:3 hexane–EtOAc) showed the conversion of **10** (R_f 0.28) into **11** (R_f 0.21) to be

complete. Triethylamine (5 mL) was added, and the mixture was diluted with CH_2Cl_2 (300 mL), filtered through Celite, washed with water, dried ($MgSO_4$), filtered, and concentrated. Column chromatography (7:3 hexane–EtOAc) of the residue gave **11**, isolated as a syrup (336 mg, 66%); $[\alpha]_D$ +40° (*c* 1); lit [18] $[\alpha]_D$ +39.4° (*c* 1.9); R_f 0.21. NMR data ($CDCl_3$): ^1H, δ 7.71–6.91 (m, 14 H, 2 Ph and Phth), 5.072 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1), 4.752 and 4.526 (2 d, each 1 H, PhC*H*$_2$O), 4.655 and 4.589 (2 d, each 1 H, PhC*H*$_2$O), 3.374 (s, 3 H, CH_3O), 3.018 (bs, 1 H, HO-4); ^{13}C, δ 167.9 and 167.5 (*C*O Phth), 137.9, 137.5, 133.5, 131.4, 128.2–127.1, and 123.0 (C_6H_5 CH_2O and Phth), 98.9 (C-1), 78.5 and 73.8 (2 C) (C-3,4,5), 74.0, 73.4, and 70.2 (C-6 and 2 PhCH_2O), 56.3 and 55.0 (C-2 and CH_3O). Anal. Calcd for $C_{29}H_{29}NO_7 \cdot 0.5H_2O$: C, 67.96; H, 5.90. Found: C, 68.00; H, 5.63.

*Methyl 4-O-{4-O-[3-O-allyl-4-O-benzoyl-6-O-*tert*-butyldimethylsilyl-2-O-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl}-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside* (**12**).—A solution of **9** (510 mg, 0.42 mmol) and **11** (335 mg, 0.67 mmol) in 1:1 1,2-dichloroethane–toluene (10 mL) containing powdered 4A molecular sieves (2.5 g) was stirred for 30 min under N_2. Then a solution of *N*-iodosuccinimide (115 mg, 0.51 mmol) and trifluoromethanesulfonic acid (6 mL, 68 mmol) in 1:1 1,2-dichloroethane–ether (5 mL) was added at room temperature. After 15 min, TLC (1:1 hexane–EtOAc) showed the disappearance of **9** (R_f 0.49), and a new compound **12** (R_f 0.36). The mixture was diluted with CH_2Cl_2 (500 mL), filtered through Celite, washed with aq 5% $Na_2S_2O_3$ (2×50 mL), aq 5% $NaHCO_3$ (2×50 mL), and water, dried ($MgSO_4$), filtered, and concentrated. Column chromatography (3:2 hexane–EtOAc) of the residue gave **12**, isolated as a white foam (364 mg, 52%); $[\alpha]_D$ −25° (*c* 1); R_f 0.16. NMR data ($CDCl_3$): ^1H, δ 8.02–6.73 (m, 33 H, 5 Ph and 2 Phth), 5.688 (m, 1 H, H_2C=C*H*CH_2O), 5.332 (t, 1 H, $J_{4'',3''} = J_{4'',5''} = 9.8$ Hz, H-4''), 5.290 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 5.175 (d, 1 H, $J_{1''',2'''}$ 1.8 Hz, H-1'''), 5.128 and 5.028 (2 m, 2 H, H_2C=CHCH_2O), 5.007 (d, 1 H, PhCH*H*O), 4.866 (d, 1 H, $J_{1',2'}$ 7.9 Hz, H-1'), 4.864 (d, 1 H, PhCH*H*O), 4.757 (m, 1 H, H-4'''), 4.666 (s, 1 H, H-1''), 3.820 (m, 1 H, H_2C=CHC*H*O), 3.274 (s, 3 H, CH_3O), 2.132, 2.124, and 2.084 (3 s, each 3 H, 3 Ac), 0.668 [s, 9 H, $(CH_3)_3CSi$], −0.183 and −0.248 [2 s, each 3 H, $(CH_3)_2Si$]; ^{13}C, δ 169.5, 169.4, and 168.4 (3 *C*OCH_3), 168.0 and 167.3 (*C*O Phth), 164.9 (*C*OPh), 138.9, 138.3, 138.1, 137.8, 134.1, 133.3, 132.6, 131.4, 131.1, 129.9, 129.3, 128.2–126.3, and 122.8 ($C_6H_5CH_2O$, C_6H_5CO, H_2C=*C*HCH_2O, and Phth), 116.6 (H_2C=CHCH_2O), 100.9, 98.8, 96.5, and 96.7 (C-1,1',1'',1'''), 79.8, 78.3, 77.4, 75.3, 75.1, 74.2 (3 C), 72.8, 69.3, 67.2, 67.0, and 66.2 (C-3,4,5,3',4',5',2'',3'',4'',5'',2''',3''',4'''), 74.7, 74.0, 73.0, 72.4, 70.4, 68.0, 67.8, 63.5, and 58.3 (C-6,6',6'',5''', 4 PhCH_2O, and H_2C=CHCH_2O), 56.3, 56.1, and 55.3 (C-2,2' and CH_3O), 25.4 [(CH_3)$_3$CSi], 20.7, 20.6, and 20.5 (3 COCH_3), 17.8 [$(CH_3)_3$*C*Si], −6.0 [$(CH_3)_2$Si]. Anal. Calcd for $C_{90}H_{100}N_2O_{26}Si$: C, 65.36; H, 6.09. Found: C, 65.07; H, 6.29.

Methyl 4-O-{4-O-[3-O-allyl-4-O-benzoyl-2-O-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl}-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**13**).—A solution of **12** (266 mg, 0.16 mmol) and *p*-toluenesulfonic acid monohydrate (150 mg, 0.79 mmol) in 9:1 MeCN–water (15 mL) was stirred for 30 min at room temperature. TLC (9:1 CH_2Cl_2–acetone) then showed a complete desilylation, and the solution was diluted with CH_2Cl_2 (250 mL), washed with aq 5% $NaHCO_3$ (25 mL) and water, dried ($MgSO_4$), filtered, and

concentrated. Column chromatography (9:1 CH_2Cl_2–acetone) of the residue gave **13**, isolated as a white foam (241 mg, 97%); $[\alpha]_D$ −29° (*c* 1); R_f 0.30. NMR data ($CDCl_3$): ^1H, δ 7.98–6.74 (m, 33 H, 5 Ph and 2 Phth), 5.726 (m, 1 H, H_2C=C*H*CH_2O), 5.330 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 5.253 (t, 1 H, $J_{4'',3''} = J_{4'',5''} = 9.6$ Hz, H-4″), 5.154 and 5.059 (2 m, 2 H, H_2C=CHCH_2O), 5.125 (d, 1 H, $J_{1''',2'''}$ 1.5 Hz, H-1‴), 5.038 (d, 1 H, PhCH*H*O), 4.889 (d, 1 H, PhCH*H*O), 4.881 (d, 1 H, $J_{1',2'}$ 7.8 Hz, H-1′), 4.764 (m, 1 H, H-4‴), 4.633 (s, 1 H, H-1″), 3.846 (m, 1 H, H_2C=CHCH*H*O), 3.282 (s, 3 H, CH_3O), 2.154, 2.133, and 2.112 (3 s, each 3 H, 3 Ac); ^{13}C, δ 169.7, 169.6, and 168.6 (3 *C*OCH_3), 168.3 and 167.5 (*C*O Phth), 165.4 (*C*OPh), 138.7, 138.5, 138.3, 137.8, 134.1, 133.7, 133.4, 133.1, 131.6, 131.2, 129.5, 128.5–126.5, 123.4, and 123.0 ($C_6H_5CH_2O$, C_6H_5CO, H_2C=*C*HCH_2O, and Phth), 116.9 (H_2C=CHCH_2O), 100.7, 98.9, 97.7, and 96.8 (C-1,1′,1″,1‴), 80.1, 78.2, 77.0, 76.6, 75.6, 74.5, 74.3, 74.2, 73.3, 68.1, 67.1 (2 C), and 66.3 (C-3,4,5,3′,4′,5′,2″,3″,4″,5″,2‴,3‴,4‴), 74.6, 74.3, 73.2, 72.5 (2 C), 70.5, 68.0, 61.7, and 58.5 (C-6,6′,6″,5‴, 4 Ph*C*H_2O, and H_2C=CH*C*H_2O), 56.4, 56.3, and 55.4 (C-2,2′ and CH_3O), 20.8 (2 C) and 20.6 (3 CO*C*H_3). Anal. Calcd for $C_{84}H_{86}N_2O_{26} \cdot 0.5H_2O$: C, 65.15; H, 5.66. Found: C, 65.05; H, 5.66.

*Methyl 4-*O*-{4-*O*-[3-*O*-allyl-4-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-acetyl-α-*D*-mannopyranosyl)-2-*O*-(2,3,4-tri-*O*-acetyl-β-*D*-xylopyranosyl)-β-*D*-mannopyranosyl]-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl}-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**14**).—A solution of **13** (99 mg, 64 mmol) and 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl trichloroacetimidate [9] (**7**; 110 mg, 0.22 mmol) in CH_2Cl_2 (3 mL) containing powdered 4A molecular sieves (250 mg) was stirred under N_2 for 30 min. Trimethylsilyl triflate (10 mL, 55 μmol) was added at −20°C and the mixture was stirred for 30 min at 0°C. TLC (95:5 CH_2Cl_2–acetone) then showed the disappearance of **13** (R_f 0.37) and a new product **14** (R_f 0.31). Pyridine (1 mL) was added, and the mixture was diluted with CH_2Cl_2 (100 mL), filtered through Celite, washed with water, dried ($MgSO_4$), filtered, and concentrated. Column chromatography (37:3 CH_2Cl_2–acetone) of the residue gave **14**, isolated as a white foam (86 mg, 71%); $[\alpha]_D$ −11° (*c* 1); R_f 0.31. NMR data ($CDCl_3$): ^1H, δ 8.01–6.76 (m, 33 H, 5 Ph and 2 Phth), 5.702 (m, 1 H, H_2C=C*H*CH_2O), 5.324 (t, 1 H, $J_{4'',3''} = J_{4'',5''} = 9.8$ Hz, H-4″), 5.304 (d, 1 H, $J_{1,2}$ 8.5 Hz, H-1), 5.058 (m, 1 H, H*H*C=CHCH_2O), 4.869 (d, 1 H, $J_{1'''',2''''}$ 1.6 Hz, H-1⁗), 4.766 (m, 1 H, $J_{4'''',5''''eq/ax}$ 2.6, $J_{4'''',5''''eq/ax}$ 5.9 Hz, H-4‴), 4.672 (s, 1 H, H-1″), 3.276 (s, 3 H, CH_3O), 2.120, 2.117, 2.063, 1.989, 1.957, 1.947, and 1.857 (7 s, each 3 H, 7 Ac); ^{13}C, δ 170.4–167.3 (*C*OCH_3 and *C*O Phth), 165.3 (*C*OPh), 138.7, 138.5, 138.3, 138.0, 134.1, 133.4, 133.0, 131.6, 131.4, 129.5, 129.4, 128.5–126.7, 123.3, and 123.0 ($C_6H_5CH_2O$, C_6H_5CO, H_2C=*C*HCH_2O, and Phth), 116.9 (H_2C=CHCH_2O), 101.0, 98.9, 97.8, and 97.1 (2 C) (C-1,1′,1″,1‴,1⁗), 80.3, 78.0, 77.0, 76.8, 75.7, 74.4, 74.3, 72.9, 72.5, 69.6, 69.2, 68.6, 68.4, 67.5, 67.2, 66.5, and 65.8 (C-3,4,5,3′,4′,5′,2″,3″,4″,5″,2‴,3‴,4‴,2⁗,3⁗,4⁗,5⁗), 74.8, 74.3, 73.2 (2 C), 72.5, 70.8, 68.0 (2 C), 62.2, and 58.6 (C-6,6′,6″,5‴,6⁗, 4 Ph*C*H_2O, and H_2C=CH*C*H_2O), 56.3 (2 C) and 55.4 (C-2,2′ and CH_3O), 20.9, 20.7, 20.6, 20.5 (2 C), and 20.4 (2 C) (7 CO*C*H_3).

*Methyl 4-*O*-{4-*O*-[4-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-acetyl-α-*D*-mannopyranosyl)-2-*O*-(2,3,4-tri-*O*-acetyl-β-*D*-xylopyranosyl)-β-*D*-mannopyranosyl]-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl}-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**15**).—A solution of **14** (83 mg, 44 mmol), tris(triphenylphosphine)-

rhodium(I) chloride (23 mg, 25 μmol), and 1,4-diazabicyclo[2.2.2]octane (9 mg, 80 μmol) in 7:3:1 EtOH–toluene–water (6 mL) was boiled under reflux for 2.5 h, then cooled, and concentrated. A solution of the residue in 9:1 acetone–M aq HCl (9 mL) was boiled under reflux for 30 min, when TLC (7:1 CH_2Cl_2–acetone) indicated a complete conversion of **14** into **15** (R_f 0.65). Then the solution was concentrated, and a solution of the residue in CH_2Cl_2 (100 mL) was washed with aq 5% $NaHCO_3$ (10 mL) and water, dried ($MgSO_4$), filtered, and concentrated. Column chromatography (7:1 CH_2Cl_2–acetone) of the residue gave **15**, isolated as a syrup (71 mg, 85%); $[\alpha]_D$ +5° (*c* 1); R_f 0.32. NMR data ($CDCl_3$): ^1H, δ 8.02–6.72 (m, 33 H, 5 Ph and 2 Phth), 4.631 (s, 1 H, H-1″), 3.269 (s, 3 H, CH_3O), 2.106, 2.102, 2.028, 2.000, 1.936, 1.910, and 1.893 (7 s, each 3 H, 7 Ac); ^{13}C, δ 170.4, 169.7, 169.6 (2 C), 169.4, 169.3, 168.8 (7 $COCH_3$), 168.1–167.3 (*C*O Phth), 165.7 (*C*OPh), 138.5 (2 C), 138.2, 137.7, 133.4, 131.6, 131.2, 129.6, 129.3, 128.5–126.7, and 123.0 ($C_6H_5CH_2O$, C_6H_5CO, and Phth), 101.3, 99.3, 98.8, and 97.0 (2 C) (C-1,1′,1″,1‴,1⁗), 56.3 (2 C) and 55.4 (C-2,2′ and CH_3O), 20.7–20.4 ($COCH_3$). Anal. Calcd for $C_{95}H_{100}N_2O_{35}\cdot H_2O$: C, 61.75; H, 5.56. Found: C, 61.54; H, 5.64.

Methyl 4-O-{4-O-[4-O-benzoyl-3,6-di-O-(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)-2-O-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl}-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**16**).—A solution of **15** (39 mg, 21 μmol) and 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl trichloroacetimidate [9] (**7**; 105 mg, 0.21 mmol) in CH_2Cl_2 (2 mL) containing powdered 4A molecular sieves (100 mg) was stirred under N_2 for 30 min. Trimethylsilyl triflate (3 μL, 17 μmol) was added and the mixture was stirred for 2 h at room temperature. TLC (95:5 CH_2Cl_2–acetone) then showed the disappearance of **15** (R_f 0.73), and a new product **16** (R_f 0.64). Pyridine (1 mL) was added, and the mixture was diluted with CH_2Cl_2 (100 mL), filtered through Celite, washed with water, dried ($MgSO_4$), filtered, and concentrated. Column chromatography (3:7 hexane–EtOAc) of the residue gave **16**, isolated as a syrup (27 mg, 59%); $[\alpha]_D$ −2° (*c* 1); R_f 0.33. NMR data ($CDCl_3$): ^1H, δ 7.97–6.74 (m, 33 H, 5 Ph and 2 Phth), 5.409 (t, 1 H, $J_{4'',3''}=J_{4'',5''}=9.8$ Hz, H-4″), 5.163 (d, 1 H, $J_{1'''',2''''}$ 1.4 Hz, H-1⁗′), 4.983 (d, 1 H, $J_{1'''',2''''}$ 1.8 Hz, H-1⁗), 3.271 (s, 3 H, CH_3O), 2.119, 2.106, 2.081, 2.056, 1.999, 1.995, 1.951, 1.881, 1.857, and 1.824 (10 s, 3,3,3,3,3,3,6,3,3,3 H, 11 Ac); ^{13}C, δ 170.5–167.3 ($COCH_3$ and *C*O Phth), 165.0 (*C*OPh), 138.6, 138.5, 138.3, 138.0, 133.4, 133.2, 131.6, 131.4, 129.6, 128.6–126.7, and 123.0 ($C_6H_5CH_2O$, C_6H_5CO, and Phth), 101.0, 99.3, 98.9, 98.2, and 97.0 (2 C) (C-1,1′,1″,1‴,1⁗,1⁗′), 56.3, 56.2, and 55.4 (C-2,2′ and CH_3O), 20.8–20.2 ($COCH_3$). Anal. Calcd for $C_{109}H_{118}N_2O_{44}$: C, 60.61; H, 5.51. Found: C, 60.37; H, 5.52.

Methyl 2-acetamido-4-O-[2-acetamido-2-deoxy-4-O-(3,6-di-O-α-D-mannopyranosyl-2-O-β-D-xylopyranosyl-β-D-mannopyranosyl)-β-D-glucopyranosyl]-2-deoxy-β-D-glucopyranoside (**4**).—A solution of **16** (26 mg, 12 μmol) in $MeNH_2$–EtOH (33%, 10 mL) was stirred for 32 h, then concentrated, and treated with Ac_2O (100 mL, 1 μmol) in MeOH (3 mL) for 2 h. The solution was concentrated, and toluene, EtOH, and CH_2Cl_2 (each 3 × 5 mL) were evaporated from the residue. Column chromatography on Sephadex LH-20 (1:1 MeOH–CH_2Cl_2) of the residue gave a white solid. To a solution of this product in MeOH (4 mL), containing AcOH (50 μL), was added 10% Pd–C (26 mg), and hydrogenolysis was performed at atmospheric pressure for 32 h. Then the mixture was filtered through Celite and concentrated, and toluene, EtOH, and CH_2Cl_2 (each 3 × 10 mL) were evaporated

from the residue. Because ^{1}H NMR analysis showed that the dephthaloylation was incomplete, a solution of the residue and hydrazine acetate (60 mg, 0.65 mmol) in EtOH (5 mL) was boiled under reflux for 16 h, then concentrated and treated with Ac_2O (300 μL, 3.1 mmol) in MeOH (3 mL) for 16 h. The solution was concentrated, and toluene, EtOH, and CH_2Cl_2 (each 3 × 10 mL) were evaporated from the residue, which was fractionated on Sephadex LH-20 (1:1 MeOH–CH_2Cl_2) to yield impure **4**. This product was then subjected to purification by RP-HPLC on a Cp tm Spher C18 column (250 × 4.6 mm, Chrompack) by elution with 95:5 water–MeOH for 5 min, followed by a linear gradient of 95:5 → 1:1 water–MeOH for 35 min, and detection at 205 nm. The fraction eluting at 5.9 min was collected and concentrated to yield **4**, isolated as a white amorphous solid (9.8 mg, 77%); $[\alpha]_D$ −8° (*c* 0.1, H_2O). For ^{1}H NMR data, see Table 1.

*Ethyl 3,6-di-*O*-benzyl-2-deoxy-4-*O*-[4,6-di-*O*-acetyl-3-*O*-allyl-2-*O*-(2,3,4-tri-*O*-acetyl-β-*D*-xylopyranosyl)-β-*D*-mannopyranosyl]-2-phthalimido-1-thio-β-*D*-glucopyranoside* (**17**).—A solution of ethyl 4-*O*-[3-*O*-allyl-2-*O*-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside [10] (**8**; 1.34 g, 1.35 mmol) in 1:1 pyridine–Ac_2O (20 mL) was kept for 16 h at room temperature, then concentrated, and toluene, EtOH, and CH_2Cl_2 (each 3 × 20 mL) were evaporated from the residue, to give **17**, isolated as a white foam (1.45 g, 99%); $[\alpha]_D$ −35° (*c* 1); R_f 0.28 (1:1 hexane–EtOAc). NMR data ($CDCl_3$): ^{1}H, δ 7.75–6.75 (m, 14 H, 2 Ph and Phth), 5.811 (m, 1 H, H_2C=C*H*CH_2O), 5.262 (d, 1 H, $J_{1,2}$ 10.4 Hz, H-1), 5.228 and 5.151 (2 m, 2 H, H_2C=CHCH_2O), 5.146 (d, 1 H, $J_{1'',2''}$ 2.4 Hz, H-1″), 5.094 (t, 1 H, $J_{4',5'}$ 9.9 Hz, H-4′), 4.983 and 4.940 (2 bt, 2 H, H-2″,3″), 4.927 and 4.369 (2 d, each 1 H, PhCH_2O), 4.760 (m, 1 H, $J_{4'',5''ax/eq}$ 2.6 and 2.9 Hz, H-4″), 4.747 and 4.534 (2 d, each 1 H, PhCH_2O), 4.613 (s, 1 H, H-1′), 4.551 and 3.524 (2 dd, each 1 H, $J_{5''ax,5''eq}$ −13.0 Hz, H-5″*ax*,5″*eq*), 4.045 (d, 1 H, $J_{2',3'}$ 3.0 Hz, H-2′), 3.175 (dd, 1 H, $J_{3',4'}$ 9.9 Hz, H-3′), 2.637 (m, 2 H, CH_3CH_2S), 2.127, 2.122, 2.076, 2.036, and 1.934 (5 s, each 3 H, 5 Ac), 1.175 (t, 3 H, C$H_3$$CH_2$S); ^{13}C, δ 170.5, 169.7, 169.4 (2 C), 168.6 (5 *C*OCH$_3$), 138.7, 137.8, 134.0, 133.5, 128.3–126.6, and 123.0 ($C_6H_5CH_2O$, H_2C=*C*HCH_2O, and Phth), 116.5 (H_2C=CHCH_2O), 101.5 and 97.7 (C-1′,1″), 81.0, 80.6, 78.6, 78.4, 78.0, 72.5, 72.1, 67.4, 67.3, 67.2, and 66.5 (C-1,3,4,5,2′,3′,4′,5′,2″,3″,4″), 74.7, 73.4, 70.2, 68.9, 62.7, and 58.6 (C-6,6′,5″, 2 Ph*C*H_2O, and H_2C=CH*C*H_2O), 54.6 (C-2), 23.6 (CH_3*C*H_2S), 20.8, 20.7, 20.6, and 20.5 (2 C) (5 CO*C*H$_3$), 14.7 (*C*$H_3$$CH_2$S). Anal. Calcd for $C_{54}H_{63}NO_{20}S$: C, 60.16; H, 5.89. Found: C, 59.97; H, 6.07.

*Methyl 3-*O*-benzyl-2-deoxy-4-*O*-{3,6-di-*O*-benzyl-2-deoxy-4-*O*-[4,6-di-*O*-acetyl-3-*O*-allyl-2-*O*-(2,3,4-tri-*O*-acetyl-β-*D*-xylopyranosyl)-β-*D*-mannopyranosyl]-2-phthalimido-β-*D*-glucopyranosyl}-6-*O*-(4-methoxybenzyl)-2-phthalimido-β-*D*-glucopyranoside* (**19**) *and 1,5-anhydro-3,6-di-*O*-benzyl-2-deoxy-4-*O*-[4,6-di-*O*-acetyl-3-*O*-allyl-2-*O*-(2,3,4-tri-*O*-acetyl-β-*D*-xylopyranosyl)-β-*D*-mannopyranosyl]-2-phthalimido-*D*-arabino-hex-1-enitol* (**20**).—A solution of **17** (637 mg, 0.59 mmol) and methyl 3-*O*-benzyl-2-deoxy-6-*O*-(4-methoxybenzyl)-2-phthalimido-β-D-glucopyranoside [18] (**18**; 470 mg, 0.88 mmol) in 2:1 1,2-dichloroethane–toluene (15 mL), containing powdered 4A molecular sieves (2 g), was stirred for 30 min under N_2. A solution of *N*-iodosuccinimide (150 mg, 0.67 mmol) and trifluoromethanesulfonic acid (8 μL, 79 μmol) in 1:1 1,2-dichloroethane–ether (4 mL) was added at room temperature. After 5 min, TLC (1:1 hexane-EtOAc) showed the disappearance of **17** (R_f 0.28), and two new products **20** (R_f 0.20) and **19** (R_f

0.16). The mixture was diluted with CH_2Cl_2 (500 mL), filtered through Celite, washed with aq 5% $Na_2S_2O_3$ (2×50 mL), aq 5% $NaHCO_3$, and water, dried ($MgSO_4$), filtered, and concentrated. Column chromatography (1:1 hexane-EtOAc) of the residue first gave **20** (120 mg, 20%) and then **19** (561 mg, 61%); $[\alpha]_D$ −29° (*c* 0.5), both isolated as a white foam. NMR data ($CDCl_3$) for **19**: ^1H, δ 7.83–6.73 (m, 27 H, 3 Ph, $MeOC_6H_4CH_2O$, and 2 Phth), 5.808 (m, 1 H, $H_2C{=}CHCH_2O$), 5.296 (d, 1 H, $J_{1,2}$ 8.5 Hz, H-1), 5.226 and 5.152 (2 m, 2 H, $H_2C{=}CHCH_2O$), 5.158 (d, 1 H, $J_{1''',2'''}$ 2.3 Hz, H-1'''), 5.098 (t, 1 H, $J_{4'',5''}$ 9.9 Hz, H-4''), 4.989 and 4.947 (2 bt, each 1 H, H-2''',3'''), 4.968 and 4.545 (2 d, each 1 H, $PhCH_2O$), 4.854 (d, 1 H, $J_{1',2'}$ 8.5 Hz, H-1'), 4.851 and 4.466 (2 d, each 1 H, $PhCH_2O$), 4.757 (m, 1 H, H-4'''), 4.605 (s, 1 H, H-1''), 3.803 (s, 3 H, $CH_3OC_6H_4CH_2O$), 3.266 (s, 3 H, CH_3O), 3.173 (dd, 1 H, $J_{3'',2''}$ 3.0, $J_{3'',4''}$ 9.9 Hz, H-3''), 2.123, 2.078, 2.071, 2.014, and 1.887 (5 s, each 3 H, 5 Ac); ^{13}C, δ 170.4, 169.9, 169.3 (2 C), and 168.5 (5 $COCH_3$), 168.0 and 167.5 (*C*O Phth), 158.8, 138.8, 137.6, 134.0, 133.3, 131.4, 131.1, 130.2, 128.8–126.4, 122.8, and 113.3 ($C_6H_5CH_2O$, $MeOC_6H_4CH_2O$, $H_2C{=}CHCH_2O$, and Phth), 116.4 ($H_2C{=}CHCH_2O$), 101.2, 98.7, 97.6, and 96.7 (C-1,1',1'',1'''), 80.5, 77.9, 77.3, 76.5, 75.4, 74.2 (2 C), 72.4, 71.9, 67.3 (2 C), 67.1, and 66.5 (C-3,4,5,3',4',5',2'',3'',4'',5'',2''',3''',4'''), 74.6, 74.1, 73.0, 72.1, 70.0, 68.0, 67.5, 62.6, and 58.4 (C-6,6',6'',5''', 3 $PhCH_2O$, $MeOC_6H_4CH_2O$, and $H_2C{=}CHCH_2O$), 56.3, 56.1, 55.3, and 54.9 (C-2,2', $CH_3OC_6H_4CH_2O$, and CH_3O), 20.7, 20.6, 20.5, 20.4, 20.3 (5 $COCH_3$). Anal. Calcd for $C_{82}H_{88}N_2O_{28}$: C, 63.56; H, 5.72. Found: C, 63.19; H, 5.83. NMR data ($CDCl_3$) for **20**: ^1H, δ 7.79–6.92 (m, 14 H, 2 Ph and Phth), 6.592 (s, 1 H, H-1), 5.842 (m, 1 H, $H_2C{=}CHCH_2O$), 5.265 and 5.176 (2 m, 2 H, $H_2C{=}CHCH_2O$), 5.261 (d, 1 H, $J_{1'',2''}$ 3.5 Hz, H-1''), 5.222 (t, 1 H, $J_{3'',2''} = J_{3'',4''} = 5.0$ Hz, H-3''), 5.182 (t, 1 H, $J_{4',3'} = J_{4',5'} = 9.7$ Hz, H-4'), 5.047 (dd, 1 H, H-2''), 4.818 (m, 1 H, H-4''), 4.721 (s, 1 H, H-1'), 4.682 and 4.407 (2 d, each 1 H, $PhCH_2O$), 4.588 (s, 2 H, $PhCH_2O$), 3.377 (dd, 1 H, $J_{3',2'}$ 2.9 Hz, H-3'), 2.143, 2.101, 2.071, 2.063, and 1.949 (5 s, each 3 H, 5 Ac); ^{13}C, δ 170.5, 169.6 (2 C), 169.3, and 168.8 (5 $COCH_3$), 167.3 (*C*O Phth), 145.1 (C-1), 138.0, 137.6, 131.6, 128.2–126.9, 123.1 ($C_6H_5CH_2O$, $H_2C{=}CHCH_2O$ and Phth), 116.8 ($H_2C{=}CHCH_2O$), 107.8 (C-2), 98.0 (C-1',1''), 77.4 (2 C), 74.4, 72.5, 72.3, 71.7, 68.0, 67.8 (2 C), and 67.2 (C-3,4,5,2',3',4',5',2'',3'',4''), 73.4, 72.0, 69.9, 67.5, 62.6, and 59.0 (C-6,6',5'', 2 $PhCH_2O$, and $H_2C{=}CHCH_2O$), 20.7 (2 C), 20.6 (2 C), and 20.4 (5 $COCH_3$).

Methyl 3-O-benzyl-2-deoxy-4-O-{3,6-di-O-benzyl-2-deoxy-4-O-[4,6-di-O-acetyl-3-O-allyl-2-O-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-2-phthalimido-β-D-glucopyranosyl}-2-phthalimido-β-D-glucopyranoside (**21**).—To a solution of **19** (490 mg, 0.32 mmol) in 9:1 MeCN–water (10 mL) was added ceric(IV) ammonium nitrate (380 mg, 0.69 mmol). When TLC (85:15 CH_2Cl_2–acetone) indicated the reaction to be complete (1 h; **21**, R_f 0.35), the mixture was diluted with CH_2Cl_2 (500 mL), washed with aq 5% $NaHSO_3$ (2×50 mL), aq 5% $NaHCO_3$, and water, dried ($MgSO_4$), filtered, and concentrated. Column chromatography of the residue (85:15 CH_2Cl_2–acetone) gave **21**, isolated as a white foam (390 mg, 86%); $[\alpha]_D$ −43° (*c* 0.7); R_f 0.35. NMR data ($CDCl_3$): ^1H, δ 7.84–6.74 (m, 23 H, 3 Ph and 2 Phth), 5.801 (m, 1 H, $H_2C{=}CHCH_2O$), 5.359 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 5.222 and 5.147 (2 m, 2 H, $H_2C{=}CHCH_2O$), 5.121 (d, 1 H, $J_{1''',2'''}$ 2.9 Hz, H-1'''), 5.088 (t, 1 H, $J_{4'',5''}$ 9.9 Hz, H-4''), 4.909 (d, 1 H, $J_{1',2'}$ 8.4 Hz, H-1'), 4.755 (m, 1 H, H-4'''), 4.593 (s, 1 H, H-1''), 4.533 (dd, 1 H, $J_{5'''ax,5'''eq}$ −13.1, $J_{5'''ax/eq,4'''}$ 2.6 Hz, H-5'''*ax* or H-5'''*eq*), 3.271 (s, 3 H, CH_3O), 3.157 (dd, 1 H, $J_{3'',2''}$ 3.0, $J_{3'',4''}$ 9.9 Hz, H-3''),

2.132, 2.126, 2.067, 2.015, and 1.898 (5 s, each 3 H, 5 Ac); ^{13}C, δ 170.4, 169.6, 169.2 (2 C), 168.5 (5 $COCH_3$), 168.0 and 167.4 (CO Phth), 138.5, 138.2, 137.5, 133.9, 133.4, 131.3, 128.2–126.5, 123.0, and 122.8 ($C_6H_5CH_2O$, $H_2C{=}CHCH_2O$, and Phth), 116.4 ($H_2C{=}CHCH_2O$), 101.2, 98.8, 97.6, and 97.2 (C-1,1′,1″,1‴), 80.5, 77.8, 77.0, 76.6, 75.6, 74.4, 74.0, 72.3, 71.9, 67.2 (2 C), 67.0, and 66.4 (C-3,4,5,3′,4′,5′,2″,3″,4″,5″,2‴,3‴,4‴), 74.2, 73.0 (2 C), 70.0, 68.2, 62.5, 60.5, and 58.4 (C-6,6′,6″,5‴, 3 $PhCH_2O$, and $H_2C{=}CHCH_2O$), 56.3, 56.1, and 55.3 (C-2,2′ and CH_3O), 20.6 (2 C), 20.4, and 20.3 (2 C) (5 $COCH_3$). Anal. Calcd for $C_{74}H_{80}N_2O_{27}\cdot H_2O$: C, 61.41; H, 5.71. Found: C, 61.40; H, 5.90.

Methyl 3-O-benzyl-2-deoxy-4-O-{3,6-di-O-benzyl-2-deoxy-4-O-[4,6-di-O-acetyl-3-O-allyl-2-O-(2,3,4-tri-O-acetyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-2-phthalimido-β-D-glucopyranosyl}-2-phthalimido-6-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside (**23**).—A mixture of **21** (320 mg, 0.22 mmol) and ethyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside [19] (**22**; 160 mg, 0.34 mmol) in 5:1 ether–1,2-dichloroethane (6 mL) containing powdered 4A molecular sieves (1 g) was stirred for 30 min under N_2. Then, iodonium dicollidine perchlorate [14] (310 mg, 0.66 mmol) was added and the mixture was stirred for 20 min at room temperature, when TLC (1:1 hexane–EtOAc) showed a complete conversion of **21** (R_f 0.05) into two new compounds **23-a** (R_f 0.11) and **23** (R_f 0.25) as the minor and major product. The mixture was diluted with CH_2Cl_2 (250 mL), filtered through Celite, washed with aq 10% $Na_2S_2O_3$ (2×25 mL) and water, dried ($MgSO_4$), filtered, and concentrated. Column chromatography (1:1 hexane–EtOAc) of the residue first gave **23** (203 mg, 49%); $[\alpha]_D$ −40° (*c* 1), and then **23-a** (127 mg); $[\alpha]_D$ −41° (*c* 1), both isolated as a white foam. NMR data ($CDCl_3$) for **23**: ^1H, δ 7.82–6.73 (m, 38 H, 6 Ph and 2 Phth), 5.811 (m, 1 H, $H_2C{=}CHCH_2O$), 5.473 (d, 1 H, $J_{1,2}$ 8.5 Hz, H-1), 5.226 and 5.151 (2 m, 2 H, $H_2C{=}CHCH_2O$), 5.078 (t, 1 H, $J_{4‴,5‴}$ 9.8 Hz, H-4‴), 5.064 (d, 1 H, $J_{1‴,2‴}$ 2.7 Hz, H-1⁗), 4.846 (d, 1 H, $J_{1″,2″}$ 8.4 Hz, H-1″), 4.800 (d, 1 H, $J_{1′,2′}$ 3.7 Hz, H-1′), 4.773 and 4.701 (2 d, each 1 H, $PhCH_2O$), 4.711 (m, 1 H, H-4⁗), 4.582 (s, 1 H, H-1‴), 4.420 (dd, 1 H, $J_{5⁗eq/ax,4⁗}$ 3.3, $J_{5⁗ax,5⁗eq}$ −12.9 Hz, H-5⁗*ax* or H-5⁗*eq*), 3.186 (s, 3 H, CH_3O), 3.132 (dd, 1 H, $J_{3‴,2‴}$ 2.9, $J_{3‴,4‴}$ 9.9 Hz, H-3‴), 2.086, 2.035, 2.010, 1.907, and 1.725 (5 s, each 3 H, 5 Ac), 1.020 (d, 3 H, $J_{6′,5′}$ 6.5 Hz, H-6′,6′,6′); ^{13}C, δ 170.5, 169.6, 169.3 (2 C), and 168.8 (5 $COCH_3$), 167.6 (CO Phth), 138.7–138.4, 137.6, 134.0, 133.5, 133.3, 131.4, 131.1, 128.3–127.1, 126.6, 126.5, and 122.9 ($C_6H_5CH_2O$, $H_2C{=}CHCH_2O$, and Phth), 116.5 ($H_2C{=}CHCH_2O$), 101.1, 98.4, 97.5, and 96.6 (C-1,1″,1‴,1⁗), 96.6 (C-1′, $J_{C\text{-}1′,H\text{-}1′}$ 168.6 Hz), 80.2, 79.2, 78.0, 77.3, 76.9, 76.4, 75.3, 74.9, 73.8, 73.6, 72.0, 71.8, 67.7, 67.3 (2 C), 66.9, and 65.7 (C-3,4,5,2′,3′,4′,5′,3″,4″,5″,2‴,3‴,4‴,5‴,2⁗, 3⁗,4⁗), 74.5, 74.4 (2 C), 73.0, 72.8, 72.3, 70.0, 68.0, 63.8, 62.6, 58.7 (C-6,6″,6‴,5⁗, 6 $PhCH_2O$, and $H_2C{=}CHCH_2O$), 56.4, 55.8, and 55.5 (C-2,2″ and CH_3O), 20.7, 20.6, 20.4 (2 C), and 20.1 (5 $COCH_3$), 16.2 (C-6′).

Methyl 4-O-{4-O-[3-O-allyl-4-O-benzoyl-2-O-(2,3,4-tri-O-benzoyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl}-3-O-benzyl-2-deoxy-2-phthalimido-6-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside (**24**).—To a solution of **23** (191 mg, 0.1 mmol) in MeOH (10 mL) was added sodium methoxide until pH 9. The solution was stirred for 1 h, when TLC (9:1 CH_2Cl_2–MeOH) showed the *O*-deacetylation to be complete (R_f 0.59), then neutralized with Dowex 50W (H^+) resin, filtered, and concentrated. To a solution of the residue in

pyridine (2 mL) was added *tert*-butyldimethylsilyl chloride (47 mg, 0.31 mmol), and the solution was stirred for 16 h, when TLC (95:5 CH_2Cl_2–MeOH) showed the silylation to be complete (R_f 0.53). Then benzoyl chloride (100 μL, 0.86 mmol) was added, and the mixture was stirred again for 16 h, diluted with CH_2Cl_2 (250 mL), washed with aq 5% $NaHCO_3$ (25 mL) and water, dried ($MgSO_4$), filtered, and concentrated. A solution of the residue and *p*-toluenesulfonic acid monohydrate (99 mg, 0.52 mmol) in 9:1 MeCN–water (7 mL) was stirred for 30 min at room temperature. TLC (3:1 toluene–acetone) then showed a complete desilylation (R_f 0.62). The solution was diluted with CH_2Cl_2 (250 mL), washed with aq 5% $NaHCO_3$ (25 mL) and water, dried ($MgSO_4$), filtered, and concentrated. Column chromatography (95:5 CH_2Cl_2–acetone) of the residue gave **24**, isolated as a syrup (152 mg, 72%); $[\alpha]_D$ −98° (*c* 1); R_f 0.56. NMR data ($CDCl_3$): ^1H, δ 8.18–6.65 (m, 58 H, 10 Ph and 2 Phth), 5.786 (m, 1 H, H_2C=C*H*CH_2O), 5.529, 5.371, and 5.143 (3 m, each 1 H, H-2‴,3‴,4‴), 5.422 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 5.243 (t, 1 H, $J_{4''',3'''} = J_{4''',5'''} = 10.2$ Hz, H-4‴), 5.222 and 5.094 (2 m, 2 H, H_2C=CHCH_2O), 4.987 (d, 1 H, $J_{1'''',2''''}$ 2.2 Hz, H-1⁗), 4.770 and 4.671 (2 d, each 1 H, PhCH_2O), 3.204 (s, 3 H, CH_3O), 1.082 (d, 3 H, $J_{6',5'}$ 6.5 Hz, H-6′,6′,6′); ^{13}C, δ 168.1, 167.7 (2 C), and 165.5 (*C*O Phth), 165.5, 165.1, 164.8, and 164.4 (4 *C*OC_6H_5), 116.9 (H_2C=CHCH_2O), 100.0, 98.5, 98.3, 97.1, and 96.5 (C-1,1′,1″,1‴,1⁗), 56.7, 55.9, and 55.5 (C-2,2″ and CH_3O), 16.4 (C-6′).

*Methyl 4-*O*-{4-*O*-[3-*O*-allyl-4-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-acetyl-α-*D*-mannopyranosyl)-2-*O* 528 points short-(2,3,4-tri-*O*-benzoyl-β-*D*-xylopyranosyl)-β-*D*-mannopyranosyl]-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl}-3-*O*-benzyl-2-deoxy-2-phthalimido-6-*O*-(2,3,4-tri-*O*-benzyl-α-*L*-fucopyranosyl)-β-*D*-glucopyranoside* (**25**).—A solution of **24** (100 mg, 49 μmol) and 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl trichloroacetimidate [9] (**7**; 57 mg, 0.12 mmol) in CH_2Cl_2 (3 mL) containing powdered 4A molecular sieves (200 mg) was stirred under N_2 for 30 min. Trimethylsilyl triflate (5 μL, 26 μmol) was added at −20°C, and the mixture was stirred for 30 min at 0°C. TLC (95:5 CH_2Cl_2–acetone) then showed the disappearance of **24** (R_f 0.56) and the formation of a new product **25** (R_f 0.46). Pyridine (1 mL) was added and the mixture was diluted with CH_2Cl_2 (250 mL), filtered through Celite, washed with water, dried ($MgSO_4$), filtered, and concentrated. Column chromatography (95:5 CH_2Cl_2–acetone) of the residue gave **25**, isolated as a syrup (53 mg, 45%); $[\alpha]_D$ −68° (*c* 1). NMR data ($CDCl_3$): ^1H, δ 7.79–6.59 (m, 58 H, 10 Ph and 2 Phth), 5.776 (m, 1 H, H_2C=C*H*CH_2O), 5.393 (d, 1 H, $J_{1,2}$ 8.5 Hz, H-1), 5.346 (t, 1 H, $J_{4''',3'''} = J_{4''',5'''} = 9.7$ Hz, H-4‴), 5.214 (m, 1 H, H*H*C=CHCH_2O), 5.142 (t, 1 H, $J_{4'''',3''''} = J_{4'''',5''''} = 10.0$ Hz, H-4⁗), 5.090 (dd, 1 H, $J_{3'''',2''''}$ 3.5 Hz, H-3⁗), 4.949 (d, 1 H, $J_{1',2'}$ 3.1 Hz, H-1′), 4.781 (dd, 1 H, H-2⁗), 4.762 (s, 1 H, H-1‴), 4.495 (d, 1 H, $J_{1'''',2''''}$ 1.8 Hz, H-1⁗), 3.189 (s, 3 H, CH_3O), 2.003, 1.966, 1.961, and 1.800 (4 s, each 3 H, 4 Ac), 1.059 (d, 3 H, $J_{6',5'}$ 6.5 Hz, H-6′,6′,6′); ^{13}C, δ 170.5, 169.8, 169.4, and 169.2 (4 *C*OCH_3), 168.1–167.3 (*C*O Phth), 165.5, 165.3, 164.7, and 164.4 (4 *C*OC_6H_5), 117.1 (H_2C=CHCH_2O), 100.1, 98.5, 98.2, 97.3, 97.1, and 96.6 (C-1,1′,1″,1‴,1⁗,1⁗), 56.6, 55.9, and 55.5 (C-2,2″ and CH_3O), 20.6–20.4 (CO*C*H_3), 16.4 (C-6′).

*Methyl 4-*O*-{4-*O*-[4-*O*-benzoyl-6-*O*-(2,3,4,6-tetra-*O*-acetyl-α-*D*-mannopyranosyl)-2-*O*-(2,3,4-tri-*O*-benzoyl-β-*D*-xylopyranosyl)-β-*D*-mannopyranosyl]-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl}-3-*O*-benzyl-2-deoxy-2-phthalimido-6-*O*-(2,3,4-tri-*O*-benzyl-α-*L*-fucopyranosyl)-β-*D*-glucopyranoside* (**26**).—A solution of **25** (53 mg,

22 μmol), tris(triphenylphosphine)rhodium(I) chloride (13 mg, 15 μmol), and 1,4-diazabicyclo[2.2.2]octane (2 mg, 18 μmol) in 7:3:1 EtOH–toluene–water (3 mL) was boiled under reflux for 2.5 h, then cooled, and concentrated. A solution of the residue in 9:1 acetone–M aq HCl (5 mL) was then boiled under reflux for 30 min, when TLC (95:5 CH_2Cl_2–acetone) indicated a complete conversion of **25** into **26** (R_f 0.36). The solution was concentrated, and a solution of the residue in CH_2Cl_2 (100 mL) was washed with aq 5% $NaHCO_3$ (10 mL) and water, dried ($MgSO_4$), filtered, and concentrated. Preparative TLC (95:5 CH_2Cl_2–acetone) of the residue gave **26**, isolated as a syrup (38 mg, 73%); $[\alpha]_D$ −23° (*c* 1); R_f 0.36. NMR data ($CDCl_3$): ^1H, δ 7.94–6.73 (m, 58 H, 10 Ph and 2 Phth), 5.630 (t, 1 H, $J_{3'''',4''''}$ 7.3 Hz, H-3''''), 5.461 (dd, 1 H, $J_{2'''',3''''}$ 7.5 Hz, H-2''''), 5.027 (d, 1 H, $J_{1'''',2''''}$ 5.4 Hz, H-1''''), 4.954 (dd, 1 H, $J_{2'''',1''''}$ 1.9 Hz, $J_{2'''',3''''}$ 2.7 Hz, H-2''''), 3.174 (s, 3 H, CH_3O), 1.976, 1.971, 1.929, and 1.842 (4 s, each 3 H, 4 Ac), 1.039 (d, 3 H, $J_{6',5'}$ 6.5 Hz, H-6',6',6').

Methyl 4-O-{4-O-[4-O-benzoyl-3,6-di-O-(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)-2-O-(2,3,4-tri-O-benzoyl-β-D-xylopyranosyl)-β-D-mannopyranosyl]-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl}-3-O-benzyl-2-deoxy-2-phthalimido-6-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside (**27**).—A solution of **26** (37 mg, 16 μmol) and 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl trichloroacetimidate [9] (**7**; 25 mg, 50 μmol) in CH_2Cl_2 (2 mL) containing powdered 4A molecular sieves (100 mg) was stirred under N_2 for 30 min. Trimethylsilyl triflate (3 μL, 17 μmol) was added at −20°C, and the mixture was stirred for 2 h at −10°C. TLC (37:3 CH_2Cl_2–acetone) then showed the disappearance of **26** (R_f 0.71), and a new product **27** (R_f 0.58). Pyridine (1 mL) was added, and the mixture was diluted with CH_2Cl_2 (100 mL), filtered through Celite, washed with water, dried ($MgSO_4$), filtered, and concentrated. Preparative TLC (4:1 toluene–acetone) of the residue gave **27**, isolated as a syrup (38 mg, 88%); $[\alpha]_D$ −45° (*c* 1, EtOAc); R_f 0.38. NMR data ($CDCl_3$): ^1H, δ 8.11–6.64 (m, 58 H, 10 Ph and 2 Phth), 3.173 (s, 3 H, CH_3O), 2.048, 2.016, 1.999, 1.968, 1.953, 1.849, 1.825, and 1.801 (8 s, each 3 H, 8 Ac), 1.036 (d, 3 H, $J_{6',5'}$ 6.5 Hz, H-6',6',6'); ^{13}C, δ 100.5, 99.1, 98.5 (2 C), 97.3, and 97.0 (2 C) (C-1,1',1'',1''',1'''',1''''',1''''''), 56.6, 55.9, and 55.5 (C-2,2'' and CH_3O), 20.6–20.2 ($COCH_3$), 16.4 (C-6').

Methyl 2-acetamido-4-O-[2-acetamido-2-deoxy-4-O-(3,6-di-O-α-D-mannopyranosyl-2-O-β-D-xylopyranosyl-β-D-mannopyranosyl)-β-D-glucopyranosyl]-2-deoxy-6-O-α-L-fucopyranosyl-β-D-glucopyranoside (**5**).—A solution of **27** (35 mg, 13 μmol) and hydrazine acetate (260 mg, 2.8 mmol) in EtOH (7.5 mL) was boiled under reflux for 16 h, then cooled, and concentrated. A solution of the residue in 1:1 pyridine–Ac_2O (4 mL) was stirred for 16 h at room temperature, then concentrated, and toluene, EtOH, and CH_2Cl_2 (each 3 × 10 mL) were evaporated from the residue. Column chromatography of the residue on Sephadex LH-20 (1:1 MeOH–CH_2Cl_2) afforded a white solid. To a solution of this product in 1:1 EtOH–EtOAc (5 mL), containing AcOH (50 μL), was added 10% Pd–C (50 mg), and hydrogenolysis was performed at atmospheric pressure for 24 h. Then the mixture was filtered through Celite and concentrated, and toluene, EtOH, and CH_2Cl_2 (each 3 × 5 mL) were evaporated from the residue. Because ^1H NMR analysis showed that the dephthaloylation was incomplete, the residue was treated with $MeNH_2$–EtOH (33%, 15 mL) for 24 h, concentrated, and treated with Ac_2O (300 μL) in MeOH (3 mL) for 24 h. The solution was concentrated, and toluene, EtOH, and CH_2Cl_2 (each 3 × 10 mL) were

evaporated from the residue, which was fractionated on Sephadex LH-20 (1:1 MeOH–CH_2Cl_2) to yield impure **5**. This product was then subjected to purification by RP-HPLC on a Cp tm Spher C18 column (250 × 4.6 mm, Chrompack) by elution with 95:5 water–MeOH for 5 min, followed by a linear gradient of 95:5 → 1:1 water–MeOH for 35 min, and detection at 205 nm. The fraction eluting at 14.3 min was collected and concentrated to yield **5**, isolated as a white amorphous solid (13 mg, 83%); $[\alpha]_D$ −24° (*c* 0.1, H_2O). For ^1H NMR data, see Table 1.

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