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Synthesis of sulfated glucuronyl glycosphingolipids; carbohydrate epitopes of neural cell-adhesion molecules †

Takahisa Nakano [a], Yukishige Ito [a] and Tomoya Ogawa [a,b,*]

[a] *The Institute of Physical and Chemical Research (RIKEN), Wako-shi, Saitama, 351-01 (Japan)*
[b] *Faculty of Agriculture, University of Tokyo, Yayoi, Bunkyo-ku, Tokyo, 113 (Japan)*

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ABSTRACT

The sulfated glucuronyl glycosphingolipids isolated from the human peripheral nervous system, HO_3S-3-β-Glc*p*A-(1 → 3)-{β-D-Gal*p*-(1 → 4)-β-D-Glc*p*NAc-(1 → 3)}$_n$-β-D-Gal*p*-(1 → 4)-β-D-Glc*p*-(1 → 1)-Cer ($n = 1, 2$) (**1** and **2**) were synthesized. The glycan part of target molecules was designed to be constructed from glucuronate, lactosamine, and lactose fragments **8**, **9** (or **10**), and **11**, which in turn were synthesized stereo- and/or regio-selectively from readily available compounds. The coupling reaction between **9** and **11** was performed by the action of trimethylsilyl trifluoromethanesulfonate (Me_3SiOTf), and subsequent manipulation of product **31** gave **33**. On the other hand, slight modification of this sequence, including repetitive glycosylation reactions using **10**, afforded hexasaccharide **46**. These compounds were reacted with nonreducing end glucuronate synthon **8** under the agency of $CuBr_2$–AgOTf–Bu_4NBr, and the resultant penta- and hepta-saccharides **34** and **47**, respectively, were transformed into glycosyl fluorides. Final coupling with the ceramide derivative **7**, followed by chemoselective deprotection of the levulinoyl group, sulfation and complete deprotection, afforded the target glycolipids **1** and **2**.

INTRODUCTION

In 1984, Ilyas and co-workers first reported[2] the presence of acidic glycolipid antigens in human peripheral nerve tissue which was recognized by IgM of patients having peripheral neuropathies and plasma cell abnormalities. The glycolipids were also shown[3] to be recognized by an antibody HNK-1 (anti-Leu-7) raised against a membrane antigen from T cell line HSB-2. Recently, these glycolipids have been isolated and chemically characterized[4]. Their structures were proposed as **1** and **2**, based on sugar analysis, enzymatic digestion, mild acid hydrolysis, permethylation, fast-atom-bombardment mass spectrometry, and NMR studies. A prominent feature of these compounds is the presence of a nonreducing-end glucuronic acid residue sulfated specifically at the C-3 position, which is carried on

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* Corresponding author.

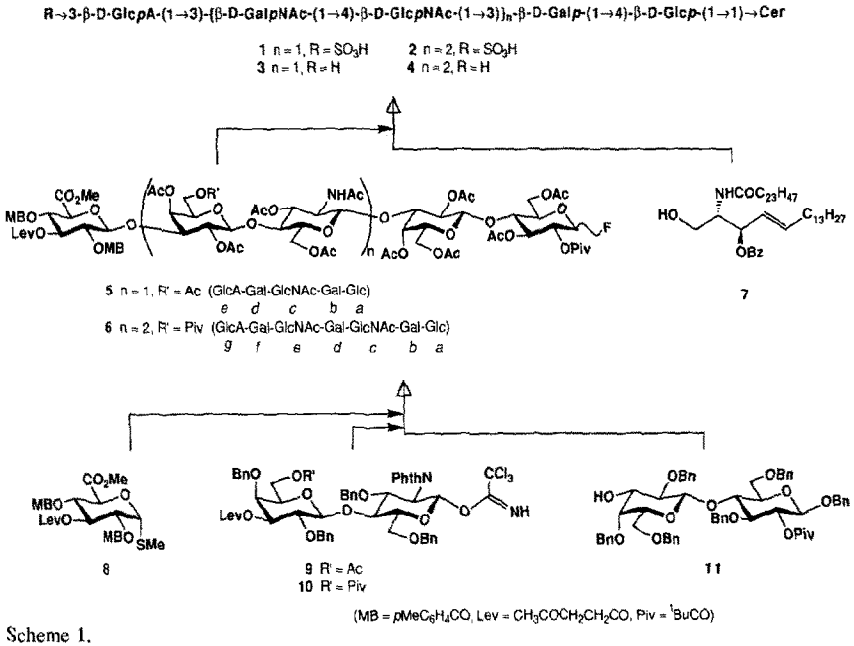
a neolacto-type backbone. This totally novel glycan sequence seems to hold an emerging importance in neurobiological sciences and quite probably in the broader field of glycobiology. For instance, neural cell-adhesion molecules L1 and N-CAM, J1 glycoprotein, and myelin-associated glycoprotein (MAG) were also shown[5] to share a carbohydrate epitope of similar structure recognized by monoclonal antibodies L2 and HNK-1. These results suggest that the epitope seems to be involved in nerve–astrocyte and astrocyte–astrocyte adhesion, acting as a ligand in cell–cell interaction[6]. Considering their potential biomedical significance, we began synthetic approaches toward these novel glycoconjugates, and our efforts have resulted in the syntheses of sulfated glucuronyl glycosphingolipids **1** (ref 7) and **2** (ref 8). Our syntheses feature the combined use of various modern glycoside bond-forming technologies (i.e., trichloroacetimidate, thioglycoside, glycosyl fluoride). Described herein is the full account of the results of this synthetic work.

RESULTS AND DISCUSSION

In order to successfully execute the synthetic path toward the target molecules, the most critical point is the construction of properly protected oligosaccharide portions so that stereoselective coupling with the lipid portion (ceramide), regioselective sulfation of the glucuronate residue, and final deprotection without touching the sulfate functionality could be achieved. In spite of recent advances in glycosphingolipid synthesis, multifunctional (carboxylate, sulfate, amide, and carbon–carbon double bond, in addition to a large number of hydroxyl groups) molecules of this magnitude, such as **1** or **2** having five and seven sugar residues, were considered a formidable challenge.

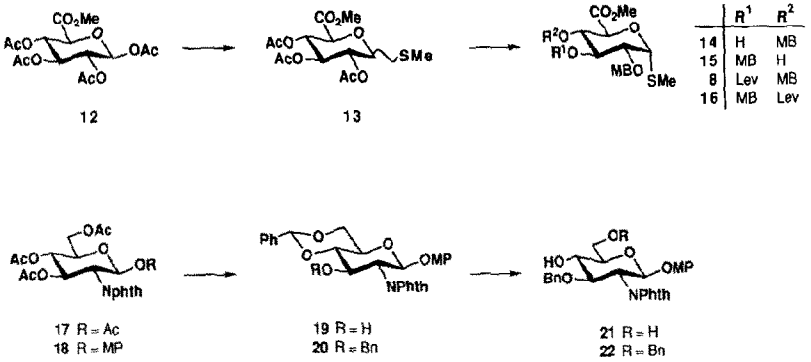
Based on the following scenario, penta- and hepta-saccharide units were designed as **5** and **6**, respectively. First of all, the sulfated function, being highly unlikely to survive under any glycosylation conditions, should be introduced after coupling with ceramide. Secondly, final deprotection must be executed under neutral or basic (preferably at low-temperature) conditions, because the sulfate group is reasonably stable only as a salt. Although the benzyl-type protecting group would be an ideal choice in this respect[9], it is not applicable to this particular case because of the presence of a carbon–carbon double bond on the ceramide moiety. Thirdly, in order to minimize practical difficulties during the end-game manipulations, the *N*-phthaloyl group, which is an obvious choice as a temporary protecting group for nitrogen, has to be converted into an *N*-acetyl group before coupling with the ceramide derivative[10]. Finally, the O-2a position had to be protected with a pivaloyl (Piv) group so that facile coupling could be assumed. Thus glycosyl donors **5** and **6** so designed were to be synthesized from mono- (**8**) and di-saccharide (**9** and **10**) derivatives, and the previously reported lactose derivative **11** (ref 11).

The glucuronyl donor, designed as a thioglycoside **8**, was synthesized from tetraacetate **12** (ref 12) in 34% overall yield as described below. Compound **12** was

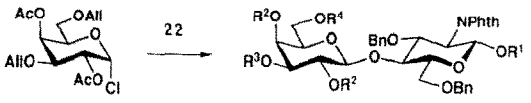


Scheme 1.

first converted into thioglycoside **13** (Bu_3SnSMe[13], $SnCl_4$ in 1,2-dichloroethane), which was subsequently deprotected and then protected, with the aid of dibutyltin oxide[14], into the di-(*p*-methylbenzoyl)ated product as a mixture of **14** and **15** in a ratio of 12:1. Although, separation of these isomers was not practical at this stage, subsequent levulinoylation into **8** and **16** allowed remarkably easy separation by silica gel column chromatography.



Scheme 2.



23

	R^1	R^2	R^3	R^4
24	MP	Ac	All	All
25	MP	H	All	All
26	MP	Bn	All	All
27	MP	Bn	H	H
28	MP	Bn	H	Ac
29	MP	Bn	Lev	Ac
30	H(α,β)	Bn	Lev	Ac
9	$C(NH)CCl_3$	Bn	Lev	Ac

Scheme 3.

The preparation of the lactosamine segment **9** basically relied upon the general strategy developed for the synthesis of the polylactosamine-type oligosaccharide[15]. A minor modification made for the present purpose was *p*-methoxypheny group protection at the anomeric position, which, although seemingly trivial, confers a substantial degree of flexibility on the whole synthetic scheme. The introduction of this protecting group was conveniently achieved by treatment of the β-acetate **17** (ref 16) with 4-methoxyphenol and Me_3SiOTf. The product was selectively protected into **22**, via **19**, **20**, and **21** in a standard manner. Reaction with the galactosyl chloride **23** (ref 15) using silver trifluoromethanesulfonate (AgOTf) as an activator gave **24** in an almost quantitative yield. Deacetylation into **25** (LiOOH in aq THF)[17] and subsequent benzylation into **26** (benzyl bromide, Ag_2O, and KI in DMF) were performed following a previously established protocol[15]. After deallylation[18], the diol **27** was selectively protected into **29** via **28**. The *p*-methoxyphenyl group was then oxidatively removed[19], and the resultant **30** was transformed into the trichloroacetimidate[20] **9**.

Glycosylation of **9** with **11** was performed by the action of Me_3SiOTf to give tetrasaccharide **31** in 86% yield, which was subjected to the following deprotection–protection sequence in order to liberate the C-3d hydroxyl group. First of all, simultaneous cleavage of the phthaloyl, acetyl, and levulinoyl groups was achieved by treatment with hydrazine hydrate in refluxing ethanol. The amino group was acetylated, and the resultant diol was selectively acetylated into **33**. Among the various conditions, the coupling with the glucuronate fragment **8** turned out to be best achieved under the agency of $CuBr_2$–Bu_4NBr–$AgOSO_2CF_3$ (ref 21) in nitromethane as solvent to give the pentasaccharide **34** in 58% yield. Conversion[22] into the fluoride **5** (α:β ratio 1:3) was performed in four steps via **35** and **36**. In this instance, because of the presence of the levulinoyl group which should be kept untouched at this stage, piperidine–acetic acid was the reagent of choice for the chemoselective cleavage of the anomeric acetyl group into **36**.

Compound **5** thus obtained was reacted with **7** ($SnCl_2$–$AgOSO_2CF_3$)[23] in

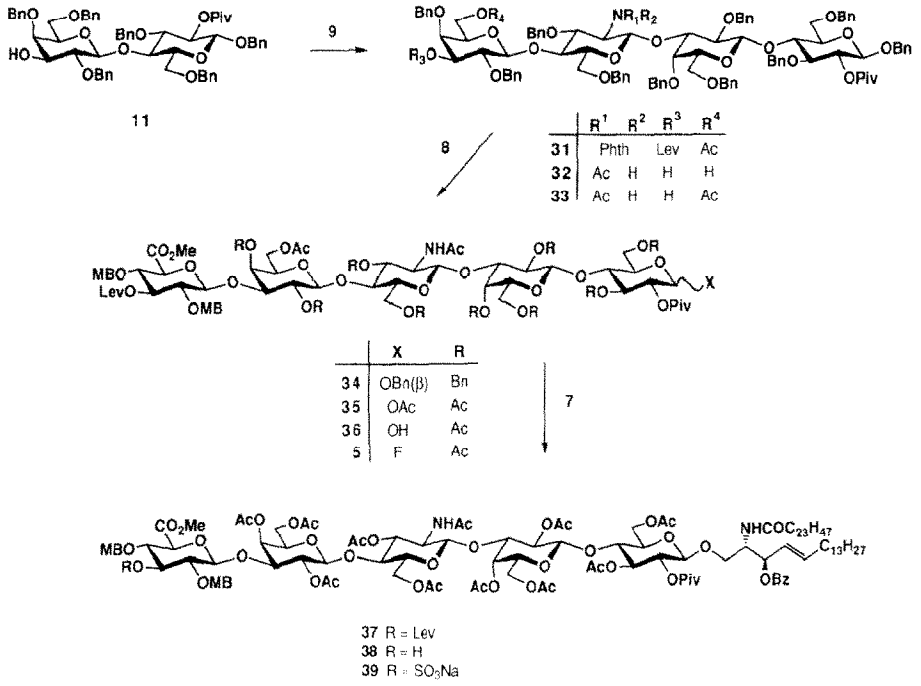
freshly distilled chloroform to afford a 55% yield of the desired **37**. It should be noted that only the β-fluoride was consumed in this transformation, and the corresponding α-counterpart was quantitatively recovered. This observation allows us to estimate that the yield based on the β-fluoride is actually > 70%. The structure of **37** was rigorously confirmed by ^{1}H NMR spectroscopy, including a COSY experiment. Further strong support was obtained from the ^{1}H NMR spectra of fully deprotected compound **3**, which revealed the presence of five anomeric protons at δ 4.681, 4.368, 4.317, 4.279, and 4.174, all assignable as that of the β-glycosidic linkage (d, J ~ 7.5 Hz).

Further conversion into the target glycolipid was executed as follows. Selective removal of levulinoyl group[24] at O-3e by hydrazine–acetic acid gave **38** in almost quantitative yield. From a COSY experiment, the H-5e and H-4e signals were found at δ 4.224 (d, J 9.5 Hz) and 5.438 (t, J 9.5 Hz), respectively. Although an unambiguous assignment could not be made for the H-3e proton whose resonance had shifted upfield after cleavage of the levulinoyl group, the absence of a corresponding signal in the region of 5.563 ppm was in accordance with the presence of a free hydroxy group at this position. Compound **38** was then treated with sulfur trioxide–trimethylamine in dry DMF for 72 h at 55°C. After extensive purification by sequential chromatography (see Experimental section), product **39** was isolated in 59% yield. The structure of **39** was confirmed by a COSY NMR experiment. Especially supportive of the structure was the downfield shift of the H-3e signal to δ4.876, confirming that a sulfate group had actually been introduced at this position.

Complete deprotection was carried out under carefully controlled conditions (1, LiOH in aq THF, −15 to 0°C; 2, NaOMe in THF–MeOH at 20°C). After purification by chromatography on Sephadex LH-20, the target glycolipid **1** was obtained in 86% yield. Although the ^{1}H NMR spectrum of synthetic **1** is not directly comparable with that of a natural sample, because the latter spectrum was recorded with a very small amount of compound, all chemical shifts and coupling constants of the anomeric protons and H-3e were in good agreement with the reported values.

Being encouraged by this result, we turned our attention to the hexaheptaosyl ceramide **2**. This compound can be viewed as a homologue of **1** with respect to the lactosamine unit. Therefore, our expectation was that only a slight modification of the synthetic route should be adequate enough for the synthesis of **2**, which turned out to be the case (*vide infra*).

The requisite protective-group manipulation of the lactosamine fragement was started by selective protection of diol **27** with pivaloyl chloride and 4-dimethylaminopyridine (DMAP) in pyridine to give **40** in 83% yield. The choice of the pivaloyl group was based on the observation in model studies that this particularly hindered acyl group is not affected under the conditions of dephthaloylation (e.g., hydrazine in refluxing EtOH), thereby allowing us to achieve the following task in a minimum number of steps. After conversion to **41**, oxidative removal of the



Scheme 4.

p-methoxyphenyl group gave the hemiacetal **42** in 87% yield, which was then converted into trichloroacetimidate **10**. Coupling of **10** with **11** using Me_3SiOTf as an activator gave an 83% yield of tetrasaccharide **43**. Selective removal of the levulinoyl group gave **44**, which was again coupled with **10** to afford hexasaccharide **45** in 81% yield. The simultaneous removal of phthaloyl and levulinoyl groups was achieved with hydrazine hydrate in refluxing EtOH, and the resultant diamino alcohol was *N*-acetylated to give compound **46** in 81% overall yield.

Attachment of the glucuronate residue was again carried out by use of the thioglycoside **8** as a glycosyl donor, and the product **47** was subjected to conventional protective group modulation as described for the preparation of **5** to give the designed glycosyl donor **6** via **48** and **49**. Compound **6** thus obtained was revealed to be a 1:4 mixture of α and β anomers.

Coupling between **6** and **7** ($SnCl_2$–AgOTf in chloroform) afforded **50** in 49% yield. This compound was converted into the target molecule **2** via **51** and **52**, as well as into neutral glycolipid **4**, following the protocol established for the preparation of **1** and **3**. Although the physical data of natural **2** is not yet reported, the ^1H NMR spectrum of the synthetic material is quite reasonable in comparison with the pentasaccharide counterpart **1** and shows, in addition to the signals for the anomeric protons, the presence of the deshielded signal for H-3g, indicating the presence of sulfate group at O-3g.

EXPERIMENTAL

General methods.—Melting points were determined with a Yanagimoto micro melting-point apparatus and are uncorrected. Optical rotations were determined with a Perkin–Elmer Model 241 MC polarimeter, for solutions in $CHCl_3$ at 25°C, unless noted otherwise. Silica gel column chromatography was performed on columns of Wako-gel C-300 (200–300 mesh). TLC and high-performance (HPTLC) were performed on Silica Gel 60 F_{254} (Merck). Molecular sieves were purchased from Nakarai Chemicals. ^1H NMR spectra were recorded with either a GNM-GSX-500, JEOL GX400, or FX90Q spectrometers. The values of δ_H are expressed in ppm downfield from the signal for internal Me_4Si. Assignments of peaks made for compounds **31, 34, 37, 38, 39, 45, 47, 50, 51,** and **52** were verified by COSY experiments.

*Methyl (methyl 2,3,4,-tri-*O*-acetyl-1-thio-α- and β-*D*-glucopyranosid)uronate* (**13**). —To a stirred mixture of **12** (5.01 g, 13.3 mmol) and Bu_3SnSMe (5.40 g, 16.0 mmol) in $(ClCH_2)_2$ (90 mL) was added dropwise $SnCl_4$ (2.1 mL, 17.9 mmol) at 0°C over 1 h. The mixture was stirred for 3 days at 20°C, evaporated in vacuo and diluted with EtOAc. The solution was vigorously stirred with aq $NaHCO_3$–KF for 3 h, filtered through Celite, washed with aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. Chromatography of the residue on SiO_2 in 10:3 toluene–EtOAc gave **13**

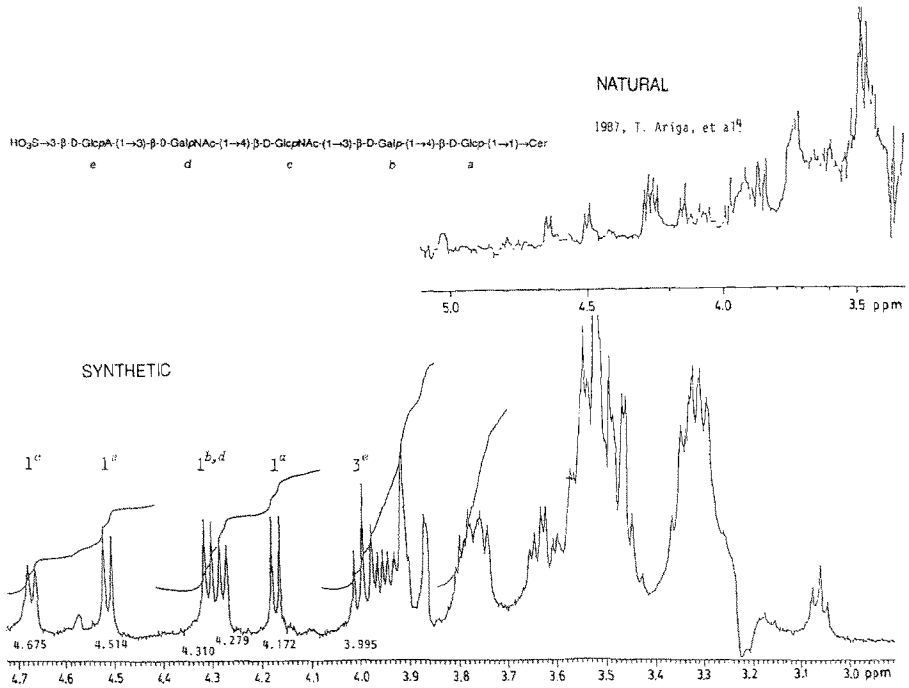
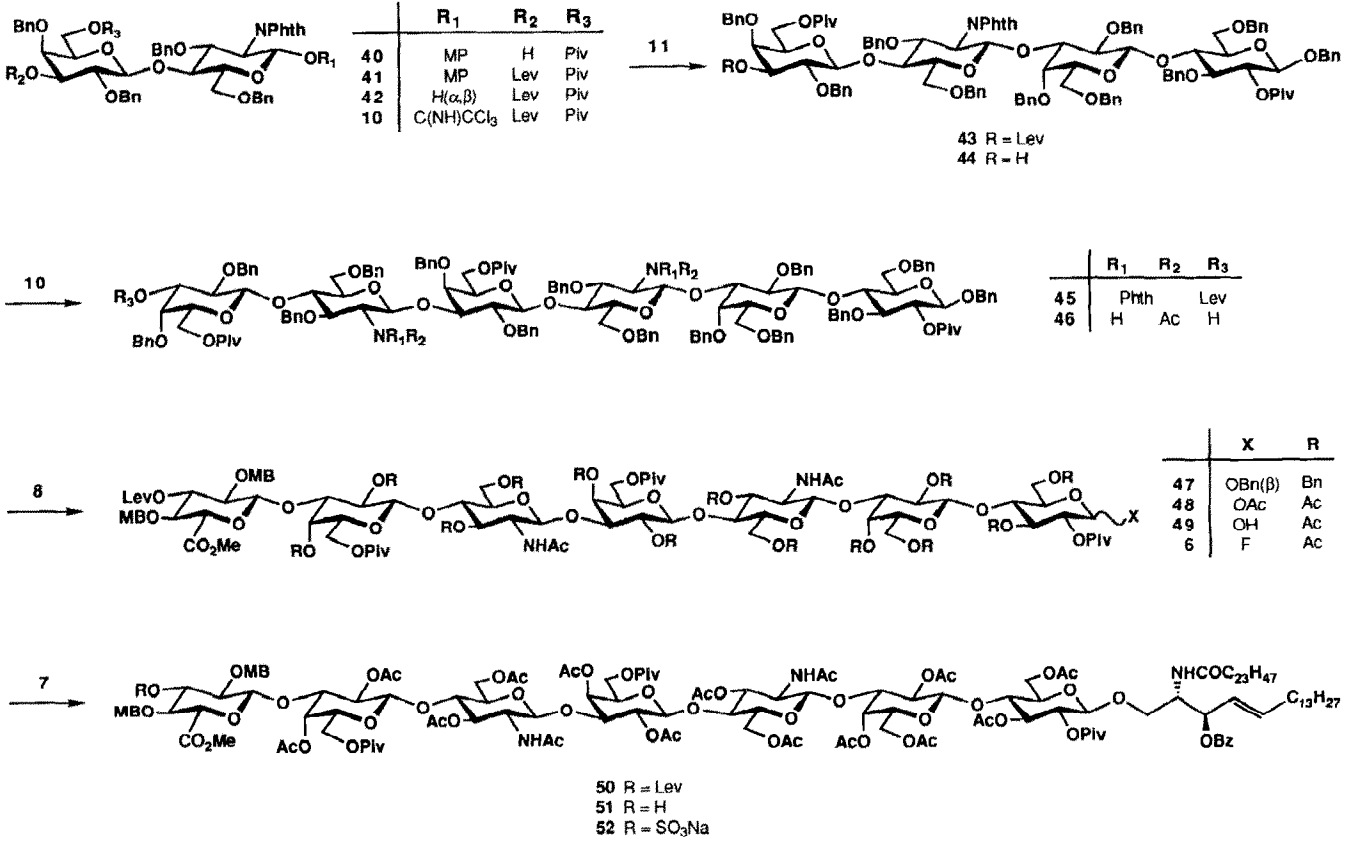


Fig. 1. 500-MHz ^1H NMR spectrum in 49:1 Me_2SO-d_6–D_2O at 60°C.

(4.37 g, 90%): R_f 0.35 (toluene–EtOAc); ^{1}H NMR ($CDCl_3$) δ 5.621 (0.63 H, d, J 5.5 Hz, H-1α), 5.396 (0.63 H, t, J 9.8 Hz, H-3α), 5.282 (0.38 H, t, 9.8 Hz, H-2,3 or 4β), 5.216 (0.38 H, t, J 9.8 Hz, H-2,3 or 4β), 5.188 (0.63 H, t, J 9.8 Hz, H-4α), 5.092 (0.38 H, t, J 9.8 Hz, H-2,3 or 4β), 5.051 (0.63 H, dd, J 9.8 and 5.5 Hz, H-2α), 4.725 (0.63 H, d, 9.8 Hz, H-5α), 4.432 (0.38 H, d, J 9.8 Hz, H-1 or 5β), 4.061 (0.38 H, d, J 9.8 Hz, H-1 or 5β), 3.762 (1.88 H, s, COOMeα), 3.753 (1.13 H, s, COOMeβ), 2.195, 2.108, 2.073, 2.071, 2.042, 2.031, 2.026, and 2.023 (12 H, 8s, 3Ac and SMe). Anal. Calcd for $C_{14}H_{20}O_9S$: C, 46.15; H, 5.53; S, 8.80. Found: C, 46.02; H, 5.58; S, 8.57.

*Methyl [methyl 2,4-di-*O*-(*p*-methylbenzoyl)-1-thio-α-*D*-glucopyranosid]uronate* (**14**) *and methyl [methyl 2,3-di-*O*-(*p*-methylbenzoyl)-1-thio-α-*D*-glucopyranosid]uronate* (**15**).—To a solution of **13** (3.90 g, 10.7 mmol) in 1:1 MeOH–THF (80 mL) was added a solution of 0.3 M NaOMe–MeOH (2.5 mL). The mixture was stirred for 2 h at 20°C, made neutral with Amberlyst-15 (H^+) and evaporated in vacuo to give the triol (2.35 g, 92%). A mixture of the triol (630 mg, 2.64 mmol) and Bu_2SnO (1.35 g, 2.64 mmol) in toluene (52 mL) was stirred for 4 h under reflux with continuous azeotropic removal of water, cooled, evaporated in vacuo, and diluted with THF (40 mL). To the solution were added, successively, *p*-methylbenzoyl chloride (0.98 mL, 7.41 mmol) and Et_3N (1.0 mL, 7.3 mmol), and the mixture was stirred for 20 h at 20°C. After the addition of MeOH, the solution was evaporated in vacuo, diluted with EtOAc, and then vigorously stirred with aq $NaHCO_3$–KF for 3 h. The precipitate was filtered off through Celite, and the filtrate was washed with aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. Chromatography of the residue on SiO_2 in 7:2 toluene–EtOAc gave a mixture of **14** and **15** (660 mg, 53%): R_f 0.44 (4:1 toluene–EtOAc). ^{1}H NMR data ($CDCl_3$): δ 5.759 (0.08 H, d, J 5.2 Hz, H-1 of **15**), 5.747 (0.92 H, d, J 5.2 Hz, H-1 of **14**), 5.699 (0.08 H, t, J 9.5 Hz, H-3 of **15**), 5.397 (0.08 H, dd, J 9.5 and 5.2 Hz, H-2 of **15**), 5.379 (0.92 H, t, J 8.9 Hz, H-4 of **14**), 5.286 (0.92 H, dd, J 8.9 and 5.2 Hz, H-2 of **14**), 4.870 (0.92 H, d, J 8.9 Hz, H-5 of **14**), 4.779 (0.08 H, d, J 9.5 Hz, H-5 of **15**), 4.365 (0.92 H, dt, J 8.9 and 3.4 Hz, H-3 of **14**), 4.152 (0.08 H, dt, J 9.5 and 3.8 Hz, H-4 of **15**), 3.836 (0.23 H, s, COOMe of **15**), 3.689 (2.77 H, s, COOMe of **14**), 2.402 (2.77 H, s, C_6H_4*Me* of **14**), 2.395 (2.77 H, s, C_6H_4*Me* of **14**), 2.345 (0.23 H, s, C_6H_4*Me* of **15**), 2.342 (0.23 H, s, C_6H_4*Me* of **15**), 2.142 (2.77 H, s, SMe of **14**), and 2.100 (0.23 H, s, SMe of **15**). Anal. Calcd for $C_{24}H_{26}O_8S \cdot 0.25H_2O$: C, 60.18; H, 5.58; S, 6.69. Found: C, 60.15; H, 5.54; S, 6.76.

*Methyl [methyl 3-*O*-levulinoyl-2,4-di-*O*-(*p*-methylbenzoyl)-1-thio-α-*D*-glucopyranosid]uronate* (**8**) *and methyl [methyl 4-*O*-levulinoyl-2,3-di-*O*-(*p*-methylbenzoyl)-1-thio-α-*D*-glucopyranosid]uronate* (**16**).—To a solution of a mixture of **14** and **15** (660 mg, 1.39 mmol) in pyridine (8 mL) were added a solution of 1.08 M levulinic anhydride in $(ClCH_2)_2$ (3.9 mL, 4.2 mmol) and DMAP. The mixture was stirred for 20 h at 20°C, and coevaporated with a mixture of EtOH and toluene. Sequential chromatography of the residue on SiO_2 first in 5:2 hexane–EtOAc and then in 3:1 toluene–EtOAc gave **8** (587 mg, 74%) and **16** (44 mg, 6%).


BnO
OR3
NPhth
R2O
OBn
OR1
40 MP H Piv
41 MP Lev Piv
42 H(α,β) Lev Piv
10 C(NH)CCl3 Lev Piv
11
OPiv
RO
43 R = Lev
44 R = H
10
R3O
NR1R2
45 Phth Lev
46 H Ac H
8
LevO
MBO
OMB
CO2Me
47 OBn(β) Bn
48 OAc Ac
49 OH Ac
6 F Ac
7
AcO
NHCOC23H47
C13H27
OBz
50 R = Lev
51 R = H
52 R = SO3Na

Scheme 5.

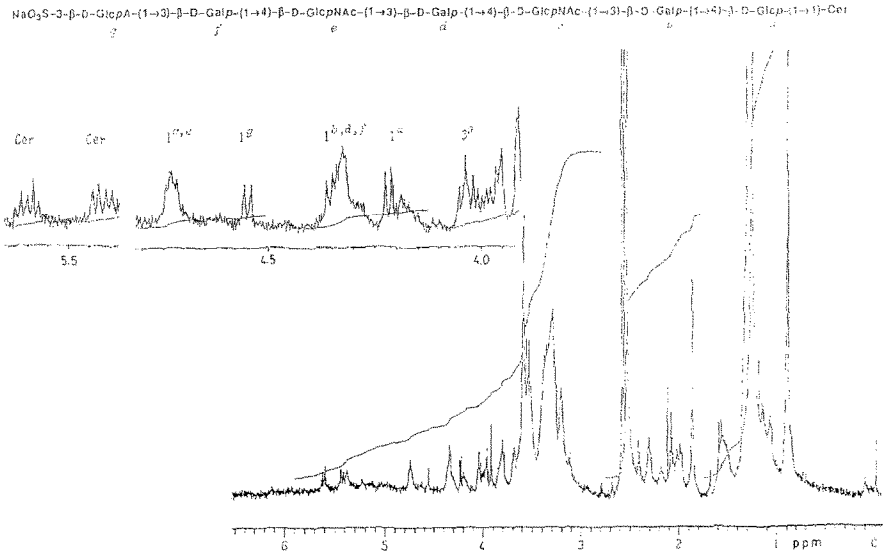


Fig. 2. 500-MHz ^{1}H NMR spectrum in 49:1 Me_2SO-d_6–D_2O at 60°C.

Compound **8** had: $[\alpha]_D$ +103° (*c* 0.9); R_f 0.35 (2:1 hexane–EtOAc). ^{1}H NMR data ($CDCl_3$): δ 5.811 (1 H, d, *J* 5.5 Hz, H-1), 5.771 (1 H, t, *J* 9.5 Hz, H-3), 5.463 (1 H, t, *J* 9.5 Hz, H-4), 5.338 (1 H, dd, *J* 9.5 and 5.5 Hz, H-2), 4.905 (1 H, d, *J* 9.5 Hz, H-5), 3.686 (3 H, s, COOMe), 2.411 (6 H, s, C_6H_4*Me*), 2.122 (3 H, s, SMe or CH_2CO*CH*$_3$), and 1.963 (3 H, s, SMe or CH_2CO*CH*$_3$). Anal. Calcd for $C_{29}H_{32}O_{10}S$: C, 60.83; H, 5.63; S, 5.60. Found: C, 60.96; H, 5.67; S, 5.54.

Compound **16** had: $[\alpha]_D$ +158° (*c* 2.1); R_f 0.29 (2:1 hexane–EtOAc). ^{1}H NMR data ($CDCl_3$): δ 5.821 (1 H, t, *J* 9.0 Hz, H-3 or 4), 5.814 (1 H, d, *J* 5.3 Hz, H-1), 5.421 (1 H, t, *J* 9.0 Hz, H-3 or 4), 5.380 (1 H, dd, *J* 9.0 and 5.3 Hz, H-2), 4.852 (1 H, d, *J* 9.0 Hz, H-5), 3.765 (3 H, s, COOMe), 2.363 (6 H, s, $C_6H_4M_e$), 2.143 (3 H, s, SMe or CH_2CO*Me*), and 2.062 (3 H, s, SMe or CH_2CO*Me*). Anal. Calcd for $C_{29}H_{32}O_{10}S$: C, 60.83; H, 5.63. Found: C, 60.83; H, 5.66.

p-*Methoxyphenyl 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**18**).—To a stirred mixture of **17** (2.16 g, 4.52 mmol) and *p*-methoxyphenol (0.87 g, 7.01 mmol) in $(ClCH_2)_2$ (30 mL) was added dropwise Me_3SiOTf (90 μL, 0.47 mmol). The mixture was stirred for 3 h at 0°C, diluted with EtOAc, washed successively with aq $NaHCO_3$ and aq NaCl, dried ($MgSO_4$), and evaporated in vacuo. Chromatography of the residue on SiO_2 in 2:1 toluene–EtOAc gave **18** (2.05 g, 84%); mp 148–149°C; $[\alpha]_D$ +51.3° (*c* 1.0). ^{1}H NMR data ($CDCl_3$): δ 5.864 (1 H, d, *J* 8.5 Hz, H-1), 5.862 (1 H, dd, *J* 10.7 and 9.0 Hz, H-3), 5.251 (1 H, dd, *J* 10.7 and 9.0 Hz, H-4), 4.579 (1 H, dd, *J* 10.7 and 8.5 Hz, H-2), 3.720 (3 H, OMe), 2.108, 2.049, and 1.892 (9 H, 3 s, 3 Ac). Anal. Calcd for $C_{27}H_{27}NO_{11}$: C, 59.88; H, 5.03; N, 2.59. Found: C, 59.37; H, 4.98; N, 2.57.

p-*Methoxyphenyl 4,6-O-benzylidene-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**19**).—To a solution of **18** (47.2 g, 87.1 mmol) in 1:1 MeOH–THF (1000 mL) were

added a solution of 0. 2M NaOMe–MeOH (43.5 mL). The mixture was stirred for 2 h at 20°C, made neutral with Amberlyst-15 (H^+), and evaporated in vacuo. The residue was dissolved in DMF (33 mL) containing α,α-dimethoxytoluene (20 mL, 130 mmol) and $TsOH \cdot H_2O$ (1.67 g, 8.76 mmol), and the solution was stirred for 20 h at 20°C. The mixture was diluted with EtOAc and washed with water. The organic layer was washed successively with aq $NaHCO_3$ and aq NaCl, dried ($MgSO_4$), and evaporated in vacuo. The residue was crystallized from MeOH to give **19** (39.2 g, 89%); mp 128–129°C; $[\alpha]_D$ +9.7° (*c* 0.8); R_f 0.49 (3:1 toluene–EtOAc). ^1H NMR data ($CDCl_3$): δ 5.799 (1 H, d, *J* 8.6 Hz, H-1), 5.590 (1 H, s, benzylidene), 4.702 (1 H, ddd, *J* 10.0, 8.5, and 3.7 Hz, H-3), 4.499 (1 H, dd, *J* 10.5 and 8.6 Hz, H-2), 3.717 (3 H, s, OMe), and 2.642 (1 H, d, *J* 3.7 Hz, OH). Anal. Calcd for $C_{28}H_{25}NO_8 \cdot 0.5H_2O$: C, 65.52; H, 5.11; N, 2.73. Found: C, 65.57; H, 4.99; N, 2.74.

p-*Methoxyphenyl 3-O-benzyl-4,6-O-benzylidene-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**20**).—To a solution of **19** (21.2 g, 42.2 mmol) in DMF (50 mL) was added NaH (2.76 g, 55% oil dispersion 63 mmol) at 0°C. To the mixture was added dropwise benzyl bromide (7.5 mL, 63 mmol) over 2 h at 0°C, and the mixture was then stirred for 20 h at 20°C. The excess NaH was carefully decomposed with MeOH. After evaporation in vacuo, a solution of the residue in $CHCl_3$ was successively washed with aq $NaHCO_3$ and aq NaCl, dried ($MgSO_4$), and evaporated in vacuo. Chromatography of the residue on SiO_2 in 5:1 toluene–EtOAc gave **20** (15.2 g, 61%) and recovered **19** (6.4 g, 30%).

Compound **20** had: $[\alpha]_D$ +72.3° (*c* 0.8); R_f 0.17 (5:1 hexane–EtOAc). ^1H NMR data ($CDCl_3$): δ 5.742 (1 H, d, *J* 8.3 Hz, H-1), 5.643 (1 H, s, benzylidene), 4.822 (1 H, d, *J* 12.4 Hz, benzyl), 4.534 (1 H, d, *J* 12.4 Hz, benzyl), 4.409 (1 H, dd, *J* 10.5 and 5.1 Hz, H-6), and 3.683 (3 H, s, OMe). Anal. Calcd for $C_{35}H_{31}NO_8$: C, 70.81; H, 5.26; N, 2.36. Found: C, 70.80; H, 5.30; N, 2.30.

p-*Methoxyphenyl 3-O-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**21**).—To a solution of **20** (19.2 g, 32.3 mmol) in MeOH–1,4-dioxane (300 mL) were added $TsOH \cdot H_2O$ (0.615 g, 3.33 mmol). The mixture was stirred for 1 h at 60°C, and for 45 min at 85°C, neutralized with Et_3N, and evaporated in vacuo. Chromatography of the residue on SiO_2 in 1:1 toluene–EtOAc gave **21** (12.6 g, 77%) and recovered **20** (0.57 g, 3%).

Compound **21** had: $[\alpha]_D$ +73.0° (*c* 1.1); R_f 0.32 (1:1 toluene–EtOAc). ^1H NMR data: δ 5.711 (1 H, d, *J* 8.1 Hz, H-1), 4.744 (1 H, d, *J* 12.2 Hz, benzyl), 4.569 (1 H, d, *J* 12.2 Hz, benzyl), and 3.696 (3 H, s, OMe). Anal. Calcd for $C_{28}H_{27}NO_8$: C, 66.53; H, 5.38; N, 2.77. Found: C, 66.16; H, 5.45; N, 2.76.

p-*Methoxyphenyl 3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**22**).—A mixture **21** (9.24 g, 18.3 mmol) and $(Bu_3Sn)_2O$ (10.9 g, 18.3 mmol) in toluene (260 mL) was stirred for 4 h under reflux, with azeotropic removal of water, and then cooled to room temperature. Benzyl bromide (11 mL, 92.5 mmol) and Bu_4NBr (0.59 g, 1.83 mmol) were added, and the mixture was stirred for 20 h at 100°C and evaporated in vacuo. A solution of the residue in EtOAc (250 mL)

was vigorously stirred with aq $NaHCO_3$–KF for 5 h and filtered through Celite. The filtrate was successively washed with aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. Chromatography of the residue on SiO_2 in 5:1 toluene–EtOAc gave **22** (9.90 g, 91%); $[\alpha]_D$ +56.1° (*c* 0.8); R_f 0.40 (4:1 toluene–EtOAc). ^1H NMR data ($CDCl_3$): δ 5.655 (1 H, d, *J* 8.5 Hz, H-1), 4.766 (1 H, d, *J* 12.2 Hz, benzyl), 4.628 (1 H, d, *J* 11.9 Hz, benzyl), 4.573 (1 H, d, *J* 11.9 Hz, benzyl), 4.560 (1 H, d, *J* 12.2 Hz, benzyl), 4.406 (1 H, dd, *J* 10.7 and 8.5 Hz, H-2), 4.305 (1 H, dd, *J* 10.7 and 8.5 Hz, H-3), 3.888 (1 H, ddd, *J* 9.5, 8.5, and 2.8 Hz, H-4), 3.690 (3 H, s, OMe), and 2.947 (1 H, d, *J* 2.8 Hz, OH). Anal. Calcd for $C_{35}H_{33}NO_8$: C, 70.57; H, 5.59; N, 2.35. Found: C, 70.24; H, 5.59; N, 2.32.

p-*Methoxyphenyl O-(2,4-di-O-acetyl-3,6-di-O-allyl-β-D-galactopyranosyl)-(1 → 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside* (**24**).—To a stirred mixture of **22** (7.11 g, 11.9 mmol), AgOTf (6.14 g, 23.9 mmol) and 4A molecular sieves (42 g) in $(ClCH_2)_2$ (150 mL) were added, at −20°C, a solution of **23** (6.49 g, 17.9 mmol) in $(ClCH_2)_2$ (100 mL) over 5 min. The mixture was diluted with $CHCl_3$ and aq $NaHCO_3$, and filtered through Celite. The filtrate was successively washed with aq $NaHCO_3$ and aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. Chromatography of the residue on SiO_2 in 4:1 toluene–EtOAc gave **24** (10.4 g, 91%); $[\alpha]_D$ +47.2° (*c* 0.6); R_f 0.44 (4:1 toluene–EtOAc). ^1H NMR data ($CDCl_3$): δ 5.615 (1 H, d, *J* 8.3 Hz, H-1a), 5.408 (1 H, d, *J* 2.7 Hz, H-4b), 5.068 (1 H, dd, *J* 10.0 and 8.1 Hz, H-2b), 4.874 and 4.766 (2 H, 2 d, *J* 12.0 Hz, benzyl), 4.565 (1 H, d, *J* 8.1 Hz, H-1b), 4.515, 4.476 (2 H, 2d, *J* 12.0 Hz, benzyl), 4.408 (1 H, dd, *J* 10.7 and 8.3 Hz, H-2a), 4.326 (1 H, dd, *J* 10.7 and 9.5 Hz, H-3a), 4.104 (1 H, dd, *J* 9.5 and 8.8 Hz, H-4a), 3.697 (3 H, s, OMe), 2.063 (3 H, s, Ac), and 2.055 (3 H, s, Ac). Anal. Calcd for $C_{51}H_{55}NO_{15}$: C, 66.44; H, 6.01; N, 1.52. Found: C, 66.47; H, 5.99; N, 1.54.

p-*Methoxyphenyl O-(3,6-di-O-allyl-β-D-galactopyranosyl)-(1 → 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside* (**25**).—To a solution of **24** (0.540 g, 0.59 mmol) in THF (15 mL) were added H_2O_2 (31%, 4.1 mL) and 1.25 N LiOH (1.45 mL). The mixture was stirred for 8 h at 0°C. The mixture was diluted with water and extracted with EtOAc. The organic layer was washed with aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. Chromatography of the residue on SiO_2 in 3:2 toluene–EtOAc gave **25** (0.329 g, 67%); $[\alpha]_D$ +68.2° (*c* 1.1); R_f 0.29 (2:1 toluene–EtOAc). ^1H NMR data ($CDCl_3$): δ 5.593 (1 H, d, *J* 8.2 Hz, H-1a), 4.562 (1 H, d, *J* 7.6 Hz, H-1b), and 3.693 (3 H, s, OMe). Anal. Calcd for $C_{47}H_{51}NO_{13} \cdot H_2O$: C, 65,95; H, 6.24; N, 1.64. Found: C, 66.34; H, 6.07; N, 1.66.

p-*Methoxyphenyl O-(3,6-di-O-allyl-2,4-di-O-benzyl-β-D-galactopyranosyl-(1 → 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside* (**26**).—To a mixture of **25** (0.293 g, 0.35 mmol), Ag_2O (0.992 g, 4.3 mmol), and KI (0.290 g, 1.8 mmol) in DMF (7 mL) was added dropwise benzyl bromide (0.5 mL, 4.2 mmol). The mixture was stirred for 1 h at 0°C and then for 1 h at 20°C. The mixture was diluted with water and Et_2O and filtered through Celite. The filtrate was washed with water and aq NaCl and evaporated in vacuo. Chromatography of the residue on SiO_2 in 5:2 hexane–EtOAc gave **26** (0.348 g, 98%); $[\alpha]_D$ +28.0° (*c* 0.9); R_f 0.42 (5:2

toluene–EtOAc). ^{1}H NMR data ($CDCl_3$): δ 5.618 (1 H, d, *J* 8.5 Hz, H-1a), 4.454 (1 H, d, *J* 7.6 Hz, H-1b), 4.427 (1 H, dd, *J* 10.7 and 8.5 Hz, H-2a), 4.096 (1 H, dd, *J* 9.8 and 8.2 Hz, H-4a), 3.854 (1 H, d, *J* 2.8 Hz, H-4b), 3.733 (1 H, dd, *J* 9.8 and 7.6 Hz, H-2b), 3.692 (3 H, s, OMe), and 3.348 (1 H, dd, *J* 9.8 and 2.8 Hz, H-3b). Anal. Calcd for $C_{61}H_{63}NO_{13}$: C, 71.96; H, 6.24; N, 1.38. Found: C, 71.75; H, 6.17; N, 1.36.

p-*Methoxyphenyl* O-*(2,4-di-*O*-benzyl-β-*D*-galactopyranosyl)-(1 → 4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**27**).—A solution of **26** (3.89 g, 3.82 mmol), in 10:5:1 MeCN–EtOH–H_2O (120 mL) was degassed by passage of N_2 for 1 h at 100°C. To this solution was then added $(Ph_3P)RhCl$ (636 mg, 0.67 mmol) and DABCO (346 mg, 3.09 mmol), and the mixture was stirred for 72 h under reflux. The mixture was concentrated in vacuo, and the residue was dissolved in 10:1 acetone–H_2O (120 mL) containing $HgCl_2$ (9.98 g, 36.8 mmol) and HgO (0.5 g, 2 mmol). The suspension was stirred for 2 h at 20°C and filtered through Celite, and the filtrate was evaporated in vacuo. The residue was dissolved in $CHCl_3$, and the solution was successively washed with 10% aq KI and aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. Chromatography of the residue on SiO_2 in 1:1 toluene–EtOAc gave **27** (2.94 g, 82%); $[\alpha]_D$ +44.2° (*c* 1.3); R_f 0.33 (3:2 toluene–EtOAc). ^{1}H NMR data ($CDCl_3$): δ 5.638 (1 H, d, *J* 8.2 H, H-1a), 4.936 (1 H, d, *J* 12.2 Hz, benzyl), 4.459 (1 H, d, *J* 7.3 Hz, H-1b), 4.426 (1 H, dd, *J* 10.2 and 8.2 Hz, H-2a or 3a), 4.383 (1 H, dd, *J* 10.2 and 8.2 Hz, H-2a or 3a), 4.111 (1 H, dd, *J* 10.1 and 8.2 Hz, H-4a), 3.693 (3 H, s, OMe), and 3.645 (1 H, dd, *J* 10.7 and 7.3 Hz, H-2b). Anal. Calcd for $C_{55}H_{55}NO_{13}$: C, 70.42; H, 5.91; N, 1.49. Found: C, 70.12; H, 5.91; N, 1.52.

p-*Methoxyphenyl* O-*(6-*O*-acetyl-2,4-di-*O*-benzyl-β-*D*-galactopyranosyl)-(1 → 4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**28**).—To an ice-cold solution of **27** (4.29 g, 4.57 mmol) in pyridine (30 mL) was added AcCl (0.68 mL, 9.6 mmol). After being stirred for 30 min at 0°C, MeOH and toluene were added, and the solution was evaporated in vacuo. Chromatography of the residue on SiO_2 in 5:2 toluene–EtOAc gave **28** (3.42 g, 76%); $[\alpha]_D$ +41.5° (*c* 1.0); R_f 0.26 (3:2 hexane–EtOAc). ^{1}H NMR data ($CDCl_3$): δ 6.623 (1 H, d, *J* 8.6 Hz, H-1a), 4.468 (1 H, d, *J* 7.0 Hz, H-1b), 4.170 (1 H, dd, *J* 11.0 and 6.4 Hz, H-6b), 3.994 (1 H, dd, *J* 11.0 and 6.4 Hz, H-6b), 3.518 (1 H, t, *J* 6.4 Hz, H-5b), and 2.004 (3 H, s, Ac). Anal. Calcd for $C_{57}H_{77}NO_{14} \cdot 0.5H_2O$; C, 69.22; H, 5.91; N, 1.42. Found: C, 69.05; H, 5.81; N, 1.34.

p-*Methoxyphenyl* O-*(6-*O*-acetyl-2,4-di-*O*-benzyl-3-*O*-levulinoyl-β-*D*-galactopyranosyl)-(1 → 4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**29**).—To a solution **28** (627 mg, 0.64 mmol) in pyridine (6 mL) were added a solution of 0.73 M levulinic anhydride in $(ClCH_2)_2$ (2.8 mL, 2.1 mmol) and a catalytic amount of DMAP. The mixture was stirred for 20 h at 20°C and then coevaporated with toluene. Chromatography of the residue on SiO_2 in 5:2 toluene–EtOAc gave **29** (689 mg, 100%); $[\alpha]_D$ +41.8° (*c* 1.6); R_f 0.32 (3:1 toluene–EtOAc). ^{1}H NMR data ($CDCl_3$): δ 5.609 (1 H, d, *J* 8.4 Hz, H-1a), 4.856 (1 H, dd, *J* 10.3 and 2.9 Hz,

H-3b), 4.511 (1 H, d, *J* 7.7 Hz, H-1b), 4.429 (1 H, t, *J* 9.5 Hz, H-3a), 4.353 (1 H, dd, *J* 9.5 and 8.4 Hz, H-2a), 3.916 (1 H, dd, *J* 11.0 and 7.0 Hz, H-6b), 3.843 (1 H, dd, *J* 11.0 and 4.4 Hz, H-6a), 3.817 (1 H, d, *J* 2.9 Hz, H-4b), 3.791 (1 H, dd, *J* 10.3 and 7.7 Hz, H-2b), 3.693 (3 H, s, OMe), 3.503 (1 H, t, *J* 7.0 Hz, H-5b), 2.151 (3 H, s, Ac or $CH_2CO\mathit{Me}$), and 1.983 (3 H, s, Ac or $CH_2CO\mathit{Me}$). Anal. Calcd for $C_{62}H_{63}NO_{16}$: C, 69.07; H, 5.89; N, 1.30. Found: C, 68.77; H, 5.91; N, 1.19.

O-(6-O-Acetyl-2,4-di-O-benzyl-3-O-levulinoyl-β-D-galactopyranosyl)-(1 → 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-D-glucopyranose (**30**).—A mixture of **29** (661 mg, 0.61 mmol) and ammonium cerium(IV) nitrate (3.37 g, 6.15 mmol) in 1:1:15:1 toluene–MeCN–H_2O (165 mL) was vigorously stirred for 7 h at 20°C, then diluted with EtoAc. The organic layer was washed successively with aq $NaHCO_3$ and aq NaCl, dried (Na_2SO_4) and evaporated in vacuo. Chromatography of the residue on SiO_2 in 3:2 toluene–EtOAc gave **30** (481 mg, 81%); R_f 0.45 and 0.35 (3:2 toluene–EtOAc). ^1H NMR data ($CDCl_3$–D_2O): δ 5.292 (1 H, d, *J* 8.5 Hz, H-1a), 4.807 (1 H, dd, *J* 10.1 and 3.1 Hz, H-3b), 4.430 (1 H, d, *J* 7.6 Hz, H-1b), 3.800 (1 H, d, *J* 3.1 Hz, H-4b), 3.763 (1 H, dd, *J* 10.1 and 7.6 Hz, H-2b), 3.452 (1 H, t, *J* 6.7 Hz, H-5b), 2.155 (3 H, s, Ac or $CH_2CO\mathit{Me}$), and 1.971 (3 H, s, Ac or $CH_2CO\mathit{Me}$). Anal. Calcd for $C_{55}H_{57}NO_{15}$: C, 67.96; H, 5.91; N, 1.44. Found: C, 67.63; H, 5.90; N, 1.37.

O-(6-O-Acetyl-2,4-di-O-benzyl-3-O-levulinoyl-β-D-galactopyranosyl)-(1 → 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl trichloroacetimidate (**9**).—To a stirred solution of **30** (165 mg, 0.17 mmol) in $(ClCH_2)_2$ (3 mL) were added CCl_3CN (0.17 mL, 1.7 mmol) and DBU (2.5 μL, 0.017 mmol) at −20°C. The mixture was stirred for 30 min at −20°C, then directly chromatographed on SiO_2 in 2:1 toluene–EtOAc to give **9** (183 mg, 97%); $[\alpha]_D$ +57.7° (*c* 1.0); R_f 0.45 (5:2 toluene–EtOAc). ^1H NMR data ($CDCl_3$): δ 8.522 (1 H, s, NH), 6.329 (1 H, d, *J* 8.8 Hz, H-1a), 4.850 (1 H, d, *J* 12.5 Hz, benzyl), 4.817 (1 H, dd, *J* 10.3 and 3.3 Hz, H-3b), 4.474 (1 H, d, *J* 10.6 and 8.8 Hz, H-2a), 4.399 (1 H, dd, *J* 10.6 and 8.4 Hz, H-3a), 4.213 (1 H, dd, *J* 9.9 and 8.4 Hz, H-4a), 3.802 (1 H, d, *J* 3.3 Hz, H-4b), 3.771 (1 H, dd, *J* 10.3 and 7.3 Hz, H-2b), 2.154 (3 H, s, Ac or $CH_2CO\mathit{Me}$), and 1.988 (3 H, s, Ac or $CH_2CO\mathit{Me}$). Anal. Calcd for $C_{57}H_{57}Cl_3N_2O_{15} \cdot 0.5$toluene: C, 62.51; H, 5.29; N, 2.41. Found: C, 63.01; H, 5.30; N, 2.34.

Benzyl O-(6-O-acetyl-2,4-di-O-benzyl-3-O-levulinoyl-β-D-galactopyranosyl)-(1 → 4)-O-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1 → 3)-O-(2,4,6-tri-O-benzyl-β-D-galactopyranosyl)-(1 → 4)-3,6-di-O-benzyl-2-O-pivaloyl-β-D-glucopyranoside (**31**).—To a stirred mixture of compounds **11** (913 mg, 0.94 mmol) and **9** (474 mg, 0.43 mmol) and 4A molecular sieves (2 g) in $(ClCH_2)_2$ (14 mL) was added Me_3SiOTf (17 μL, 0.088 mmol) at −20°C. The mixture was stirred for 30 min at −20°C, quenched with Et_3N, diluted with EtOAc, and filtered through Celite. The filtrate was washed successively with aq $NaHCO_3$ and aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. The residue was chromatographed on SiO_2 in 3:2 hexane–EtOAc to give **31** (703 mg, 86%); $[\alpha]_D$ −3.8° (*c* 1.7); R_f 0.46 (3:1 toluene–EtOAc). ^1H NMR data: δ 5.369 (1 H, d, *J* 8.5 Hz, H-1c), 5.021 (1 H, dd, *J*

9.2 and 8.0 Hz, H-2a), 4.856 (1 H, dd, *J* 10.3 and 3.3 Hz, H-3d) 4.526 (1 H, d, *J* 7.7 Hz, H-1d), 4.493 (1 H, dd, *J* 10.8 and 8.5 Hz, H-3c), 4.286 (1 H, d, *J* 8.0 Hz, H-1a), 4.262 (1 H, dd, *J* 10.8 and 8.5 Hz, H-2c), 4.225 (1 H, d, *J* 7.7 Hz, H-1b), 3.956 (1 H, d, *J* 3.1 Hz, H-4b), 3.808 (1 H, d, *J* 3.3 Hz, H-4d), 3.788 (1 H dd, *J* 10.3 and 7.7 Hz, H-2d), 3.530 (1 H, dd, *J* 9.8 and 3.1 Hz, H-3b), 3.440 (1 H, dd, *J* 9.7 and 7.7 Hz, H-2b), 3.395 (1 H, t, *J* 9.2 Hz, H-3a), 2.153 (3 H, s, Ac or $CH_2CO\mathit{Me}$), 1.935 (3 H, s, Ac or $CH_2CO\mathit{Me}$), and 1.082 (9 H, s, ^{t}Bu). Anal. Calcd for $C_{114}H_{121}NO_{26}$ C, 71.27; H, 6.35; N, 0.73. Found: C, 71.01; H, 6.36; N, 0.55.

Benzyl O-*(6-*O*-acetyl-2,4-di-*O*-benzyl-β-*D*-galactopyranosyl)-(1 → 4)-*O*-(2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranosyl)-(1 → 3)-(2,4,6-tri-*O*-benzyl-β-*D*-galactopyranosyl)-(1 → 4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-*D*-glucopyranoside* (**33**).—To a solution of **31** (703 mg, 0.37 mmol) in EtOH (45 mL) were added $NH_2NH_2 \cdot H_2O$ (1.36 mL, 27 mmol). The mixture was stirred for 48 h under reflux, and then evaporated in vacuo. To the solution of the residue in MeOH (18 mL) was added Ac_2O (1 mL, 10 mmol), and the mixture was stirred for 30 min at 20°C and then coevaporated with toluene. Chromatography of the residue on SiO_2 in toluene–EtOAc gave **32** (206 mg, 34%) and **33** (411 mg, 65%).

Compound **32** had: $[\alpha]_D$ −5.7° (*c* 0.9); R_f 0.14 (5:2 toluene–EtOAc). ^{1}H NMR data ($CDCl_3$) δ 5.092 (1 H, dd, *J* 9.5 and 8.1 Hz, H-2a), 5.031 (1 H, d, *J* 8.4 Hz, N*H*Ac), 4.948 (1 H, d, *J* 8.1 Hz, H-1c), 1.418 (3 H, s, NAc), and 1.118 (9 H, s, ^{t}Bu). Anal. Calcd for $C_{101}H_{113}NO_{22}$: C, 71.65; H, 6.73; N, 0.86. Found: C, 71.30; H, 6.72; N, 0.66.

Compound **33** had: $[\alpha]_D$ −12.7° (*c* 0.7); R_f 0.37 (5:2 toluene–EtOAc). ^{1}H NMR data ($CDCl_3$): δ 5.100 (1 H, d, *J* 8.1 Hz, N*H*Ac), 5.090 (1 H, dd, *J* 9.5 and 8.1 Hz, H-2a), 4.972 (1 H, d, *J* 7.7 Hz, H-1c), 3.444 (1 H, t, *J* 6.6 Hz, H-5b or 5d), 1.921 (3 H, s, Ac), 1.491 (3 H, s, NAc), and 1.116 (9 H, s, ^{t}Bu). Anal. Calcd for $C_{103}H_{115}NO_{23}$: C, 71.30; H, 6.68; N, 0.81. Found: C, 71.01; H, 6.70; N, 0.66.

To an ice-cold solution of **32** (162 mg, 0.096 mmol) in pyridine (3 mL) was added AcCl (20 μL, 0.28 mmol). The mixture was stirred for 1.5 h at 0°C, and coevaporated with toluene–MeOH in vacuo. Chromatography of the residue on SiO_2 in 5:2 toluene–EtOAc gave **33** (142 mg, 86%).

Benzyl O-*[methyl 3-*O*-levulinoyl-2,4-di-*O*-(p-methylbenzoyl)-β-*D*-glucopyranosyl uronate]-(1 → 3)-*O*-(6-*O*-acetyl-2,4-di-*O*-benzyl-β-*D*-galactopyranosyl)-(1 → 4)-*O*-(2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranosyl)-(1 → 3)-*O*-(2,4,6-tri-*O*-benzyl-β-*D*-galactopyranosyl)-(1 → 4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-*D*-glucopyranoside* (**34**).—To a mixture of $CuBr_2$ (415 mg, 1.86 mmol), AgOTf (491 mg, 1.19 mmol), Bu_4NBr (41 mg, 0.127 mmol) and 4A molecular sieves (0.13 g) was added a solution of compounds **8** (435 mg, 0.765 mmol) and **33** (215 mg, 0.124 mmol) in $MeNO_2$ (9 mL). The mixture was stirred for 48 h at 20°C, diluted with EtOAc and aq $NaHCO_3$, and then filtered through Celite. The filtrate was washed with aq NaCl, dried (Na_2SO_4) and evaporated in vacuo. The residue was purified by successive chromatography first on Bio-Beads S-X3 (22 × 900 mm) in toluene and then on SiO_2 in 3:1 toluene–EtOAc to give **34** (163 mg, 58%); $[\alpha]_D$ −17.9° (*c*

0.9); R_f 0.42 (5:2 toluene–EtOAc). ^{1}H NMR data: δ 5.622 (1 H, t, J 9.9 Hz, H-3e), 5.494 (1 H, t, J 9.9 Hz, H-4e), 5.359 (1 H, dd, J 9.9 and 7.7 Hz, H-2e), 5.219 (1 H, d, J 7.7 Hz, H-1e), 4.884 (1 H, d, J 7.7 Hz, H-1a or d), 4.174 (1 H, d, J 9.9 Hz, H-5e), 3.873 (2 H, d, J 2.6 Hz, H-4b and 4d), 3.672 (3 H, s, COOMe), 2.421, 2.340 (6 H, 2s, C_6H_4*Me*), 1.953 (3 H, s, Ac or CH_2CO*Me*), 1.888 (3 H, s, Ac or CH_2CO*Me*), and 1.112 (9 H, s, ^{t}Bu). Anal. Calcd for $C_{131}H_{143}NO_{33}$: C, 69.63; H, 6.38; N, 0.62. Found: C, 69.52; H, 6.48; N, 0.61.

O-[*Methyl 3-O-levulinoyl-2,4-di-O-(*p*-methylbenzoyl)-β-*D*-glucopyranosyluronate]-(1 → 3)-*O*-(2,4,6-tri-O-acetyl-β-*D*-galactopyranosyl)-(1 → 4)-*O*-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-*D*-glucopyranosyl)-(1 → 3)-*O*-(2,4,6-tri-O-acetyl-β-*D*-galactopyranosyl)-(1 → 4)-3,6-di-O-acetyl-2-O-pivaloyl-*D*-glucopyranosyl acetate* (**35**).—A mixture of **34** (356 mg, 0.16 mmol) and 10% Pd–C (380 mg) in MeOH (38 mL) was stirred under H_2 for 20 h at 50°C, diluted with $CHCl_3$ and filtered through Celite. The filtrate was concentrated in vacuo. To a solution of the residue in pyridine (12 mL) were added Ac_2O (4 mL) and DMAP. The mixture was stirred for 1 h at 20°C and then coevaporated with EtOH and toluene in vacuo. Chromatography of the residue on SiO_2 in 4:3 toluene–acetone gave **35** (228 mg, 81%) as a 1:1 mixture of α and β anomers; R_f 0.30 (1:1 toluene–acetone). ^{1}H NMR data ($CDCl_3$): δ 6.285 (0.5 H, d, J 3.7 Hz, H-1aα), 5.691 (0.5 H, d, J 8.1 Hz, H-1aβ), 5.563 (1 H, t, J 9.5 Hz, H-3e or 4e), 5.457 (1 H, d, J 7.3 Hz, H-1e), 5.457 (1 H, d, J 3.3 Hz, H-4b or 4d), 5.288 (1 H, d, J 3.3 Hz, H-4b or 4d), 5.201 (1 H, dd, J 9.5 and 7.3 Hz, H-2e), 4.837 (1 H, d, J 7.3 Hz, H-1c), 4.566 (1 H, d, J 8.1 Hz, H-1b or 1d), 4.189 (1 H, d, J 9.5 Hz, H-5e), 3.690 (3 H, s, COOMe), 2.411, 2.403 (6 H, 2 s, C_6H_4*Me*), 2.156-1.892 (36 H, multi s, 11 Ac and CH_2CO*Me*), 1.689 (3 H, s, NAc), 1.130, and 1.117 (9 H, 2s, ^{t}Bu). Anal. Calcd for $C_{81}H_{103}NO_{43} \cdot 0.5H_2O$: C, 53.61; H, 5.79; N, 0.77. Found: C, 53.34; H, 5.77; N, 0.85.

O-[*Methyl 3-O-levulinoyl-2,4-di-O-(*p*-methylbenzoyl)-β-*D*-glucopyranosyluronate]-(1 → 3)-*O*-(2,4,6-tri-O-acetyl-β-*D*-galactopyranosyl)-(1 → 4)-*O*-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-*D*-glucopyranosyl)-(1 → 3)-*O*-(2,4,6-tri-O-acetyl-β-*D*-galactopyranosyl)-(1 → 4)-3,6-di-O-acetyl-2-O-pivaloyl-*D*-glucopyranose* (**36**).—A mixture of **35** (122 mg, 0.069 mmol) and piperidine acetate (98 mg, 0.68 mmol) in THF (10 mL) was stirred for 22 h at 20°C. The mixture was diluted with water and extracted with EtOAc. The organic layer was washed with aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. Chromatography of the residue on SiO_2 in 4:5 toluene–acetone gave **36** (94.4 mg, 79%), along with recovered **35** (18.4 mg, 15%). Compound **36** had: R_f 0.19 (1:1 toluene–acetone). ^{1}H NMR data ($CDCl_3$–D_2O): δ 5.565 (1 H, t, J 9.5 Hz, H-3e or 4e), 5.480 (1 H, t, J 9.5 Hz, H-3e or 4e), 5.359 (d, J 3.7 Hz, H-1aα), 5.200 (1 H, dd, J 9.5 and 7.3 Hz, H-2e), 4.836 (1 H, d, J 7.3 Hz, H-1c or 1e), 4.379 (1 H, d, J 8.1 Hz, H-1b or 1d), 4.192 (1 H, d, J 9.5 Hz, H-5e), 3.687 (3 H, s, COOMe), 2.411, 2.403 (6 H, 2s, C_6H_4*Me*), 2.148–1.880 (33 H, multi s, 11 Ac and CH_2CO*Me*), 1.699 (3 H, s, NAc), and 1.174 (9 H, s, ^{t}Bu). Anal. Calcd for $C_{79}H_{101}NO_{42} \cdot H_2O$: C, 54.08; H, 5.92; N, 0.80. Found: C, 54.00; H, 6.00; N, 0.76.

O-[Methyl 3-O-levulinoyl-2,4-di-O-(p-methylbenzoyl)-β-D-glucopyranosyluronate]-(1 → 3)-O-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-3,6-di-O-acetyl-2-O-pivaloyl-D-glucopyranosyl fluoride (**5**). —To a solution of **36** (80 mg, 0.046 mmol) in $(ClCH_2)_2$ (2.5 mL) was added diethylaminosulfur trifluoride (20 μL, 0.16 mmol). The mixture was stirred for 10 min at 20°C, diluted with $CHCl_3$, and washed successively with aq $NaHCO_3$ and aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. Chromatography of the residue on SiO_2 in 1:1 toluene–acetone gave **5** (75.4 mg, 93%) as a 1:3 mixture of α and β anomers; R_f 0.37 (1:1 toluene–acetone). ^1H NMR data ($CDCl_3$): δ 5.698 (0.25 H, dd, *J* 53.1 and 2.1 Hz, H-1aα), 5.561 (1 H, t, *J* 9.5 Hz, H-3e), 5.487 (1 H, t, *J* 9.5 Hz, H-4e), 5.313 (0.75 H, dd, *J* 52.5 and 5.8 Hz, H-1aβ), 4.838 (1 H, d, *J* 7.0 Hz, H-1c), 4.378 (1 H, d, *J* 7.6 Hz, H-1b or 1d), 4.190 (1 H, d, *J* 9.5 Hz, H-5e), 3.691 (3 H, s, COOMe), 2.411, 2.402 (6 H, 2s, C_6H_4*Me*), 1.187, and 1.183 (9 H, 2s, ^{t}Bu α and β). Anal. Calcd for $C_{79}H_{100}FNO_{41} \cdot 3H_2O$: C, 52.93; H, 5.96; N, 0.78. Found: C, 53.02; H, 5.70; N, 0.64.

O-[Methyl 3-O-levulinoyl-2,4-di-O-(p-methylbenzoyl)-β-D-glucopyranosyluronate]-(1 → 3)-O-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-O-(3,6-di-O-acetyl-2-O-pivaloyl-β-D-glucopyranosyl)-(1 → 1)-3-O-benzoyl-2R,3S,4E-2-N-tetracosanoylsphingenine (**37**).—To a stirred mixture of $SnCl_2$ (34.4 mg, 0.17 mmol), AgOTf (45.1 mg, 0.18 mmol) and 4A molecular sieves (0.36 g) was added a solution of **5** (73 mg, 0.042 mmol) and **7** (41.2 mg, 0.055 mmol) in freshly distilled $CHCl_3$ (3.5 mL) at −20°C. The mixture was gradually warmed over a period of 20 h to 20°C, diluted with $CHCl_3$, and filtered through Celite. The filtrate was washed successively with aq $NaHCO_3$ and aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. Chromatography of the residue on SiO_2 in 3:2 toluene–acetone gave **37** (57 mg, 55%) and recovered α-fluoride (19.9 mg, 27%).

Compound **37** had: $[\alpha]_D$ +12.4° (*c* 0.6); R_f 0.30 (3:2 toluene–acetone). ^1H NMR data ($CDCl_3$): δ 5.871 (1 H, dt, *J* 14.7 and 7.0 Hz, H-5Cer), 5.744 (1 H, d, *J* 9.5 Hz, NHCer), 5.563 (1 H, t, *J* 9.5 Hz, H-3e), 5.483 (1 H, t, *J* 9.5 Hz, H-4e), 5.268 (1 H, d, *J* 3.4 Hz, H-4b or d), 5.202 (1 H, dd, *J* 9.5 and 7.3 Hz, H-2e), 5.175 (1 H, t, *J* 9.5 Hz, H-3a), 4.947 (1 H, dd, *J* 9.8 and 7.6 Hz, H.2b or d), 4.884 (1 H, dd, *J* 9.5 and 7.9 Hz, H.2a), 4.834 (1 H, d, *J* 7.3 Hz, H-1e), 4.539 (1 H, d, *J* 7.6 Hz, H-1c), 4.409 (1 H, d, *J* 7.9 Hz, H-1a), 4.369 (1 H, d, *J* 7.9 Hz, H-1b or 1d), 4.274 (1 H, d, *J* 7.6 Hz, H-1b or d), 4.189 (1 H, d, *J* 9.5 Hz, H-5e), 3.784 (1 H, t, *J* 6.4 Hz, H-5b or 5d), 3.690 (3 H, s, COOMe), 2.413 and 2.403 (6 H, 2s, $2C_6H_4$*Me*), 1.139 (9 H, s, ^{t}Bu), and 0.879 (6 H, t, *J* 7.0 Hz, $2CH_2$*Me*). Anal. Calcd for $C_{128}H_{186}N_2O_{45} \cdot H_2O$: C, 61.72; H, 7.53; N, 1.12. Found: C, 61.76; H, 7.58; N, 1.05.

O-β-D-Glucopyranosyluronic acid-(1 → 3)-O-β-D-galactopyranosyl-(1 → 4)-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-β-D-galactopyranosyl-(1 → 4)-O-β-D-glucopyranosyl-(1 → 1)-2R,3S,4E-2-N-tetracosanoylsphingenine, sodium salt

(**3**).—To a solution of **37** (3.4 mg, 1.4 μmol) in 24:1 THF–H_2O (1 mL) was added a solution of 1.25 N LiOH (30 μL). The mixture was stirred for 1 h at −15°C, and then gradually warmed to 0°C over 3 h. The resultant mixture was diluted with toluene and evaporated in vacuo. A solution of the residue in 0.15 M NaOMe 1:1 MeOH–THF (1 mL) was stirred for 3 h at 20°C. The mixture was purified by chromatography on a column of Sephadex LH-20 in 6:4:1 $CHCl_3$–MeOH–H_2O to give **3** (1.8 mg, 86%); R_f 0.29 (6:4:0.8 $CHCl_3$–MeOH–H_2O). ^{1}H NMR data (49:1 Me_2SO-d_6—D_2O, 60°C): δ 5.555 (1 H, dt, *J* 15.0 and 7.3 Hz, H-5Cer), 5.372 (1 H, dd, *J* 15.0 and 7.3 Hz, H-4Cer), 4.681 (1 H, d, *J* 7.6 Hz, H-1c), 4.368 (1 H, d, *J* 7.6 Hz, H-1e), 4.317 (1 H, d, *J* 7.6 Hz, H-1b or 1d), 4.279 (1 H, d, *J* 7.3 Hz, H-1b or 1d), 4.174 (1 H, d, *J* 7.6 Hz, H-1a), 1.832 (3 H, s, NAc), and 0.854 (6 H, t, $2CH_2$).

*O-[Methyl 2,4-di-O-(*p*-methylbenzoyl)-β-*D*-glucopyranosyluronate]-(1 → 3)-O-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-O-(3,6-di-O-acetyl-2-O-pivaloyl-β-D-glucopyranosyl)-(1 → 1)-3-O-benzoyl-2*R,*3*S,*4*E-*2*-N-tetracosanoylsphingenine* (**38**).—A mixture of **37** (11.2 mg, 4.5 μmol) and hydrazine–acetic acid (1.4 mg, 15 μmol) in EtOH (1 mL) was stirred for 1 h at 20°C. The mixture was diluted with $CHCl_3$, and then washed successively with aq $NaHCO_3$ and aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. Chromatography of the residue on SiO_2 in 3:2 toluene–acetone gave **38** (1 mg, 100%); R_f 0.28 (3:2 toluene–acetone); [α]D +11.6° (*c* 0.9). ^{1}H NMR data ($CDCl_3$–D_2O): δ 5.872 (1 H, dt, *J* 15.9 and 7.3 Hz, H-5Cer), 5.534 (1 H, t, *J* 7.3 Hz, H-3Cer), 5.449 (1 H, dd, *J* 15.9 and 7.3 Hz, H-4Cer), 5.438 (1 H, t, *J* 9.5 Hz, H-4e), 5.278 (1 H, d, *J* 3.4 Hz, H-4b or d), 4.948 (1 H, dd, *J* 9.8 and 7.9 Hz, H-2b or d), 4.558 (1 H, d, *J* 7.6 Hz, H-1c), 4.409 (1 H, d, *J* 7.9 Hz, H-1a, b or d), 4.403 (1 H, d, *J* 8.2 Hz, H-1a, b or d), 4.274 (1 H, d, *J* 7.9 Hz, H-1a, b or d), 4.224 (1 H, d, *J* 9.5 Hz, H-5e), 3.818 (1 H, t, *J* 6.7 Hz, H-5b or d), 3.708 (3 H, s, COOMe), 2.419 and 2.413 (6 H, 2 s, $2C_6H_4$*Me*), 1.140 (9 H, s, ^{t}Bu), and 0.879 (6 H, t, $2CH_2$*Me*). Anal. Calcd for $C_{123}H_{180}N_2O_{43} \cdot H_2O$: C, 61.74; H, 7.67; N, 1.17. Found: C, 61.64; H, 7.61; N, 1.19.

*O-[Methyl 2,4-di-O-(*p*-methylbenzoyl)-3-O-sulfo-β-*D*-glucopyranosyluronate]-(1 → 3)-O-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-O-(3,6-di-O-acetyl-2-O-pivaloyl-β-D-glucopyranosyl)-(1 → 1)-3-O-benzoyl-2*R,*3*S,*4*E-*2*-N-tetracosanoylsphingenine, sodium salt* (**39**).—A solution of **38** (16 mg, 6.4 μmol) and sulfur trioxide–trimethylamine complex (27.4 mg, 200 μmol) in DMF (0.6 mL) was stirred at 55°C for three days and then cooled to room temperature. MeOH (0.5 mL) and $CHCl_3$ (0.5 mL) were added, and the solution was applied to a column of Sephadex LH-20 and was eluted with 1:1 MeOH–$CHCl_3$. Glycolipid-containing fractions were subsequently passed through a column of Dowex-50 × 2 (Na^+) resin in 9:1 MeOH–H_2O. Final purification on SiO_2 in 8:1 $CHCl_3$–MeOH gave **39** (9.8 mg, 59%) and recovered **38** (4.2 mg, 26%).

Compound **39** had: [α]D +7.7° (*c* 0.4, MeOH); R_f 0.49 (8:1 $CHCl_3$–MeOH).

^{1}H NMR data (CD_3OD): δ 5.775 (1 H, dt, J 15.3 and 7.3 Hz, H-5Cer), 5.461 (1 H, t, J 7.3 Hz, H-3Cer), 5.398 (1 H, dd, J 15.3 and 7.3 Hz, H-4Cer), 5.369 (1 H, d, J 3.4 Hz, H-4b or d), 5.261 (1 H, d, J 3.7 Hz, H-4b or d), 5.199 (1 H, t, J 9.5 Hz, H-4e), 5.006 (1 H, dd, J 9.5 and 7.9 Hz, H-2e), 4.970 (1 H, dd, J 10.4 and 8.9 Hz, H-3c), 4.896 (1 H, d, J 7.9 Hz, H-1e), 4.876 (1 H, t, J 9.5 Hz, H-3e), 4.536 (1 H, d, J 7.9 Hz, H-1b or d), 4.527 (1 H, d, J 8.2 Hz, H-1c), 4.371 (1 H, d, J 7.9 Hz, H-1a, b or d), 4.355 (1 H, d, J 8.2 Hz, H-1a, b or d), 4.214 (1 H, d, J 9.5 Hz, H-5e), 3.743 (3 H, s, COOMe), 3.532 (3 H, s, COOMe), 2.403 and 2.389 (6 H, 2s, $2C_6H_4$*Me*), 1.282 (9 H, s, ^{t}Bu), and 0.895 (6 H, t, $2CH_2$*Me*). Anal. Calcd for $C_{123}H_{179}N_2NaO_{46}S \cdot 2H_2O$: C, 58.79; H, 7.34; N, 1.11. Found: C, 58.78; H, 7.38; N, 1.10.

O-*(3-O-Sulfo-β-*D*-glucopyranosyluronic acid)-(1 → 3)-*O*-β-*D*-galactopyranosyl)-(1 → 4)-*O*-(2-acetamido-2-deoxy-β-*D*-glucopyranosyl)-(1 → 3)-*O*-β-*D*-galactopyranosyl-(1 → 4)-*O*-β-*D*-glucopyranosyl-(1 → 1)-2*R,*3*S,*4*E*-2-N-tetracosanoylsphingenine, disodium salt* (**1**).—To a solution of **39** (3.8 mg, 1.5 μmol) in 24:1 THF–H_2O (1 mL) was added a solution of 1.25 N LiOH (45 μL). The mixture was stirred for 1.5 h at −15°C and then gradually warmed over 5 h to 0°C. The resultant mixture was diluted with toluene and evaporated in vacuo. A solution of the residue in 0.15 M NaOMe 1:1 MeOH–THF (1 mL) was stirred for 3 h at 20°C and then purified on a column of Sephadex LH-20 in 50:45:10 $CHCl_3$–MeOH–H_2O to give **1** (2.5 mg, 99%); R_f 0.26 (6:4:0.8 $CHCl_3$–MeOH–H_2O). ^{1}H NMR data (49:1 Me_2SO-d_6–D_2O, 60°C); δ 5.541 (1 H, dt, J 15.0 and 7.0 Hz, H-5Cer), 5.372 (1 H, dd, J 15.0 and 7.0 Hz, H-4Cer), 4.675 (1 H, d, J 8.2 Hz, H-1c), 4.514 (1 H, d, J 7.6 Hz, H-1e), 4.310 (1 H, d, J 7.6 Hz, H-1b or 1d), 4.280 (1 H, d, J 7.3 Hz, H-1b or -1d), 4.172 (1 H, d, J 7.9 Hz, H-1a), 3.995 (1 H, t, J 9.1 Hz, H-3e), 1.827 (3 H, s, NAc), and 0.856 (6 H, t, J 6.8 Hz, $2CH_2$*Me*).

p-*Methoxyphenyl* O-*(2,4-di-*O*-benzyl-6-*O*-pivaloyl-β-*D*-galactopyranosyl)-(1 → 4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside* (**40**).—To a solution of **27** (968 mg, 1.0 mmol) in pyridine (15 mL) were added pivaloyl chloride (0.29 mL, 2.4 mmol) and a catalytic amount of DMAP. The mixture was stirred for 2 h at 20°C and then coevaporated with EtOH and toluene. The residue was diluted with EtOAc, and washed with aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. Chromatography of the residue on SiO_2 in 7:1 toluene–EtOAc gave **40** (1.00 g, 95%); $[\alpha]_D$ +52.4° (*c* 1.0); R_f 0.25 (7:1 toluene–EtOAc). ^{1}H NMR data ($CDCl_3$): δ 5.617 (1 H, d, J 7.9 Hz, H-1a), 4.451 (1 H, d, J 8.2 Hz, H-1b), 4.399 and 4.361 (2 H, 2dd, J 10.7 and 7.9 Hz, H-2a, 3a), 4.191 (1 H, dd, J 11.0 and 6.1 Hz, H-6b), 4.106 (1 H, dd, J 10.7 and 7.9 Hz, H-4a), 4.017 (1 H, dd, J 11.0 and 6.1 Hz, H-6b), 3.881 and 3.828 (2 H, 2dd, J 11.0 and 4.3 Hz, H-6a), 3.713 (1 H, d, J 1.8 Hz, H-4b), 3.695 (3 H, s, OMe), 3.522 (1 H, t, J 6.1 Hz, H-5b), and 1.212 (9 H, s, ^{t}Bu). Anal. Calcd for $C_{60}H_{63}NO_{14}$: C, 70.50; H, 6.21; N, 1.37. Found: C, 70.34; H, 6.23; N, 1.39.

p-*Methoxyphenyl* O-*(2,4-di-*O*-benzyl-3-*O*-levulinoyl-6-*O*-pivaloyl-β-*D*-galactopyranosyl)-(1 → 4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranoside*

(**41**).—To a solution of **40** (979 mg, 0.96 mmol) in pyridine (15 mL) were added a solution of 1.08 M levulinic anhydride in $(ClCH_2)_2$ (2.7 mL, 2.9 mmol) and a catalytic amount of DMAP. The mixture was stirred for 20 h at 20°C, and then coevaporated with toluene. Chromatography of the residue on SiO_2 in 6:1 toluene–EtOAc gave **41** (1.00 g, 93%); $[\alpha]_D$ +55.3° (*c* 0.9); R_f 0.32 (3:2 hexane–EtOAc). ^1H NMR data ($CDCl_3$): δ 5.602 (1 H, d, *J* 8.2 Hz, H-1a), 4.843 (1 H, dd, *J* 10.1 and 3.1 Hz, H-3b), 4.487 (1 H, d, *J* 7.6 Hz, H-1b), 4.391 (1 H, dd, *J* 10.7 and 8.2 Hz, H-2a or 3a), 4.346 (1 H, dd, *J* 10.7 and 8.2 Hz, H-2a or 3a), 4.148 (1 H, dd, *J* 11.0 and 6.4 Hz, H-6b), 4.101 (1 H, dd, *J* 9.8 and 8.2 Hz, H-4a), 3.947 (1 H, dd, *J* 11.0 and 6.4 Hz, H-6b), 3.851 (1 H, dd, *J* 11.0 and 4.3 Hz, H-6a), 3.784 (1 H, d, *J* 3.1 Hz, H-4b), 3.695 (3 H, s, OMe), 3.510 (1 H, t, *J* 6.4 Hz, H-5b), 2.140 (3 H, s, $CH_2CO\mathit{Me}$), and 1.200 (9 H, s, ^{t}Bu). Anal. Calcd for $C_{65}H_{69}No_{16}$: C, 69.69; H, 6.21; N, 1.25. Found: C, 69.55; H, 6.23; N, 1.18.

O-2,4-di-O-Benzyl-3-O-levulinoyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranose (**42**).—A mixture of **41** (1.00 g, 0.89 mmol) and ammonium cerium(IV) nitrate (4.917 g, 8.97 mmol) in 1:1.15:1 toluene–MeCN–H_2O (230 mL) was vigorously stirred for 3.5 h at 20°C, then diluted with EtOAc. The organic layer was washed successively with aq $NaHCO_3$ and aq NaCl, dried (Na_2SO_4) and evaporated in vacuo. Chromatography of the residue on SiO_2 in 5:2 toluene–EtOAc gave **42** (785 mg, 87%); R_f 0.35 and 0.30 (5:2 toluene–EtOAc). ^1H NMR data ($CDCl_3$–D_2O): δ 5.318 (0.33 H, d, *J* 3.7 Hz, H-1aα), 5.280 (0.67 H, d, *J* 8.6 Hz, H-1aβ), 3.458 (0.67 H, t, *J* 6.7 Hz, H-5bβ), 3.411 (0.33 H, t, *J* 6.7 Hz, H-5bα), 2.143 (3 H, s, $CH_2CO\mathit{Me}$), 1.185, and 1.167 (9 H, 2s, ^{t}Buα and β). Anal. Calcd for $C_{58}H_{63}NO_{15}$: C, 68.69; H, 6.26; N, 1.38. Found: C, 68.54; H, 6.32; N, 1.30.

O-(2,4-di-O-Benzyl-3-O-levulinoyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl trichloroacetimidate (**10**).—To a stirred solution of **42** (494 mg, 0.49 mmol) in $(ClCH_2)_2$ (4 mL) were added CCl_3CN (0.49 mL, 4.99 mmol) and DBU (14 μL, 0.094 mmol) at −20°C. The mixture was stirred for 1 h at −20°C, then directly chromatographed on SiO_2 in 4:1 toluene–EtOAc to give **10** (550 mg, 98%); $[\alpha]_D$ +65.1° (*c* 0.9); R_f 0.41 (4:1 toluene–EtOAc). ^1H NMR data ($CDCl_3$): δ 8.521 (1 H, s, NH), 6.386 (1 H, d, *J* 8.2 Hz, H-1a), 4.808 (1 H, d, *J* 10.1 and 3.1 Hz, H-3b), 4.142 and 3.943 (2 H, 2dd, *J* 11.0 and 6.7 Hz, H-6b), 3.470 (1 H, t, *J* 6.7 Hz, H-5b), 2.143 (3 H, s, $CH_2CO\mathit{Me}$), and 1.198 (9 H, s, ^{t}Bu). Anal. Calcd for $C_{60}H_{63}Cl_3N_2O_{15}$: C, 62.21; H, 5.48; N, 2.42. Found: C, 62.13; H, 5.51; N, 2.32.

Benzyl O-(2,4-di-O-benzyl-3-O-levulinoyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-O-(3,6-di-O-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1 → 3)-O-(2,-4,6-tri-O-β-D-galactopyranosyl)-(1 → 4)-3,6-di-O-benzyl-2-O-pivaloyl-β-D-glucopyranoside (**43**).—To a stirred mixture of compounds **11** (859 mg, 0.89 mmol) and **10** (543 mg, 0.47 mmol) and 4A molecular sieves (1.8 g) in $(ClCH_2)_2$ (12 mL) was added a solution of 0.84 M Me_3SiOTf in $(ClCH_2)_2$ (111 μL, 0.093 mmol) at −20°C. The mixture was stirred for 2 h at −20°C, neutralized with Et_3N, diluted

with EtOAc, and filtered through Celite. The filtrate was washed successively with aq $NaHCO_3$ and aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. The residue was chromatographed on SiO_2 in 5:1 toluene–EtOAc to give **43** (762 mg, 83%); $[\alpha]_D$ −0.7° (*c* 1.1); R_f 0.31 (5:1 toluene–EtOAc). ^1H NMR data ($CDCl_3$); δ 5.365 (1 H, d, *J* 8.5 Hz, H-1c), 5.011 (1 H, dd, *J* 9.2 and 7.9 Hz, H-2a), 4.841 (1 H, d, *J* 9.2 and 3.4 Hz, H-3d), 3.957 (1 H, d, *J* 3.1 Hz, H-4b), 3.770 (1 H, d, *J* 3.4 Hz, H-4d), 3.768 (1 H, dd, *J* 9.8 and 7.4 Hz, H-2d), 3.529 (1 H, dd, *J* 9.8 and 3.1 Hz, H-3b), 3.440 (1 H, dd, *J* 9.8 and 7.9 Hz, H-2b), 3.397 (1 H, t, *J* 9.2 Hz, H-3a), 2.143 (3 H, s, $CH_2CO\mathit{Me}$), 1.133 and 1.082 (18 H, 2s, 2^{t}Bu). Anal. Calcd for $C_{117}H_{127}NO_{26}$: C, 71.58; H, 6.52; N, 0.71. Found: C, 71.37; H, 6.50; N, 0.67.

Benzyl O-*(2,4-di-*O*-benzyl-6-*O*-pivaloyl-β-*D*-galactopyranosyl)-(1 → 4)-*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)-(1 → 3)-*O*-(2,4,6-tri-*O*-benzyl-β-*D*-galactopyranosyl)-(1 → 4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-*D*-glucopyranoside* (**44**). —A mixture of **43** (739 mg, 0.38 mmol) and hydrazine–acetic acid (173 mg, 19 mmol) in 4:1 EtOH–THF (70 mL) was stirred for 1.5 h at 20°C. The mixture was diluted with $CHCl_3$ and then washed with aq $NaHCO_3$, aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. Chromatography of the residue on SiO_2 in 2:1 hexane–EtOAc gave **44** (426 mg, 61%); $[\alpha]_D$ 0° (*c* 1.3); R_f 0.27 (2:1 hexane–EtOAc). ^1H NMR data $CDCl_3$) δ 5.379 (1 H, d, *J* 8.5 Hz, H-1c), 5.012 (1 H, dd, *J* 9.5 and 8.2 Hz, H-2a), 4.289 (1 H, d, *J* 7.9 Hz, H-1a, 1b or 1d), 4.237 (1 H, d, *J* 7.6 Hz, H-1a, 1b or 1d), 4.226 (1 H, dd, *J* 9.8 and 8.5 Hz, H-2c or 3c), 4.141 (1 H, dd, *J* 11.0 and 6.7 Hz, H-6d), 4.094 (1 H, dd, *J* 9.8 and 8.9 Hz, H-4c), 3.985 (1 H, d, *J* 2.4 Hz, H-4b), 3.700 (1 H, d, *J* 1.5 Hz, H-4d), 3.446 (1 H, dd, *J* 9.8 and 7.6 Hz, H-2b), 3.399 (1 H, t, *J* 9.5 Hz, H-3a), 1.144 and 1.082 (18 H, 2s, 2^{t}Bu). Anal. Calcd for $C_{112}H_{121}NO_{24}$: C, 72.12; H, 6.54; N, 0.75. Found: C, 72.25; H, 6.57; N, 0.81.

Benzyl O-*(2,4-di-*O*-benzyl-3-*O*-levulinoyl-6-*O*-pivaloyl-β-*D*-galactopyranosyl)-(1 → 4)-*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)-(1 → 3)-*O*-(2,4-di-*O*-benzyl-6-*O*-pivaloyl-β-*D*-galactopyranosyl)-(1 → 4)-*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-*D*-glucopyranosyl)-(1 → 3)-*O*-(2,4,6-tri-*O*-benzyl-β-*D*-galactopyranosyl)-(1 → 4)-3,6-di-*O*-benzyl-2-*O*-pivaloyl-β-*D*-glucopyranoside* (**45**).—To a stirred mixture of compounds **44** (624 mg, 0.34 mmol) and **10** (412 mg, 0.36 mmol) and 4A molecular sieves (1.9 g) in $(ClCH_2)_2$ (10 mL) was added a solution of 0.84 M Me_3SiOTf in $(ClCH_2)_2$ (60 μL, 0.05 mmol) at −20°C. The mixture was stirred for 1 h at −20°C, quenched with Et_3N, diluted with EtOAc, and filtered through Celite. The filtrate was washed successively with aq $NaHCO_3$ and aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. The residue was purified by successive chromatography, first on SiO_2 in 3:2 hexane–EtOAc and then on Bio-Beads S-X3 (22 × 900 mm) in toluene to give **45** (773 mg, 81%); $[\alpha]_D$ −0.4° (*c* 0.8); R_f 0.43 (5:1 toluene–EtOAc). ^1H NMR data $CDCl_3$); δ 5.387 (1 H, d, *J* 8.3 Hz, H-1c or 1e), 5.191 (1 H, d, *J* 8.3 Hz, H-1c or 1e), 4.933 (1 H, dd, *J* 9.5 and 8.1 Hz, H-2a), 4.819 (1 H, dd, *J* 10.0 and 3.2 Hz, H-3f), 4.267 (2 H, 2d, *J* 8.1 Hz, H-1a and 1b or 1d), 4.299 and 4.101 (2 H, 2dd, *J* 10.7 and 8.3 Hz, H-2c,2e), 3.806 (1 H, d, *J* 3.2 Hz, H-4f), 3.756 (1 H, d, *J* 3.2 Hz, H-4b or 4d), 2.146 (3 H, s, $CH_2CO\mathit{Me}$), 1.139 (9 H,

s, ^{t}Bu), and 1.072 (18 H, s, 2^{t}Bu). Anal. Calcd for $C_{170}H_{182}NO_{38}$: C, 71.36; H, 6.41; N, 0.98. Found: C, 71.37; H, 6.46; N, 0.96.

Benzyl O-(2,4-di-O-benzyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4-di-O-benzyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4,6-tri-O-benzyl-β-D-galactopyranosyl)-(1 → 4)-3,6-di-O-benzyl-2-O-pivaloyl-β-D-glucopyranoside (**46**).—To a solution of **45** (457 mg, 0.16 mmol) in EtOH (40 mL) were added hydrazine hydrate (1.25 mL, 26 mmol). The mixture was stirred for 50 h under reflux and evaporated in vacuo. The residue was purified by chromatography on SiO_2 in 3:1 toluene–EtOAc and then evaporated in vacuo. To the solution of the residue in MeOH (11 mL) was added Ac_2O (0.4 mL, 4.2 mmol), and the mixture was stirred for 2 h at 20°C and coevaporated with toluene. Chromatography of the residue on SiO_2 in 3:1 toluene–EtOAc gave **46** (335 mg, 81%); $[\alpha]_D$ −1.8° (*c* 0.9); R_f 0.33 (5:2 toluene–EtOAc). ^{1}H NMR data ($CDCl_3$); δ 5.176 (1 H, d, *J* 8.2 Hz, NHAc), 5.125 (1 H, dd, *J* 9.5 and 7.9 Hz, H-2a), 5.092 (1 H, d, *J* 7.9 Hz, H-1c or 1e), 5.073 (1 H, d, *J* 7.9 Hz, H-1c or 1d), 1.423 and 1.390 (6 H, 2s, 2NAc), 1.143, 1.113, and 1.073 (27 H, 3s, 3^{t}Bu). Anal. Calcd for $C_{153}H_{176}NO_{34} \cdot 0.5H_2O$: C, 70.54; H, 6.89; N, 1.08. Found: C, 70.51; H, 6.84; N, 1.05.

Benzyl O-[methyl 3-O-levulinoyl-2,4-di-O-(p-methylbenzoyl)-β-D-glucopyranosyluronate]-(1 → 3)-O-(2,4-di-O-benzyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4-di-O-benzyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4,6-tri-O-benzyl-β-D-galactopyranosyl)-(1 → 4)-3,6-di-O-benzyl-2-O-pivaloyl-β-D-glucopyranoside (**47**).—To a mixture of $CuBr_2$ 424 mg, 1.9 mmol), AgOTf (600 mg, 2.3 mmol), Bu_4NBr (31 mg, 0.099 mmol), and 4A molecular sieves (1 g) was added a solution of compounds **8** (320 mg, 0.56 mmol) and **46** (233 mg, 0.09 mmol) in $MeNO_2$ (8 mL), and the mixture was stirred at 20°C. After 3 h, a solution of **8** (102 mg, 0.178 mmol) in $MeNO_2$ (1.5 mL) was added, and stirring was continued for additional 2 h at 20°C. The mixture was diluted with EtOAc and aq $NaHCO_3$ and then filtered through Celite. The filtrate was washed with aq NaCl, dried (Na_2SO_4) and evaporated in vacuo. The residue was purified by successive chromatography, first on Bio-Beads S-X4 (22 × 900 mm) in toluene and then on SiO_2 in 1:1 hexane–EtOAc, to give **47** (174 mg, 62%); R_f 0.27 (1:1 hexane–EtOAc); $[\alpha]_D$ −13.1° (*c* 1.3). ^{1}H NMR data ($CDCl_3$): δ 5.626 (1 H, t, *J* 9.5 Hz, H-3g), 5.506 (1 H, t, *J* 9.5 Hz, H-4g), 5.469 (1 H, dd, *J* 9.5 and 7.6 Hz, H-2g), 5.186 (1 H, d, *J* 7.6 Hz, H-1g), 5.124 (1 H, d, *J* 7.9 Hz, N*H*Ac), 5.083 (1 H, dd, *J* 9.8 and 7.9 Hz, H-2a), 5.057 (1 H, d, *J* 8.2 Hz, N*H*Ac), 4.189 (1 H, d, *J* 9.5 Hz, H-5g), 3.666 (3 H, s, COOMe), 2.418, 2.327 (6 H, 2s, 2C_6H_4*Me*), 1.885 (3 H, s, CH_2CO*Me*), 1.393 and 1.385 (6 H, 2s, 2NAc), 1.134, 1.113, and 1.058 (27 H, 3s, 3^{t}Bu). Anal. Calcd for $C_{181}H_{204}N_2O_{44}$: C, 69.87; H, 6.61; N, 0.90. Found: C, 69.55; H, 6.62; N, 0.81.

O-[Methyl 3-O-levulinoyl-2,4-di-O-(p-methylbenzoyl)-β-D-glucopyranosyluronate]-(1 → 3)-O-(2,4-di-O-acetyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4-di-O-acetyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-O-3,6-di-O-acetyl-2-O-pivaloyl-D-glucopyranosyl acetate (**48**).—A mixture of **47** (210 mg, 0.068 mmol) and 10% Pd–C (240 mg) in MeOH (34 mL) was stirred under H_2 for 20 h at 50°C, diluted with $CHCl_3$ and filtered through Celite. The filtrate was concentrated in vacuo. To a solution of the residue in pyridine (12 mL) were added Ac_2O (4 mL) and DMAP. The mixture was stirred for 1 h at 20°C and then coevaporated with EtOH and toluene. Chromatography of the residue on SiO_2 in 4:5 toluene–acetone gave **48** (137 mg, 83%) as a 1:1 mixture of the α and β anomers; R_f 0.34 (4:5 toluene–EtOAc). ^{1}H NMR data ($CDCl_3$): δ 6.288 (0.5 H, d, *J* 3.7 Hz, H-1aα), 5.694 (0.5 H, d, *J* 8.2 Hz, H-1aβ), 5.562 (1 H, t, *J* 9.5 Hz, H-3g), 5.489 (1 H, t, *J* 9.5 Hz, H-4g), 5.430 (1 H, d, *J* 3.7 Hz, H-4b, 4d or 4f), 5.196 (1 H, dd, *J* 9.5 and 7.3 Hz, H-2g), 4.819 (1 H, d, *J* 7.3 Hz, H-1g), 4.604 (1 H, d, *J* 7.3 Hz, H-1c), 4.343 and 4.335 (2 H, 2d, *J* 7.9 Hz, H-1b, 1d or 1f), 4.176 (1 H, d, *J* 9.5 Hz, H-5g), 3.679 (3 H, s, COOMe), 2.410 and 2.402 (6 H, 2s, $2C_6H_4Me$). Anal. Calcd for $C_{111}H_{148}N_2O_{58} \cdot H_2O$: C, 54.28; H, 6.16; N, 1.14. Found: C, 54.17; H, 6.03; N, 1.37.

O-[Methyl 3-O-levulinoyl-2,4-di-O-(p-methylbenzoyl)-β-D-glucopyranosyluronate]-(1 → 3)-O-(2,4-di-O-acetyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4-di-O-acetyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-O-3,6-di-O-acetyl-2-O-pivaloyl-D-glucopyranose (**49**).—A mixture of **48** (137 mg, 0.056 mmol) and piperidine acetate (65 mg, 0.45 mmol) in THF (10 mL) was stirred for 49 h at 20°C. The mixture was diluted with water and extracted with $CHCl_3$. The organic layer was washed with aq NaCl, dried (Na_2SO_4) and evaporated in vacuo. Chromatography of the residue on SiO_2 in 2:3 toluene–acetone gave **49** (118 mg, 88%); R_f 0.36 (2:3 toluene–acetone). ^{1}H NMR data ($CDCl_3$): δ 5.556 (1 H, t, *J* 9.5 Hz, H-3g), 5.483 (1 H, t, *J* 9.5 Hz, H-4g), 5.434 (1 H, d, *J* 3.1 Hz, H-4b, 4d or 4f), 5.350 (1 H, d, *J* 3.7 Hz, H-4b, 4d or 4f), 5.198 (1 H, dd, *J* 9.5 and 7.6 Hz, H-2g), 4.821 (1 H, d, *J* 7.6 Hz, H-1g), 4.600 (1 H, d, *J* 7.6 Hz, H-1c or 1e), 4.355 and 4.328 (2 H, 2d, *J* 7.9 Hz, H-1b, 1d or 1f), 4.180 (1 H, d, *J* 9.5 Hz, H-5g), 3.670 (3 H, s, COOMe), 2.411, 2.403 (6 H, 2s, C_6H_4Me), 1.212, 1.209, 1.203, 1.117, and 1.172 (27 H, 5s, ^{t}Bu). Anal. Calcd for $C_{109}H_{146}N_2O_{57} \cdot$ toluene: C, 55.99; H, 6.24; N, 1.13. Found: C, 56.25; H, 6.68; N, 1.37.

O-[Methyl-3-O-levulinoyl-2,4-di-O-(p-methylbenzoyl)-β-D-glucopyranosyluronate]-(1 → 3)-O-(2,4-di-O-acetyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4-di-O-acetyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-O-

3,6-di-O-acetyl-2-O-pivaloyl-D-glucopyranosyl fluoride (**6**).—To a solution of **49** (48 mg, 20 μmol) in $(ClCH_2)_2$ (2.5 mL) was added diethylaminosulfur trifluoride (10 μL, 82 μmol). The mixture was stirred for 10 min at 0°C and then 1.5 h at 20°C. The mixture was diluted with $CHCl_3$ and washed successively with aq $NaHCO_3$ and aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. Chromatography of the residue on SiO_2 in 4:5 toluene–acetone gave **6** (44 mg, 92%) as a 1:4 mixture of the α and β anomers; R_f 0.36 (4:5 toluene–acetone). ^1H NMR data ($CDCl_3$): δ 5.649 (0.2 H, dd, *J* 53.4 and 2.7 Hz, H-1aα), 5.563 (1 H, t, *J* 9.5 Hz, H-3g), 5.488 (1 H, t, *J* 9.5 Hz, H-4g), 5.311 (0.8 H, dd, *J* 52.8 and 5.8 Hz, H-1aβ), 5.305 (1 H, d, *J* 2.7 Hz, H-4b, 4d or 4f), 5.289 (1 H, d, *J* 3.7 Hz, H-4b, 4d or 4f), 5.197 (1 H, dd, *J* 9.5 and 7.3 Hz, H-2g), 4.820 (1 H, d, *J* 7.3 Hz, H-1g), 4.689 and 4.608 (2 H, 2d, *J* 7.6 Hz, H-1c and 1e), 4.333 (1 H, d, *J* 7.9 Hz, H-1b, 1d or 1f), 4.177 (1 H, d, *J* 9.5 Hz, H-5g), 3.678 (3 H, s, COOMe), 2.410, 2.402 (6 H, 2s, $2C_6H_4$*Me*), 1.212 (9 H, s, ^{t}Bu), 1.209 (9 H, s, ^{t}Bu), 1.189 and 1.186 (9 H, 2s, ^{t}Bu). Anal. Calcd for $C_{109}H_{145}FN_2O_{56}$ · toluene: C, 55.94; H, 6.19; N, 1.12. Found: C, 56.17; H, 6.50; N, 1.13.

O-*[Methyl 3-O-levulinoyl-2,4-di-O-(*p*-methylbenzoyl)-β-D-glucopyranosyluronate]-(1 → 3)-O-(2,4-di-O-acetyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4-di-O-acetyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-O-(3,6-di-O-acetyl-2-O-pivaloyl-β-D-glucopyranosyl)-(1 → 1)-3-O-benzoyl-2*R, *3*S,*4*E-*2*-N-*tetracosanoylsphingenine* (**50**).—To a stirred mixture of $SnCl_2$ (57 mg, 0.29 mmol), AgOTf (45 mg, 0.29 mmol) and 4A molecular sieves (0.32 g) was added a solution of **6** (92 mg, 0.038 mmol) and **7** (44 mg, 0.058 mmol) in freshly distilled $CHCl_3$ (3.5 mL) at −20°C. The mixture was gradually warmed up over 20 h to 20°C, diluted with $CHCl_3$, and filtered through Celite. The filtrate was washed successively with aq $NaHCO_3$ and aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. Chromatography of the residue on SiO_2 in 4:3 toluene–acetone gave **50** (55 mg, 46%) and recovered α-fluoride (13 mg, 14%).

Compound **50** had: $[\alpha]_D$ +10.5° (*c* 1.1); R_f 0.20 (4:3 CCl_4–acetone). ^1H NMR data ($CDCl_3$): δ 5.870 (1 H, dt, *J* 15.0 and 7.6 Hz, H-5Cer), 5.723 (1 H, d, *J* 9.5 Hz, N*H*Cer), 5.563 (1 H, t, *J* 9.5 Hz, H-3g), 5.573 (1 H, t, *J* 7.6 Hz, H-3Cer), 5.489 (1 H, t, *J* 9.5 Hz, H-4g), 5.454 (1 H, dd, *J* 15.0 and 7.6 Hz, H-4Cer), 5.431 (1 H, d, *J* 3.1 Hz, H-4b, 4d or 4f), 5.372 (1 H, d, *J* 7.9 Hz, N*H*Ac), 5.326 (1 H, d, *J* 8.2 Hz, N*H*Ac), 5.285 (1 H, d, *J* 3.4 Hz, H-4b, 4d or 4f), 5.196 (1 H, dd, *J* 9.5 and 7.3 Hz, H-2g), 5.180 (1 H, t, *J* 9.5 Hz, H-3a), 4.887 (1 H, dd, *J* 9.5 and 7.9 Hz, H-2a), 4.819 (1 H, d, *J* 7.3 Hz, H-1g), 4.652 (1 H, d, *J* 7.6 Hz, H-1c or 1e), 4.599 (1 H, d, *J* 7.3 Hz, H-1c or 1e), 4.412 (1 H, d, *J* 7.9 Hz, H-1b, 1d or 1f), 4.284 (1 H, d, *J* 8.2 Hz, H-1b, 1d or 1f), 4.176 (1 H, d, *J* 9.5 Hz, H-5g), 3.679 (3 H, s, COOMe), 2.409 and 2.401 (6 H, 2s, $2C_6H_4$*Me*), 1.212, 1.206, and 1.141 (27 H, 3s, 3^{t}Bu), and 0.879 (6 H, t, *J* 7.0 Hz, $2CH_2$*Me*). Anal. Calcd for $C_{158}H_{231}N_3O_{60}$ · $3H_2O$: C, 59.55; H, 7.50; N, 1.32. Found: C, 59.29; H, 7.36; N, 1.21.

O-β-D-Glucopyranosyluronic acid-(1 → 3)-O-β-D-galactopyranosyl-(1 → 4)-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-β-D-galactopyranosyl-(1 → 4)-O-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-β-D-galactopyranosyl-(1 → 4)-O-β-D-glucopyranosyl-(1 → 1)-2R,3S,4E-2-N-tetracosanoylsphingenine, sodium salt (**4**).—To a solution of **50** (6.0 mg, 1.9 μmol) in 97:3 THF–H_2O (2 mL) was added a solution of 1.25 N LiOH (70 μL). The mixture was stirred for 1 h at −15°C and then gradually warmed over 4 h to 0°C. The resultant mixture was diluted with toluene and evaporated in vacuo. A solution of the residue in 0.15 M NaOMe–1:1 MeOH–THF (1 mL) was stirred for 6 h at 20°C, neutralized with solid CO_2, and then evaporated in vacuo. Chromatography of the residue over Sephadex LH-20 in 6:4:1 $CHCl_3$–MeOH–H_2O gave **4** (2.5 mg, 68%); R_f 0.54 (6:3:0.8 $CHCl_3$–MeOH–H_2O). ^{1}H NMR data (49:1 Me_2SO-d_6–D_2O, 60°C): δ 5.558 (1 H, dt, *J* 15.4 and 7.0 Hz, H-5Cer), 5.375 (1 H, dd, *J* 15.4 and 7.0 Hz, H-4Cer), 4.688 (2 H, d, *J* 8.1 Hz, H-1c, 1e), 4.369 (1 H, d, *J* 7.7 Hz, H-1g), 4.318 (1 H, d, *J* 7.7 Hz, H-1b, 1d or 1f), 4.283 (2 H, d, 7.7 Hz, H-1b, 1d or 1f), 4.174 (1 H, d, *J* 7.7 Hz, H-1a), and 0.856 (6 H, t, *J* 7.0 Hz, $2CH_2CH_3$).

O-[Methyl-2,4-di-O-(p-methylbenzoyl)-β-D-glucopyranosyluronate]-(1 → 3)-O-(2,4-di-O-acetyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4-di-O-acetyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-O-(3,6-di-O-acetyl-2-O-pivaloyl-β-D-glucopyranosyl)-(1 → 1)-3-O-benzoyl-2R,3S,4E-2-N-tetracosanoylsphingenine (**51**).—A mixture of **50** (21 mg, 6.7 μmol) and hydrazine–acetic acid (1.4 mg, 15 μmol) in EtOH (3 mL) was stirred for 1 h at 20°C. The mixture was diluted with $CHCl_3$ and then washed successively with aq $NaHCO_3$ and aq NaCl, dried (Na_2SO_4), and evaporated in vacuo. Subsequent purification on preparative TLC (4:3 CCl_4–acetone) gave **51** (15.5 mg, 76%); $[\alpha]_D$ +11.6° (*c* 1.0); R_f 0.26 (5:4 toluene–acetone). ^{1}H NMR data ($CDCl_3$): δ 5.870 (1 H, dt, *J* 15.3 and 7.6 Hz, H-5Cer), 5.721 (1 H, d, *J* 9.2 Hz, NHAc), 5.535 (1 H, t, *J* 9.5 Hz, H-3Cer), 5.363 (1 H, d, *J* 8.6 Hz, NHAc), 5.177 (1 H, t, *J* 9.5 Hz, H-3a), 5.085 (1 H, dd, *J* 9.6 and 6.4 Hz, H-2g), 5.069, 4.992, and 4.955 (3 H, 3dd, *J* 9.8 and 7.9 Hz, H-2b,2d,2f), 4.884 (1 H, d, *J* 6.4 Hz, H-1g), 4.883 (1 H, dd, *J* 9.8, 7.6 Hz, H-2a), 4.652 and 4.610 (2 H, 2d, *J* 7.6 Hz, H-1c or 1e), 4.408 (1 H, d, *J* 7.6 Hz, H-1a), 4.208 (1 H, d, *J* 9.8 Hz, H-5g), 3.698 (3 H, s, COOMe), 2.418 and 2.411 (6 H, 2s, $2C_6H_4Me$), 1.214, 1.209, and 1.141 (27 H, 3s, 3^tBu), and 0.879 (6 H, t, *J* 7.0 Hz, $2CH_2Me$). Anal. Calcd for $C_{153}H_{225}N_3O_{58}\cdot H_2O$: C, 60.20; H, 7.50; N, 1.38. Found: C, 59.88; H, 7.44; N, 1.46.

O-[Methyl 2,4-di-O-(p-methylbenzoyl)-3-O-sulfo-β-D-glucopyranosyluronate]-(1 → 3)-O-(2,4-di-O-acetyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4-di-O-acetyl-6-O-pivaloyl-β-D-galactopyranosyl)-(1 → 4)-O-(2-acetamido-3,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-O-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1 → 4)-O-(3,6-di-O-acetyl-2-O-pivaloyl-β-D-glucopyranosyl)-(1 → 1)-3-O-benzoyl-2R,3S,4E-2-N-

tetracosanoylsphingenine, sodium salt (**52**).—A solution of **51** (9.4 mg, 3.1 μmol) and sulfur trioxide–trimethylamine complex (18 mg, 130 μmol) in DMF (0.8 mL) was stirred for 66 h at 55°C and then cooled to room temperature. MeOH (0.5 mL) and $CHCl_3$ (0.5 mL) were added, and the solution was applied to a column of Sephadex LH-20 packed in 1:1 MeOH–$CHCl_3$, and elution was carried out in the same solvent. Conversion into the sodium salt by passage through a column of Dowex-50 × 2 (Na^+) resin in 9:1 MeOH–H_2O and purification on preparative TLC (10:1 $CHCl_3$–MeOH) gave **52** (6.9 mg, 71%), together with recovered **51** (2.4 mg, 26%).

Compound **52** had: $[\alpha]_D$ +16.5° (*c* 0.6, MeOH); R_f 0.45 (10:1 $CHCl_3$–MeOH). ^1H NMR data (CD_3OD); δ 5.883 (1 H, dt, *J* 15.3 and 7.0 Hz, H-5Cer), 5.568 (1 H, t, *J* 7.0 Hz, H-3Cer), 5.488 (1 H, dd, *J* 15.3 and 7.0 Hz, H-4Cer), 5.440, 5.362, and 5.348 (3 H, 3d, *J* 3.7 Hz, H-4b,4d,4f), 5.191 (1 H, dd, *J* 9.5 and 7.9 Hz, H-2g), 5.181 (1 H, t, *J* 9.5 Hz, H-3a), 4.976 (1 H, t, *J* 9.5 Hz, H-3g), 4.965 (1 H, d, *J* 7.9 Hz, H-1g), 4.851 (1 H, dd, *J* 9.5 and 7.9 Hz, H-2a), 4.687 and 4.650 (2 H, 2d, *J* 7.9 Hz, H-1c,1e), 4.606 (1 H, d, *J* 7.9 Hz, H-1a), 4.472, 4.432, and 4.420 (3 H, 3d, *J* 7.9 Hz, H-1b,1d,1f), 4.294 (1 H, d, *J* 9.5 Hz, H-5g), 3.628 (3 H, s, COOMe), 2.403, 2.390 (6 H, 2s, $2C_6H_4$*Me*), 1.235, 1.229, and 1.153 (27 H, 3s, 3^tBu), and 0.894 (6 H, t, $2CH_2$*Me*). Anal. Calcd for $C_{153}H_{224}N_3NaO_{61}S \cdot 5H_2O$: C, 56.95; H, 7.31; N, 1.30. Found: C, 56.66; H, 6.96; N, 1.25.

O-*(3-O-Sulfo-β-*D*-glucopyranosyluronic acid)-(1 → 3)*-O-*β-*D*-*galactopyranosyl)-(1 → 4)*-O-*(2-acetamido-2-deoxy-β-*D*-glucopyranosyl)-(1 → 3)*-O-*β-*D*-*galactopyranosyl-(1 → 4)*-O-*(2-acetamido-2-deoxy-β-*D*-glucopyranosyl)-(1 → 3)*-O-*β-*D*-*galactopyranosyl-(1 → 4)*-O-*β-*D*-glucopyranosyl)-(1 → 1)-2*R*,3*S*,4*E*-2-N-tetracosanoylsphingenine, disodium salt* (**2**).—To a solution of **52** (4.6 mg, 1.5 μmol) in 97:3 THF–H_2O (2 mL) was added a solution of 1.25 N LiOH (85 μL) at −15°C. The mixture was gradually warmed over 1 h to 0°C. The resultant mixture was diluted with toluene and evaporated in vacuo. A solution of the residue in 0.15 M NaOMe–1:1 MeOH–THF (0.9 mL) was stirred for 2.5 h at 20°C, neutralized with solid CO_2, and then evaporated in vacuo. Chromatography of the residue over Sephadex LH-20 in 5:5:1 $CHCl_3$–MeOH–H_2O gave **2** (1.1 mg, 37%); R_f 0.47 (6:3:0.8 $CHCl_3$–MeOH–H_2O). ^1H NMR data (49:1 Me_2SO-d_6–D_2O, 60°C): δ 5.605 (1 H, dt, *J* 15.4 and 7.0 Hz, H-5Cer), 5.423 (1 H, dd, *J* 15.4 and 7.0 Hz, H-4Cer), 4.730 (2 H, d, *J* 7.7 Hz, H-1c and 1e), 4.553 (1 H, d, *J* 7.7 Hz, H-1g), 4.359 (1 H, d, *J* 7.3 Hz, H-1b,1d or 1f), 4.332 (2 H, d, *J* 7.3 Hz, H-1b,1d or 1f), 4.221 (1 H, d, *J* 7.7 Hz, H-1a), 4.039 (1 H, t, *J* 8.8 Hz, H-3g), and 0.905 (6 H, t, *J* 7.3 Hz, $2CH_2$*Me*).

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