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Synthesis of lipid A type pyran carboxylic acids with ether chains and their biological activities

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Abstract

Synthesis of lipid A type pyran carboxylic acids having ether chains at both the C-3′ and C-4 positions and their bioactivities toward human U937 cells are described.

Keywords: Lipid A; Endotoxin; LPS-agonist; LPS-antagonist; TNFα production inhibitor

1. Introduction

Endotoxin (lipopolysaccharide; LPS)[1] is a toxic substance of Gram-negative bacteria and one of the components of their outer surface membrane. It is also a highly potent stimulator of the immune system.[2] A variety of responses, both beneficial and harmful, can be elicited by LPS. One of these harmful responses is fatal endotoxic shock (bacterial sepsis) caused as a consequence of acute inflammatory response, and this fatal shock has precluded the clinical use of LPS. Most of the biological activities of LPS reside in a relatively small portion of the molecule, that is, the terminal disaccharide phospholipid subunit known as lipid A, which is a hydrophobic anchor substance holding an essentially linear polysaccharide chain to the cell wall. Analogues of both the nonreducing distal subunit and the reducing sugar part of lipid A are usually still biologically active.[3]

LPS and its related compounds have mainly been investigated as anticancer drugs[4] that function as LPS-agonists by activating macrophages. However, in recent years, lipid A-related compounds have been studied as LPS-antagonists, which may have potential as immunosuppressants,[5] and in autoimmune diseases[5] and septicemia[6] by deactivating LPS-induced aggressive macrophages. For example, Qureshi's group[7] isolated a nontoxic lipid A-related compound from *Rhodobacter sphaeroides* as an LPS antagonist, and an Eisai group recently developed a related compound, E5564,[6,8] as a highly potent anti-septicemia drug.

On the other hand, during our investigation of the biological activities of compounds related to GLA-60,[3a] which is a nonreducing

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distal subunit analogue in the lipid A molecule, we also found that most of them had LPS-agonistic activity, but a few of them behaved as LPS antagonists. The anomeric carboxymethyl GLA-60 analogue **A**[9] and the pyran carboxylic acid **B**[10] exhibited fairly strong LPS-antagonistic activity, and also lipid A-type disaccharides constructed from pyran carboxylic acid **C**[11] showed a strong LPS-antagonistic activity toward human U937 cells. Compound **C** has an acetamido group in the 2′-position, four fatty acid chains, and a carboxylic acid at the anomeric position. Therefore, by using this information on the characteristics of **C**, we synthesized the title compounds which have both C-4–O and C-3′–O ether bonds instead of ester bonds in compound **C**, in order to stabilize the compound and to increase its activity. Herein we report the synthesis of lipid A-type pyran carboxylic acid analogues with ether chains and their activities (Fig. 1).

2. Results and discussion

Synthesis.—First, in Scheme 1, mesylates **5** as side-chain material was prepared from optically active starting diol **2**. The starting diol **2**, easily obtained by lithium aluminum hydride reduction[12] in THF of commercially available (*R*)-3-hydroxytetradecanoic acid, was treated with 4-methoxybenzaldehyde dimethylacetal using *p*-TsOH·H_2O as a catalyst to yield single acetal **3**. The configurations of two substituents of compounds **3** should be equatorial toward the [1,3]dioxane ring, because the equatorial configuration should be more stable than axial. DIBAL reduction of compound **3** in CH_2Cl_2 gave **4** exclusively without detection of a secondary alcohol. Mesylation of **4** with methanesulfonyl chloride using Et_3N as a base yielded **5**.

Pyran carboxylic acid **1**[13] as a glycosyl acceptor should be coupled with the glycosyl donors, the imidates obtained from compounds **15**, **22**, **24**, **54**, **59** and **61**, to yield the pseudo-disaccharides **28**, **29**, **30**, **62**, **63** and **64**, respectively (Schemes 5 and 9). Therefore, we converted trifluoroacetamide **6**[14] to compounds **15**, **22**, **24**, **54**, **59** and **61** as shown in Schemes 2–4, 7 and 8.

The glycosyl donor precursor **15** was synthesized from trifluoroacetamide **6** as follows (Scheme 2). The C-3 hydroxy compound **6** was alkylated with (*R*)-3-(4-methoxybenzyl)-1-(methanesulfonyloxy)tetradecane and sodium hydride in *N*,*N*-dimethylformamide (DMF) at room temperature to give **7**. The trifluoroacetamide of **7** was hydrolyzed with aqueous 1

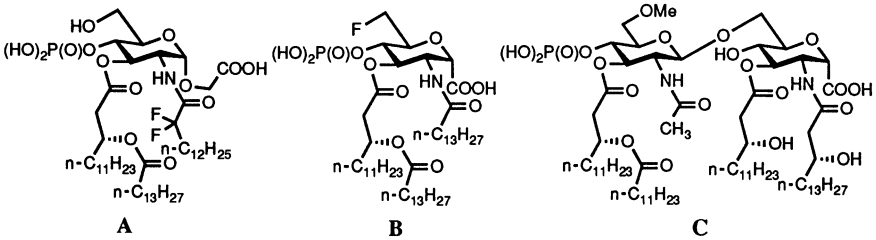
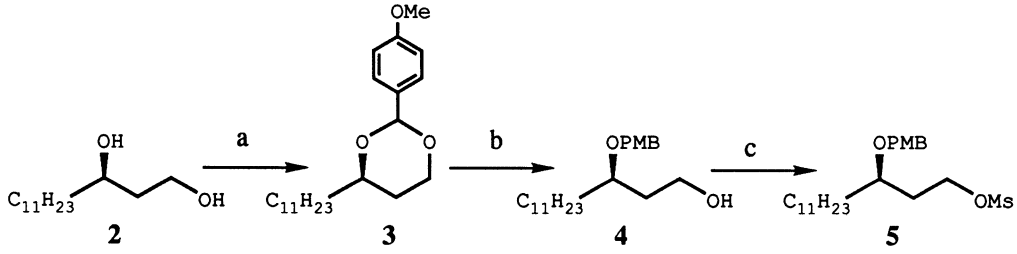
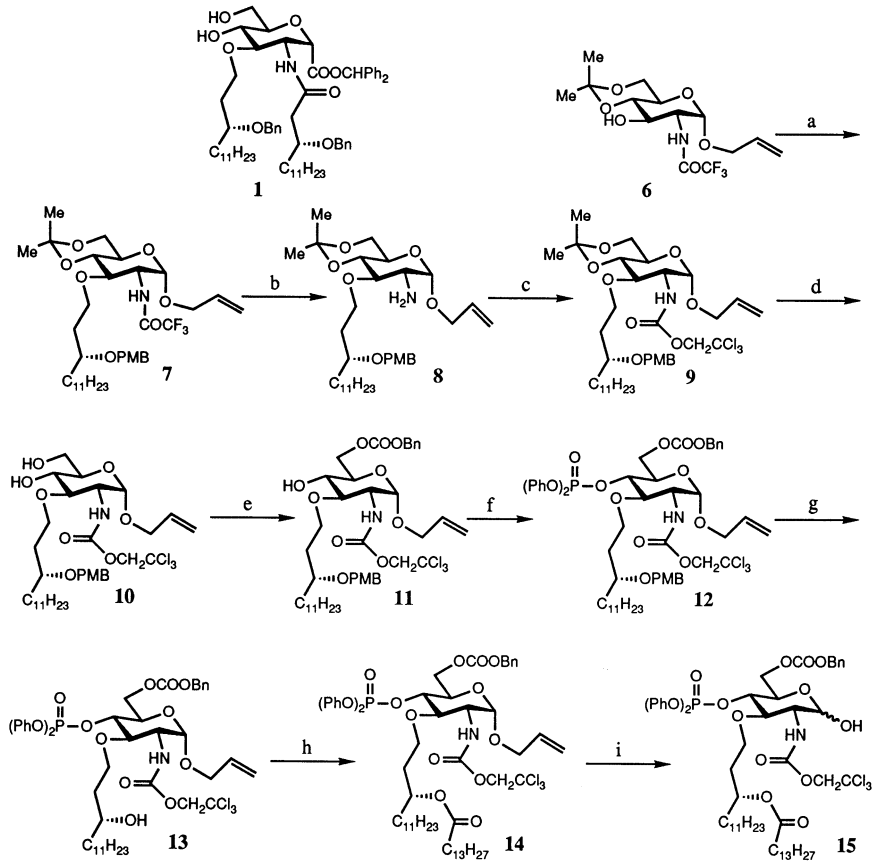


Fig. 1. LPS-antagonists towards human U937 cells.



Scheme 1. Reagents and conditions: PMB = *p*-methoxybenzyl; (a) 4-methoxybenzaldehyde dimethylacetal, *p*-TsOH, DMF, 99%; (b) DIBAL, CH_2Cl_2, −78 °C, 93%; (c) MsCl, Et_3N, CH_2Cl_2, 0 °C, 99%.



Scheme 2. Reagents and conditions: (a) (*R*)-3-(4-methoxybenzyloxy)-1-(methanesulfonyloxy) tetradecane, NaH, DMF, rt, 18 h, 84%; (b) aq 1 M NaOH, EtOH, 60 °C, 3 h, 99%; (c) $ClCOOCH_2CCl_3$, satd aq $NaHCO_3$, CH_2Cl_2, rt, 30 min, 94%; (d) 80% aq AcOH, 60 °C, 1 h, 83%; (e) ClCOOBn, pyridine, CH_2Cl_2, rt, 2 h, 97%; (f) $(PhO)_2P(O)Cl$, DMAP, CH_2Cl_2, rt, 1 h, 94%; (g) DDQ, CH_2Cl_2–water, rt, 1 h, 94%; (h) $C_{13}H_{27}COCl$, Et_3N, THF, rt, 18 h, 93%; (i) $[C_8H_{12}Ir(PMePh_2)_2]$ PF_6, THF, rt, 3 h; then THF, water, pyridine, I_2, rt, 1 h, 81%.

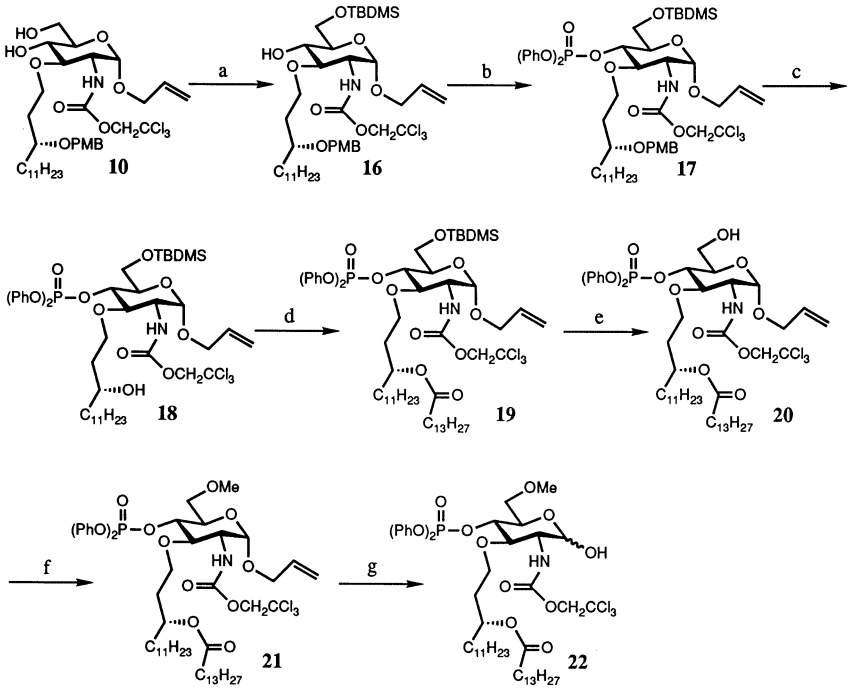
M NaOH in EtOH to convert to amine **8**. Treatment of **8** with 2,2,2-trichloroethyl chloroformate and satd aqueous $NaHCO_3$ as a base in dichloromethane gave carbamate **9**. The *O*-isopropylidene group of **9** was removed by treatment with aqueous 80% AcOH at 60 °C for 3 h to give diol **10**. The overall yield of **10** from **6** was 65% in four steps. Treatment of **10** with benzyl chloroformate and pyridine in dichloromethane gave carbonate **11**, regioselectively. Phosphorylation of the C-4 alcohol of **11** with diphenyl chlorophosphate and 4-dimethylaminopyridine (DMAP) yielded phosphate **12** without formation of cyclic carbonate in those two steps from **10**. Deprotection of the 4-methoxybenzyl group on the alkyl side chain of **12** by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) gave alcohol **13**. Acylation of the alcohol group of **13** with tetradecanoyl chloride and triethylamine in tetrahydrofuran (THF) yielded ester **14**. Double bond migration of the anomeric allyl group of **14** to anomeric vinyl ether by treatment with (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate, and successive oxidative hydrolysis with water–pyridine–iodine in THF afforded cyclic hemiacetal **15** in 65% overall yield from **10** in five steps.

The glycosyl donor precursor **22**, a methoxylated compound at the C-6 position, was synthesized from diol **10** as follows (Scheme 3). Regioselective silylation of the primary C-6–OH group of **10** with *tert*-butyldimethylsilyl chloride (TBDMSCl) and DMAP as a base gave silyl ether **16**. Compound **16** was converted to **19** via **17** and **18** by the same procedure as in the formation of **14** from **11**. Desilylation of **19** was performed by treatment with aqueous 3 M HCl in THF

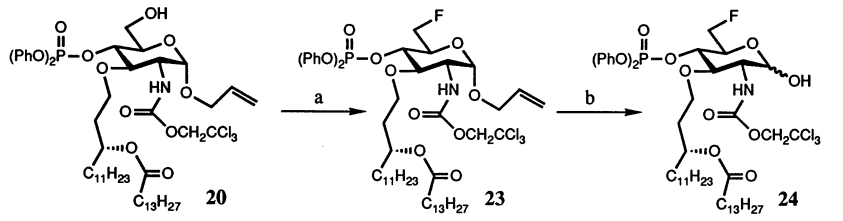
to give alcohol **20** in 74% overall yield from **10** in five steps. Methylation of the C-6–OH group of **20** using trimethyloxonium tetrafluoroborate and 2,6-di-*tert*-butyl-4-methylpyridine as a base gave C-6–OMe ether **21**, which was further converted to cyclic hemiacetal **22** according to the same deallylation procedure from **14** to **15**. The yield of **22** from **20** was 66% in two steps.

The glycosyl donor precursor **24**, a fluorinated compound at the C-6 position, was synthesized from the primary alcohol **20** as follows (Scheme 4). Fluorination of the C-6–OH group of **20** using diethylaminosulfur trifluoride (DAST) gave C-6–F compound **23**, which was further converted to cyclic hemiacetal **24** according to the same deallylation procedure from **14** to **15**. The yield of **24** from **20** was 58% in two steps.

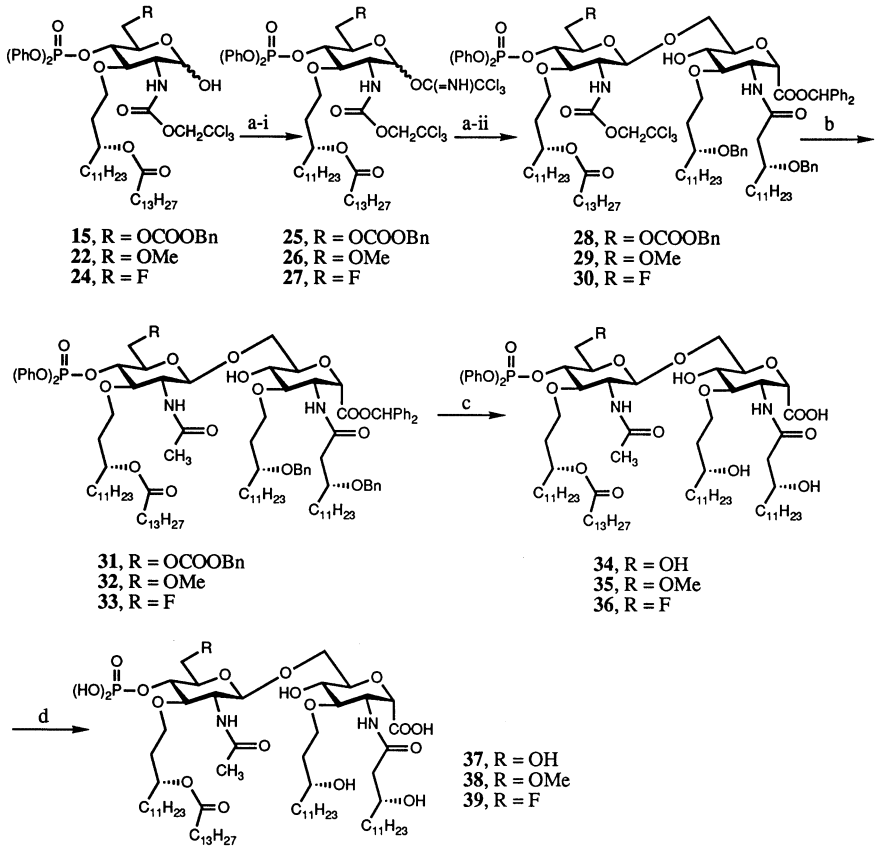
The coupling of **15**, **22**, and **24** via the corresponding imidates **25**, **26**, and **27** with **1**, and successive conversion to corresponding 2′-acetamides **37**, **38**, and **39** are shown in Scheme 5. Treatment of **15**, **22**, and **24** with trichloroacetonitrile using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a base gave imidates **25**, **26**, and **27**, which were independently condensed with **1** using both trimethylsilyl trifluoromethanesulfonate (TMSOTf) and 4 Å molecular sieves (MS4A) as condensing reagents to afford **28**, **29**, and **30**, respectively. Each trichloroethoxycarbonyl



Scheme 3. Reagents and conditions: (a) TBDMSCl, DMAP, CH_2Cl_2, rt, 3 h, 96%; (b) $(PhO)_2POCl$, DMAP, CH_2Cl_2, rt, 1 h, 98%; (c) DDQ, CH_2Cl_2–water, rt, 1 h, 91%; (d) $C_{13}H_{27}COCl$, Et_3N, DMAP, THF, rt, 24 h, 95%; (e) 3 M HCl, THF, rt, 2 h, 91%; (f) Me_3OBF_4, 2,6-di-*tert*-butyl-4-methylpyridine, CH_2Cl_2, rt, 3 h, 91%; (g) $[C_8H_12Ir(PMePh_2)_2]PF_6$, THF, rt, 2 h; then THF, water, pyridine, I_2, rt, 2 h, 73%.



Scheme 4. Reagents and conditions: (a) DAST, DME, 0 °C, 3 h, 80%; (b) $[C_8H_{12}Ir(PMePh_2)_2]PF_6$, THF, rt, 3 h; then water, pyridine, I_2, THF, 2 h, 73%.



Scheme 5. Reagents and conditions: (a) (i) Cl_3CCN, cat. DBU, CH_2Cl_2, 0 °C, 1 h; (ii) **1**, cat. TMSOTf, MS4A, CH_2Cl_2, −78 °C, 2 h, **28** (88%): **29** (72%): **30** (72%); (b) (i) Zn, AcOH, rt, 24 h; (ii) Ac_2O, pyridine, THF–water, rt, 4 h, **31** (70%): **32** (65%): **33** (66%); (c) H_2, 20% $Pd(OH)_2$–C, EtOH, rt, 14 h, **34** (52%): **35** (72%): **36** (64%); (d) H_2, PtO_2, THF, rt, 18 h, **37** (95%): **38** (96%): **39** (98%).

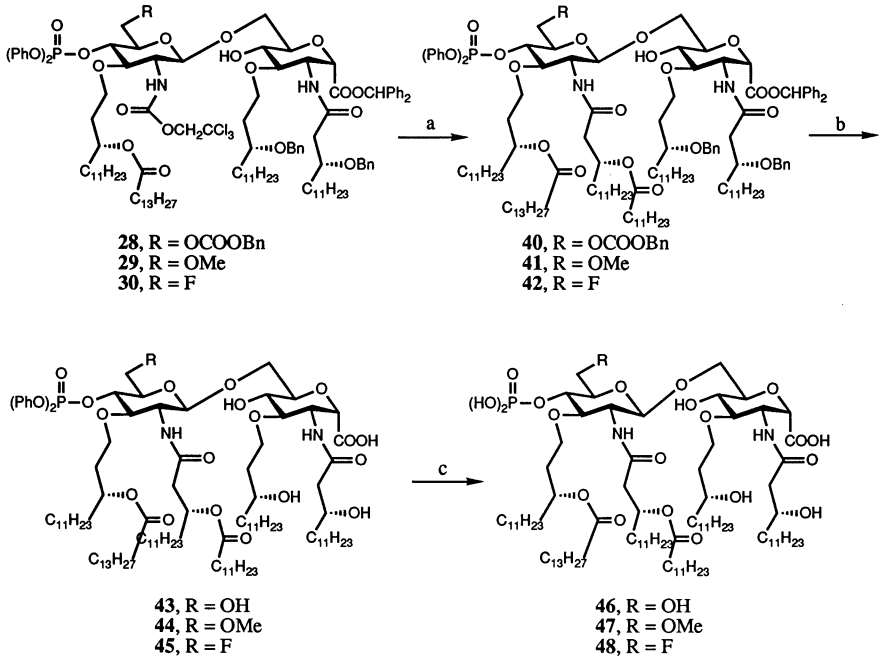
(Troc) group as an amine protecting group of **28**, **29**, and **30** was removed with zinc–acetic acid, and successive treatment of each corresponding amine with acetic anhydride–pyridine yielded acetamides **31**, **32**, and **33**. The protecting groups for hydroxy and ester groups of **31**, **32**, and **33** were removed by hydrogenolysis using palladium hydroxide-on-charcoal to give **34**, **35**, and **36**, which were successively deprotected to **37**, **38**, and **39** by hydrogenolysis using platinum oxide as a catalyst.

Compounds **46**, **47**, and **48** having a [(*R*)-3-dodecanoyloxytetradecanamido] group at the C-2′-amide position were synthesized from **28**, **29**, and **30**, respectively, as follows (Scheme 6). The amines derived from **28**, **29**, and **30** were treated with 3-(*R*)-3-dodecanoyloxytetradecanoic acid and dicyclohexylcarbodiimide (DCC) to give amides **40**, **41**, and **42**, respectively. These amides were further converted to **46**, **47**, and **48** via **43**, **44**, and **45** according to the same deprotection procedure in the formation of **37**, **38**, and **39** from **31**, **32**, and **33**, respectively.

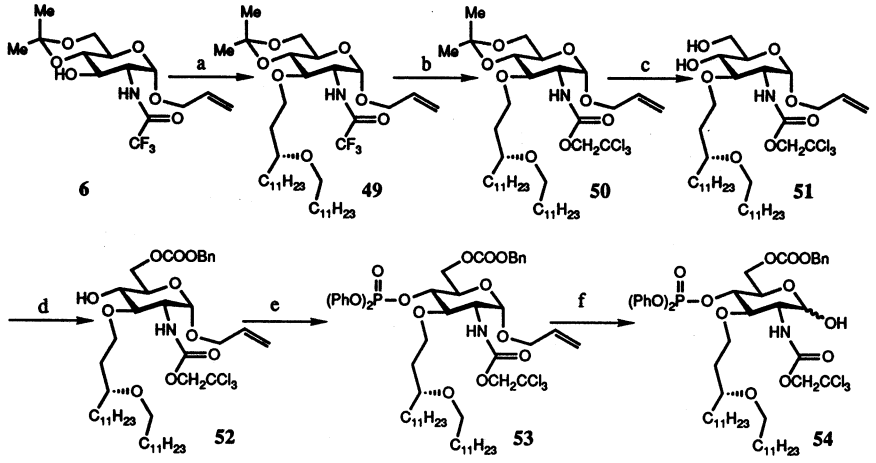
Next, (*R*)-3′-*O*-dodecyloxytetradecyl analogues **71**, **72**, and **73** were synthesized as follows (Schemes 7–9). The glycosyl donor precursor **54** was synthesized from trifluoroacetamide **6**[14] according to almost the same procedures as in the formation of **15** from **6** as follows (Scheme 7). C-3–OH compound **6** was alkylated with (*R*)-3-(dodecyloxy)-1-(methanesulfonyloxy)tetradecane[14] and NaH in DMF at room temperature to give C-3 ether **49**. The trifluoroacetamide of **49** was hydrolyzed with aqueous 1 M NaOH in EtOH to convert it to the corresponding amine, which was treated with 2,2,2-trichloroethyl chloroformate and satd aqueous $NaHCO_3$ as a base in dichloromethane to give carbamate **50**. The *O*-isopropylidene group of **50** was deprotected

by treatment with aqueous 80% AcOH at 60 °C for 3 h to give diol **51** in 62% from **6**. Treatment of **51** with benzyl chloroformate and pyridine in CH_2Cl_2 gave carbonate **52** regioselectively. Phosphorylation of the C-4–OH group of **52** with diphenyl chlorophosphate and DMAP yielded phosphate **53**. Double bond migration of the anomeric allyl group of **53** to anomeric vinyl ether by treatment with (1,5-cyclooctadiene)bis(methyldiphenylphosphine)iridium(I) hexafluorophosphate, and successive oxidative hydrolysis with water–pyridine–iodine in THF afforded cyclic hemiacetal **54** in 64% yield from **51**.

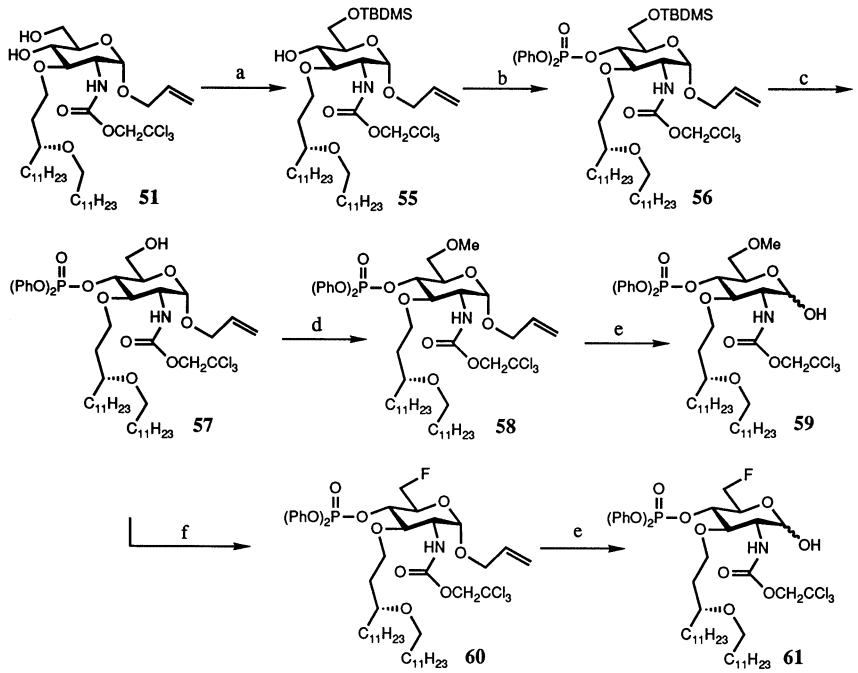
Additionally, C-6-methoxy and C-6-fluoro compounds **59** and **61** as glycosyl donors were also synthesized from diol **51** according to almost the same procedures as in the forma-



Scheme 6. Reagents and conditions: (a) (i) Zn, AcOH, rt, 20 h; (ii) (*R*)-3-(dodecanoyloxy)tetradecanoic acid, DCC, $(ClCH_2)_2$, rt, 6 h, **40** (54%), **41** (71%), and **42** (58%), respectively; (b) H_2, 20% $Pd(OH)_2$–C, EtOH, rt, 14 h, **43** (49%), **44** (77%), and **45** (58%), respectively; (c) H_2, PtO_2, THF, rt, 18 h, **46** (98%), **47** (77%), and **48** (88%), respectively.



Scheme 7. Reagents and conditions: (a) (*R*)-3-(dodecyloxy)-1-(methanesulfonyloxy)tetradecane, NaH, DMF, rt, 3 h, 75%; (b) 1 M aq NaOH, EtOH, 60 °C, 4 h; then $ClCOOCH_2CCl_3$, satd aq $NaHCO_3$, CH_2Cl_2, rt, 1 h, 87%; (c) 80% aq AcOH 60 °C, 4 h, 95%; (d) ClCOOBn, pyridine, CH_2Cl_2, rt, 3 h, 94%; (e) $(PhO)_2P(O)Cl$, DMAP, CH_2Cl_2, rt, 2 h, 96%; (f) $[C_8H_{12}Ir(PMePh_2)_2]PF_6$, THF, rt, 3 h; then water, pyridine, I_2, THF, rt, 1 h, 71%.

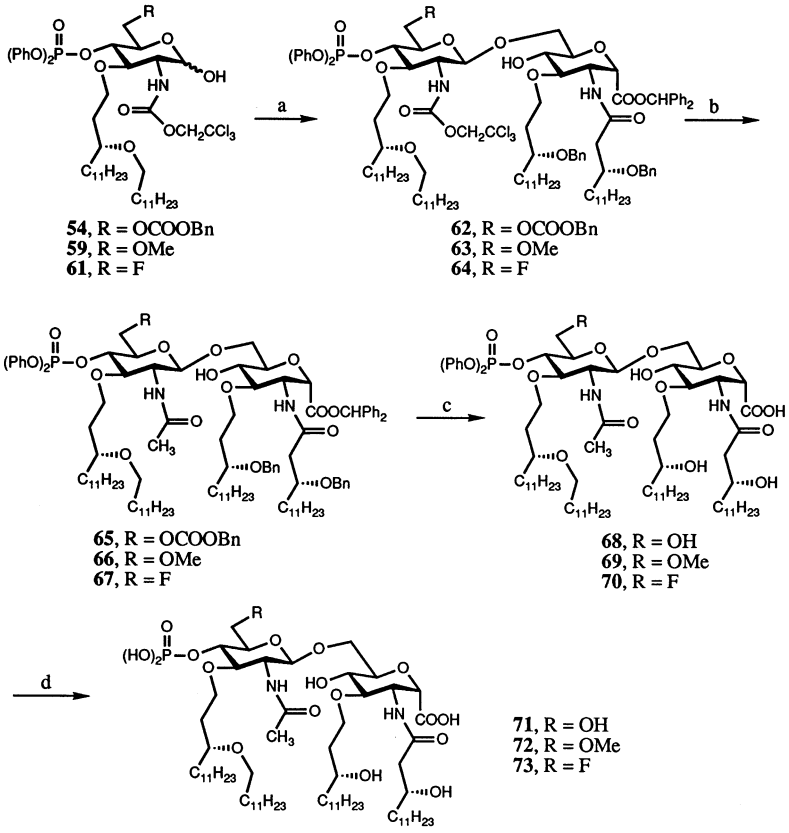


Scheme 8. Reagents and conditions: (a) TBDMSCl, DMAP, CH_2Cl_2, rt, 3 h, 99%; (b) $(PhO)_2P(O)Cl$, DMAP, CH_2Cl_2, rt, 2 h, 99%; (c) 3 M HCl, THF, rt, 3 h, 89%; (d) Me_3OBF_4, 2,6-di-*tert*-butyl-4-methylpyridine, CH_2Cl_2, rt, 3 h, 91%; (e) $[C_8H_{12}Ir(PMePh_2)_2]PF_6$, THF, rt, 3 h; then water, pyridine, I_2, THF, rt, 1 h, 72% (**59** from **58**) and 82% (**61** from **60**), respectively; (f) DAST, DME, −40 °C, 30 min, then rt, 2 h, 83%.

tion of **22** and **24** from **10** as follows (Scheme 8). The diol **51** was selectively protected as silyl ether **55** using TBDMSCl and DMAP and was further converted to phosphate **56** using diphenyl chlorophosphate and DMAP. Treatment of **56** with aqueous 3 M HCl in THF afforded alcohol **57**, which was converted to C-6–OMe compound **58** or C-6–F compound **60** by treatment with Me_3OBF_4 or DAST. Anomeric allyl group deprotection of **58** and **60** according to the same procedure as in the formation of **15** from **14** was performed to give cyclic hemiacetals **59** and **61**, respectively. The yields of **59** and **61** from **51** were 57 and 59%, respectively.

Pseudodisaccharides **71**, **72**, and **73** were synthesized from **54**, **59** and **61**, respectively, by coupling reaction with **1**, and by a series of conversions of corresponding disaccharides according to almost the same procedures as in the formation of **37**, **38** and **39** from **15**, **22** and **24** (Scheme 9). Activation of the anomeric hydroxy group of **54**, **59** and **61** with trichloroacetonitrile using catalytic amount of cesium carbonate afforded corresponding trichloroacetimidate compounds, which were immediately used for subsequent glycosylation with diol **1** in the presence of TMSOTf and MS4A to give pseudodisaccharides **62**, **63** and **64**, respectively. Deprotection of the C-2′–*N*-Troc groups of **62**, **63** and **64** with zinc dust in acetic acid, and successive acetylation of the corresponding amines with acetic anhydride and pyridine gave acetamides **65**, **66** and **67**, respectively. Treatment of **65**, **66** and **67** in hydrogen using 20% palladium hydroxide-on-charcoal as a catalyst gave carboxylic acids **68**, **69** and **70**, respectively. Finally, hydrogenolysis of **68**, **69** and **70** using PtO_2 as a catalyst gave phosphoric acids **71**, **72** and **73**, respectively. The yields of **71**, **72** and **73** from **54**, **59** and **61** were 37, 45, and 41%, respectively.

Biological activity.—The inhibitory activity of compounds **37**, **38**, **39**, **46**, **47**, **48**, **71**, **72** and **73** on LPS-induced TNFα production was investigated in vitro using human monoblastic U937 cells. Compounds **37**, **38**, **39**, **71**, **72** and **73**, which have four chains in their molecules, inhibited TNFα production as LPS-antagonists, and the IC_{50} (nM) values of these six compounds were 0.86, 0.61, 1.2, 11, 6.4 and 10, respectively. Compound **47**, having six chains in the molecule, was almost inactive.



Scheme 9. Reagents and conditions: (a) Cl_3CCN, cat. Cs_2CO_3, CH_2Cl_2, rt, 1 h; then **1**, cat. TMSOTf, MS4A, CH_2Cl_2, −40 °C, 2 h, 75% (**62**), 68% (**63**) and 80% (**64**), respectively; (b) Zn, AcOH, rt, 5 h; then Ac_2O, pyridine, THF–water, rt, 2 h, 71% (**65**), 74% (**66**) and 68% (**67**), respectively; (c) H_2, 20% $Pd(OH)_2$–C, EtOH, rt, 18 h, 72% (**68**), 89% (**69**) and 80% (**70**), respectively; (d) H_2, PtO_2, THF, rt, 5 h, 96% (**71**), 100% (**72**) and 94% (**73**), respectively.

On the other hand, compounds **46** and **48** having six chains in the molecules, showed moderate acceleration of TNFα production as LPS-agonists as shown in Figs. 2 and 3.

Judging from the activity of these compounds, the total number of chains in the molecules plays an important role in whether or not the compound exhibits LPS-antagonism or LPS-agonism. If the total number of chains is four, the compounds are LPS-antagonists. However, if it is six, the compounds are LPS-agonists or inactive. And, also the three C-6 substitution patterns having hydroxy, methoxy and fluorine groups were investigated. However, there were no big differences between them in their activity. This tendency is correlated with the previous results.[11] The difference between 3-tetradecanoyloxytetradecyl and 3-dodecyloxytetradecyl in the C-3′–O substituent is not critical for inhibitory activity toward human monoblastic U937 cells.

3. Experimental

Melting points are uncorrected. Optical rotations were obtained by the use of a JASCO P-1030 polarimeter. IR absorption spectra were recorded on a JASCO IR A-2 spectrophotometer. ^1H NMR spectra were recorded with a JEOL-GSX 400 spectrometer using Me_4Si as an internal standard, and mass

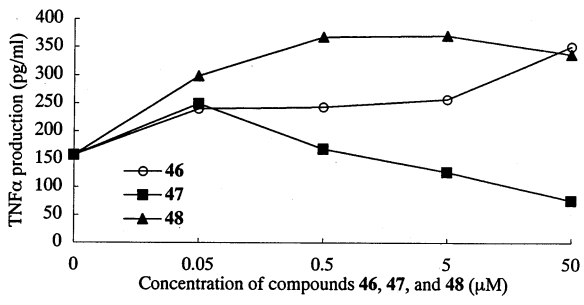


Fig. 2. Inhibitions of TNFα release from TPA-treated U937 cells stimulated by LPS (30 ng/mL) in the presence of lipid A-type pyrancarboxylic acid derivatives.

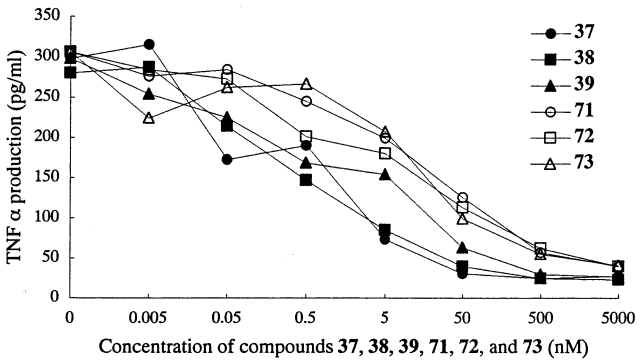


Fig. 3. Inhibitions of TNFα release from U937 cells from TPA-treated U937 cells stimulated by LPS (30ng/mL) in the presence of lipid A-type pyrancarboxylic acid derivatives.

spectra were obtained with a JMS-700 mass spectrometer. Elemental analyses were performed by the Institute of Science and Technology, Inc. Separation of the compounds by column chromatography was carried out with Silica Gel 60 (E. Merck, 0.040–0.063 mm) at slightly elevated pressure (1.1–1.5 atm) for easy elution, and the quantity of the used silica gel was 50–100 times the weight of the purified compounds. Analytical chromatography was performed on E. Merck Art 5715 Silica Gel 60-F_{254} plates. THF was distilled in the presence of radical anions generated by Na–benzophenone ketyl. Dichloromethane was dried by being passed through an ICN Alumina B-Super I, and DMF and pyridine were dried by storage over 4 Å molecular sieves.

(R)-1-Methanesulfonyloxy-3-(4-methoxybenzyloxy)tetradecane (**5**).—(i) To a solution of (*R*)-1,3-dihydroxytetradecane (**2**, 1.85 g, 8.0 mmol) in DMF (20 mL) were added 4-methoxybenzaldehyde dimethylacetal (2.90 g, 16.0 mmol) and *p*-TsOH·H_2O (152 mg, 0.80 mmol). After stirring at rt for 2 h, the reaction mixture was diluted with EtOAc, washed with satd $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to give a mixture, which was chromatographed on a silica-gel column. Elution with 9:1 cyclohexane–EtOAc gave 2-(4-methoxyphenyl)-4-(*R*)-undecyl-[1,3]dioxane (**3**, 2.78 g, 99%) as an oil. IR $\nu_{max}(CHCl_3)$ 2928, 2856, 1616 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.88 (3 H, t, *J* 6.5 Hz), 1.19–1.56 (20 H, m), 1.60–1.81 (2 H, m), 3.75–3.82 (m, 4 H, containing 3 H, s, at δ 3.80), 3.94 (1 H, m), 4.24 (1 H, m), 5.46 (1 H, s), 6.89 (2 H, d, *J* 8.6 Hz), 7.42 (2 H, d, *J* 8.7 Hz). FABMS (positive-ion): *m/z* 349 $[M+H]^+$. HRFABMS (positive-ion): Calcd for $C_{22}H_{37}O_3$: 349.2743; Found: 349.2751. Anal. Calcd for $C_{22}H_{36}O_3$ (348.5): C, 75.82; H, 10.41. Found: C, 75.60; H, 10.68.

(ii) To a solution of the above-obtained **3** (2.71 g, 7.80 mmol) in CH_2Cl_2 (25 mL) was added DIBAL (1.0 M solution in CH_2Cl_2, 24 mL, 24.0 mmol) at −78 °C under N_2. After stirring for 2 h at 0 °C, the reaction mixture was quenched with satd NH_4Cl at 0 °C, and 0.5 M aq Rochelle salt was added to this mixture. After stirring for 30 min at rt, the mixture was extracted with CH_2Cl_2, washed with water and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to give a mixture that was chromatographed on a silica-gel column. Elution with 7:3 cyclohexane–EtOAc gave (*R*)-1-hydroxy-3-(4-methoxybenzyloxy)tetradecane (**4**, 2.54 g, 93%) as an oil. IR $\nu_{max}(CHCl_3)$ 3626, 3499, 2929, 2857, 1613 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.88 (3 H, t, *J* 6.6 Hz), 1.27–1.84 (22 H, m), 2.44 (1 H, t, *J* 5.4 Hz, OH), 3.62 (1 H, m), 3.69–3.82 (5 H, m, containing 3 H, s, at δ 3.80), 4.41, 4.54 (2 H, AB-q, *J* 11.1 Hz), 6.88 (2 H, d, *J* 8.6 Hz), 7.26 (2 H, d, *J* 8.6 Hz). FABMS (positive-ion): *m/z* 373 $[M+Na]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{22}H_{38}O_3$: 350.2821; Found: 350.2800. Anal. Calcd for $C_{22}H_{38}O_3$ (350.5): C, 74.77; H, 11.10. Found: C, 75.08; H, 10.93.

(iii) To a solution of **4** (2.50 g, 7.10 mmol) in CH_2Cl_2 (20 mL) were added Et_3N (1.5 mL, 10.7 mmol) and methanesulfonyl chloride (1.22 g, 10.7 mmol) at 0 °C. After stirring for 1 h at 0 °C, the reaction mixture was diluted with EtOAc, washed with water and brine, dried over $MgSO_4$, filtered, concentrated in vacuo, and chromatographed on a silica-gel column. Elution with 7:3 cyclohexane–EtOAc gave **5** (3.02 g, 99%) as an oil. IR $\nu_{max}(CHCl_3)$ 2929, 2857, 1613 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.88 (3 H, t, *J* 6.6 Hz), 1.27 (18 H, bs), 1.43–1.66 (2 H, m), 1.81–1.98 (2 H, m), 2.95 (3 H, s), 3.54 (1 H, m), 3.80 (3 H, s), 4.26–4.51 (4 H, m, containing 2 H, AB-q, *J* 11.0 Hz, at δ 4.38, 4.51), 6.88 (2 H, d, *J* 8.7 Hz), 7.26 (2 H, d, *J* 8.6 Hz). FABMS (posi-

tive-ion): m/z 451 $[M + Na]^+$, 428 $[M^{+\bullet}]$. HR-FABMS (positive-ion), Calcd for $C_{23}H_{40}O_5S$: 428.2596; Found: 428.2584.

*Allyl 2-deoxy-4,6-*O*-isopropylidene-3-*O*-[(*R*)-3-(4-methoxybenzyloxy)tetradecyl]-2-trifluoroacetamide-α-*D*-glucopyranoside* (**7**).—To a solution of allyl 2-deoxy-4,6-*O*-isopropylidene-2-trifluoroacetamido-α-D-glucopyranosid e (**6**, 1.28 g, 3.60 mmol) in DMF (15 mL) was gradually added NaH (55% oil dispersion, 205 mg, 4.70 mmol) at 0 °C with stirring. After 15 min, (*R*)-3-(4-methoxybenzyloxy)-1-methanesulfonyloxytetradecane (1.29 g, 3.00 mmol) was added to this solution, which was then stirred for 18 h at rt. The reaction mixture was quenched with water, extracted with EtOAc, washed with water and brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated in vacuo to give a mixture that was chromatographed on a silica-gel column. Elution with 3:1 cyclohexane–EtOAc gave **7** (1.74 g, 84%) as a wax. IR $\nu_{max}(CHCl_3)$ 3429, 2929, 2857, 1734 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.88 (3 H, t, J 6.5 Hz), 1.26–1.49 (26 H, m, containing 3 H, s, at δ 1.40, and 3 H, s, at δ 1.49), 1.64–1.78 (2 H, m), 3.41–3.91 (11 H, m, containing 3 H, s, at δ 3.80), 3.99 (1 H, m), 4.13–4.21 (2 H, m), 4.36, 4.43 (2 H, AB-q, J 11.2 Hz), 4.87 (1 H, d, J 3.8 Hz), 5.24–5.32 (2 H, m), 5.87 (1 H, m), 6.41 (1 H, d, J 9.3 Hz, NH), 6.87 (2 H, d, J 8.6 Hz), 7.25 (2 H, d, J 7.9 Hz). FABMS (positive-ion): m/z 710 $[M + Na]^+$. FABMS (negative-ion): m/z 686 $[M - H]^-$. HRFABMS (positive-ion): m/z Calcd for $C_{36}H_{56}F_3NNaO_8$: 710.3856; Found: 710.3851. Anal. Calcd for $C_{36}H_{56}F_3NO_8$ (687.8): C, 62.86; H, 8.21; F, 8.19; N, 2.04. Found: C, 62.56; H, 8.15; F, 7.94; N, 2.07.

*Allyl 2-amino-2-deoxy-4,6-*O*-isopropylidene-3-*O*-[(R)-3-(4-methoxybenzyloxy)tetradecyl]-α-D-glucopyranoside* (**8**).—A solution of **7** (1.45 g, 2.11 mmol) in EtOH (10 mL) and 1 M NaOH aq (10 mL) was stirred at 60 °C for 3 h. The solution was concentrated in vacuo, diluted with EtOAc, washed with water and brine, dried over $MgSO_4$, filtered, concentrated, and chromatographed on a silica-gel column. Elution with 2:3 cyclohexane–EtOAc gave **8** (1.23g, 99%) as a gum. IR $\nu_{max}(CHCl_3)$ 2928, 2855, 1612 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.88 (3 H, t, J 6.6 Hz), 1.26–1.62 (28 H, m, containing 3 H, s, at δ 1.39, and 3 H, s, at δ 1.48), 1.71–1.85 (2 H, m), 2.72 (1 H, dd, J 3.7, 9.5 Hz), 3.27 (1 H, t, J 9.1 Hz), 3.49–3.86 (9 H, m, containing 3 H, s, at δ 3.80), 4.17 (1 H, m), 4.40, 4.47 (2 H, AB-q, J 11.2 Hz), 4.86 (1 H, d, J 3.6 Hz), 5.19–5.34 (2 H, m), 5.88 (1 H, m), 6.87 (2 H, d, J 8.6 Hz), 7.26 (2 H, d, J 8.6 Hz). FABMS (positive-ion): m/z 592 $[M + H]^+$. HRFABMS (positive-ion): m/z Calcd for $C_{34}H_{58}NO_7$: 592.4213; Found: 592.4207. Anal. Calcd for $C_{34}H_{57}NO_7$ (591.8): C, 69.00; H, 9.71; N, 2.37. Found: C, 68.86; H, 10.21; N, 2.31.

*Allyl 2-deoxy-4,6-*O*-isopropylidene-3-*O*-[(R)-3-(4-methoxybenzyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-D-glucopyranoside* (**9**).—To a solution of **8** (1.20 g, 2.03 mmol) in CH_2Cl_2 (8 mL) were added satd $NaHCO_3$ (8 mL) and chloroformic acid 2,2,2-trichloroethyl ester (534 mg, 2.52 mmol). After stirring for 30 min at rt, the mixture was diluted with EtOAc, washed with water and brine, dried over $MgSO_4$, filtered, concentrated, and chromatographed on a silica-gel column. Elution with 4:1 cyclohexane–EtOAc gave **9** (1.47 g, 94%) as a gum. IR $\nu_{max}(CHCl_3)$ 3440, 2929, 2857, 1744, 1613 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.88 (3 H, t, J 6.6 Hz),1.26–1.48 (26 H, m, containing 3 H, s, at δ 1.40, and 3 H, s, at δ 1.48), 1.62–1.78 (2 H, m), 3.38–4.02 (13 H, m, containing 3 H, s, at δ 3.80), 4.16 (1 H, m), 4.39, 4.45 (2 H, AB-q, J 11.2 Hz), 4.68, 4.74 (2 H, AB-q, J 12.0 Hz), 4.86 (1 H, d, J 3.7 Hz), 5.13–5.32 (3 H, m), 5.89 (1 H, m), 6.88 (2 H, d, J 8.6 Hz), 7.27 (2 H, d, J 8.5 Hz). FABMS (positive-ion): m/z 788 $[M + Na]^+$. FABMS (negative-ion): m/z 764 $[M - H]^-$. HRFABMS (positive-ion): m/z Calcd for $C_{37}H_{58}Cl_3NO_9$: 788.3075; Found: 788.3077. Anal. Calcd for $C_{37}H_{58}Cl_3NNaO_9$ (767.2): C, 57.92; H, 7.62; Cl, 13.86; N, 1.83. Found: C, 57.50; H, 7.38; Cl, 13.87; N, 1.85.

*Allyl 2-deoxy-3-*O*-[(R)-3-(4-methoxybenzyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-D-glucopyranoside* (**10**).—A solution of **9** (885 mg, 1.15 mmol) in 80% AcOH aq (10 mL) was stirred at 60 °C for 1 h. The solution was diluted with EtOAc, washed with satd aq $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, concentrated in vacuo, and chromatographed on a silica-gel column. Elu-

tion with 1:1 cyclohexane–EtOAc gave **10** (696 mg, 83%) as a white powder. IR $\nu_{max}(CHCl_3)$ 3601, 3436, 2928, 1742, 1612 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.88 (3 H, t, *J* 6.6 Hz), 1.26 (18 H, bs), 1.43–1.80 (4 H, m), 2.08 (1 H, broad, OH), 3.41–3.54 (4 H, m), 3.56–3.91 (9 H, m, containing 3 H, s, at δ 3.80), 3.99 (1 H, dd, *J* 6.3, 12.8 Hz), 4.18 (1 H, dd, *J* 5.3, 12.8 Hz), 4.39, 4.45 (2 H, AB-q, *J* 11.2 Hz), 4.68, 4.75 (2 H, AB-q, *J* 12.0 Hz), 4.85 (1 H, d, *J* 3.5 Hz), 5.21–5.32 (3 H, m), 5.89 (1 H, m), 6.88 (2 H, d, *J* 8.8 Hz), 7.26 (2 H, d, *J* 8.5 Hz). FABMS (positive-ion) 748 $[M+Na]^+$. FABMS (negative-ion): *m/z* 724 $[M-H]^-$. HRFABMS (positive-ion): *m/z* Calcd for $C_{34}H_{54}Cl_3NNaO_9$: 748.2762; Found: 748.2744. Anal. Calcd for $C_{34}H_{54}Cl_3NO_9$ (727.2): C, 56.16; H, 7.49; Cl, 14.63; N, 1.93. Found: C, 56.10; H, 7.36; Cl, 14.60; N, 1.96.

Allyl 6-O-benzyloxycarbonyl-2-deoxy-3-O-[(R)-3-(4-methoxybenzyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-D-glucopyranoside (**11**).—To a solution of **10** (366 mg, 0.503 mmol) in CH_2Cl_2 (5 mL) were added pyridine (60.4 mg, 0.764 mmol) and benzyloxycarbonyl chloride (90 μL, 0.630 mmol) at 0 °C under N_2. After stirring for 2 h at rt, the solution was diluted with EtOAc, washed with 1 N NH_4Cl, satd aq $NaHCO_3$, and brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated in vacuo, and chromatographed on a silica-gel column. Elution with 3:1 cyclohexane–EtOAc gave **11** (419 mg, 97%) as a wax. IR $\nu_{max}(CHCl_3)$ 3436, 2928, 2856, 1744, 1612 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.88 (3 H, t, *J* 6.6 Hz), 1.26–1.78 (22 H, m), 3.37–3.53 (4 H, m, containing OH), 3.69–3.99 (8 H, m, containing 3 H, s, at δ 3.79 ppm), 4.15 (1 H, dd, *J* 5.3, 13.0 Hz), 4.37–4.47 (4 H, m), 4.67, 4.74 (2 H, AB-q, *J* 12.1 Hz), 4.84 (1 H, d, *J* 3.7 Hz), 5.18–5.30 (5 H, m), 5.87 (1 H, m), 6.87 (2 H, d, *J* 8.6 Hz), 7.25 (2 H, d, *J* 7.3 Hz), 7.33–7.41 (5 H, m). FABMS (positive-ion): *m/z* 882 $[M+Na]^+$. FABMS (negative-ion): *m/z* 858 $[M-H]^-$. HRFABMS (negative-ion): *m/z* Calcd for $C_{42}H_{59}Cl_3NO_{11}$: 858.3154; Found: 858.3133. Anal. Calcd for $C_{42}H_{60}Cl_3NO_{11}$ (861.3): C, 58.57; H, 7.02; Cl, 12.35; N, 1.63. Found: C, 58.38; H, 6.93; Cl, 12.58; N, 1.61.

Allyl 6-O-benzyloxycarbonyl-2-deoxy-4-O-(diphenylphosphono)-3-O-[(R)-3-(4-methoxybenzyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-D-glucopyranoside (**12**).—To a solution of **11** (390 mg, 0.453 mmol) and DMAP (84 mg, 0.679 mmol) in CH_2Cl_2 (3 mL) was added dropwise diphenyl chlorophosphate (140 μL, 0.675 mmol). After stirring for 1 h at rt, the reaction mixture was diluted with EtOAc, washed with satd aq $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to give a residue, which was chromatographed on a silica-gel column. Elution with 3:1 cyclohexane–EtOAc gave **12** (467 mg, 94%) as a gum. IR $\nu_{max}(CHCl_3)$ 3435, 2928, 2855, 1747, 1612 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.88 (3 H, t, *J* 6.6 Hz), 1.17–1.72 (22 H, m), 3.37 (1 H, m), 3.65–3.84 (6 H, m, containing 3 H, s, at δ 3.78), 3.93–4.04 (3 H, m), 4.14 (1 H, dd, *J* 5.3, 12,9 Hz), 4.20–4.39 (4 H, m), 4.63 (1 H, m), 4.49, 4.76 (2 H, AB-q, *J* 12.1 Hz), 4.87 (1 H, d, *J* 3.6 Hz), 5.06, 5.12 (2 H, AB-q, *J* 12.2 Hz), 5.21–5.30 (3 H, m), 5.86 (1 H, m), 6.83 (2 H, d, *J* 8.6 Hz), 7.11–7.37 (17 H, m). FABMS (positive-ion): *m/z* 1114 $[M+Na]^+$. FABMS (negative-ion): *m/z* 1090 $[M-H]^-$. HRFABMS (negative-ion): *m/z* Calcd for $C_{54}H_{68}Cl_3NO_{14}P$: 1090.3443; Found: 1090.3431. Anal. Calcd for $C_{54}H_{69}Cl_3NO_{14}P$ (1093.5): C, 59.32; H, 6.36; Cl, 9.73; N, 1.28; P, 2.83. Found: C, 59.35; H, 6.35; Cl, 9.80; N, 1.21; P, 3.04.

Allyl 6-O-benzyloxycarbonyl-2-deoxy-4-O-(diphenylphosphono)-3-O-[(R)-3-(hydroxy)-tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)-amino]-α-D-glucopyranoside (**13**).—A mixture of **12** (338 mg, 0.309 mmol), water (0.3 mL), and DDQ (85 mg, 0.373 mmol) in CH_2Cl_2 (3 mL) was stirred for 1 h at rt. The mixture was diluted with EtOAc, washed with satd aq $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, concentrated in vacuo, and chromatographed on a silica-gel column. Elution with 7:3 cyclohexane–EtOAc gave **13** (283 mg, 94%) as a gum. IR $\nu_{max}(CHCl_3)$ 3435, 2927, 2855, 1746, 1592 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.88 (3 H, t, *J* 6.6 Hz), 1.25–1.75 (22 H, m), 3.64–3.85 (4 H, m), 3.95–4.08 (3 H, m), 4.15 (1 H, dd, *J* 5.3, 12.7 Hz), 4.23–4.38 (2 H, m), 4.63–4.75 (3 H, m),

4.93 (1 H, d, *J* 3.6 Hz), 5.04, 5.11 (2 H, AB-q, *J* 12.2 Hz), 5.22–5.31 (2 H, m), 5.44 (1 H, d, *J* 9.2 Hz, NH), 5.88 (1 H, m), 7.11–7.34 (15 H, m). FABMS (positive-ion): *m/z* 994 $[M+Na]^+$; 972 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{46}H_{62}Cl_3NO_{13}P$: 972.3024; Found: 972.3010. Anal. Calcd for $C_{46}H_{61}Cl_3NO_{13}P$ (973.3): C, 56.77; H, 6.32; Cl, 10.93; N, 1.44; P, 3.18. Found: C, 56.60; H, 6.49; Cl, 11.17; N, 1.45; P, 3.33.

Allyl 6-O-benzyloxycarbonyl-2-deoxy-4-O-(diphenylphosphono)-3-O-[(R)-3-(tetradecanoyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-D-glucopyranoside (**14**).—To a solution of **13** (271 mg, 0.278 mmol) in THF (3 mL) were added Et_3N (60 μL, 0.427 mmol), DMAP (51 mg, 0.420 mmol), and tetradecanoyl chloride (0.12 mL, 0.438 mmol) with stirring. After stirring for 18 h at rt, the mixture was diluted with EtOAc, washed with satd aq $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, concentrated, and chromatographed on a silica-gel column. Elution with 4:1 cyclohexane–EtOAc gave **14** (305 mg, 93%) as a gum. IR $\nu_{max}(CHCl_3)$ 3435, 2927, 2855, 1746 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.88 (3 H, t, *J* 6.6 Hz), 1.19–1.71 (44 H, m), 2.20 (2 H, t, *J* 7.5 Hz), 3.50 (1 H, m), 3.68 (1 H, m), 3.82 (1 H, m), 3.92–4.01 (3 H, m), 4.15 (1 H, dd, *J* 5.3, 13.0 Hz), 4.28–4.41 (2 H, m), 4.63 (1 H, m), 4.75 (2 H, s), 4.84–4.93 (2 H, m, containing 1 H, d, *J* 3.6 Hz, at δ 4.90), 5.05, 5.11 (2 H, AB-q, *J* 12.2 Hz), 5.20–5.34 (2 H, m), 5.78 (1 H, d, *J* 10.7 Hz, NH), 5.87 (1 H, m), 7.12–7.34 (15 H, m). FABMS (positive-ion): *m/z* 1182 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{60}H_{88}Cl_3NO_{14}P$: 1182.5008; Found: 1182.5021. Anal. Calcd for $C_{60}H_{87}Cl_3NO_{14}P$ (1183.7): C, 60.88; H, 7.41; Cl, 8.99; N, 1.18; P, 2.62. Found: C, 61.12; H, 7.46; Cl, 9.18; N, 1.13; P, 2.72.

6-O-Benzyloxycarbonyl-2-deoxy-4-O-(diphenylphosphono)-3-O-[(R)-3-(tetradecanoyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-D-glucopyranose (**15**).—To a solution of **14** (136 mg, 0.114 mmol) in THF (3 mL) was added $[C_8H_{12}Ir(PMePh_2)_2]PF_6$ (3.6 mg). The air in the reaction flask was completely replaced with N_2 and then further replaced with hydrogen to activate the iridium complex. Immediately after 2 min, when the red color solution of iridium complex had become almost colorless, the hydrogen was completely replaced with N_2. This solution was stirred for 3 h at rt. After confirming a double bond shift to an enol ether from the 1-allyloxy group (as indicated by a slightly higher R_f value on the TLC), water (0.3 mL), pyridine (15 mg), and I_2 (22 mg) were added to this solution. After 1 h stirring at rt, the mixture was diluted with EtOAc, washed with aq 10% $Na_2S_2O_3$, satd $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated to give a mixture that was chromatographed on a silica-gel column. Elution with 7:3 cyclohexane–EtOAc gave **15** (106 mg, 81%) as a gum. IR $\nu_{max}(CHCl_3)$ 3599, 3434, 3326, 2927, 2855, 1746 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.88 (3 H, t, *J* 6.6 Hz), 1.20–1.77 (44 H, m), 2.21 (2 H, t, *J* 7.5 Hz), 3.41–3.53 (2 H, m, containing OH), 3.75 (1 H, m), 3.83–3.95 (2 H, m), 4.19–4.43 (3 H, m), 4.58–4.79 (3 H, m), 4.92 (1 H, m), 5.04, 5.11 (2 H, AB-q, *J* 12.1 Hz), 5.29 (1 H, m), 6.03 (1 H, d, *J* 8.6 Hz, NH), 7.12–7.34 (15 H, m). FABMS (positive-ion): *m/z* 1142 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{57}H_{83}Cl_3NNaO_{14}P$: 1164.4518; Found: 1164.4518. Anal. Calcd for $C_{57}H_{83}Cl_3NO_{14}P$ (1143.6): C, 59.87; H, 7.37; Cl, 9.03; N, 1.23; P, 2.71. Found: C, 59.84; H, 7.29; Cl, 9.05; N, 1.46; P, 2.76.

*Allyl 6-O-(*tert*-butyldimethylsilyl)-2-deoxy-3-O-[(R)-3-(4-methoxybenzyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-D-glucopyranoside* (**16**).—To a solution of **15** (1.15 g, 1.58 mmol) in CH_2Cl_2 (5 mL) were added DMAP (304 mg, 2.49 mmol) and *tert*-butyldimethylsilyl chloride (364 mg, 2.42 mmol). After stirring for 3 h at rt, the mixture was diluted with EtOAc, washed with water, satd aq $NaHCO_3$, and brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated in vacuo, and chromatographed on a silica-gel column. Elution with 4:1 cyclohexane–EtOAc gave **16** (1.28 g, 96%) as a gum. IR $\nu_{max}(CHCl_3)$ 3437, 2955, 2929, 2856, 1742, 1613 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.09 (6 H, s), 0.86–0.91 (12 H, m), 1.26 (18 H, bs), 1.40–1.80 (4 H, m), 3.34–3.67 (4 H, m, containing OH), 3.76–3.93 (9 H, m, containing 3 H, s, at δ 3.80), 3.98 (1 H, dd, *J* 6.3, 12.8

Hz), 4.18 (1 H, dd, *J* 5.2, 12.9 Hz), 4.40, 4.45 (2 H, AB-q, *J* 11.5 Hz), 4.70 (2 H, s), 4.84 (1 H, d, *J* 3.6 Hz), 5.19–5.32 (3 H, m, containing NH), 5.90 (1 H, m), 6.87 (2 H, d, *J* 8.6 Hz), 7.26 (2 H, d, *J* 8.6 Hz). FABMS (positive-ion): *m/z* 878 $[M+K]^+$. FABMS (negative-ion): *m/z* 838 $[M-H]^-$. HRFABMS (negative-ion): *m/z* Calcd for $C_{40}H_{68}Cl_3NNaO_9Si$: 862.3627; Found: 862.3622. Anal. Calcd for $C_{40}H_{68}Cl_3NO_9Si$ (841.4): C, 57.10; H, 8.15; Cl, 12.64; N, 1.67. Found: C, 57.54; H, 8.13; Cl, 12.72; N, 1.57.

Allyl 6-O-tert-*butyldimethylsilyl-2-deoxy-4*-O-*(diphenylphosphono)-3*-O-*[(*R*)-3-(4-methoxybenzyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-*α-D-*glucopyranoside* (**17**).—To a solution of **16** (1.26 g, 1.50 mmol) in CH_2Cl_2 (5 mL) were added DMAP (278 mg, 2.28 mmol) and diphenyl chlorophosphate (0.46 mL, 2.23 mmol). After stirring for 1 h at rt, the mixture was diluted with EtOAc, washed with satd aq $NaHCO_3$ and brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated in vacuo, and chromatographed on a silica-gel column. Elution with 4:1 cyclohexane–EtOAc gave **17** (1.57 g, 98%) as an oil. IR $\nu_{max}(CHCl_3)$ 3435, 2955, 2929, 2856, 1743, 1613 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.002 (6 H, s), 0.86–0.92 (12 H, m), 1.26 (18 H, bs), 1.66–1.74 (4 H, m), 3.37 (1 H, m), 3.69–3.87 (9 H, m, containing 3 H, s, at δ 3.79), 3.94–4.04 (2 H, m), 4.22 (1 H, dd, *J* 5.3, 12.7 Hz), 4.30 (2 H, s), 4.43–4.61 (2 H, m), 4.75 (1 H, m) 4.89 (1 H, d, *J* 3.6 Hz), 5.20–5.34 (3 H, m, containing NH), 5.91 (1 H, m), 6.84 (2 H, d, *J* 8.6 Hz), 7.14–7.33 (12 H, m). FABMS (positive-ion): *m/z* 1094 $[M+Na]^+$; 1072 $[M+H]^+$. HR-FABMS (positive-ion): *m/z* Calcd for $C_{52}H_{77}Cl_3NNaO_{12}PSi$: 1094.3916; Found: 1094.3905. Anal. Calcd for $C_{52}H_{77}Cl_3NO_{12}PSi$ (1073.6): C, 58.18; H, 7.23; Cl, 9.91; N, 1.31; P, 2.89. Found: C, 57.85; H, 7.05; Cl, 10.57; N, 1.27; P, 2.16.

Allyl 6-O-*(*tert-*butyldimethylsilyl)-2-deoxy-4*-O-*(diphenylphosphono)-3*-O-*[(*R*)-3-(hydroxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-*α-D-*glucopyranoside* (**18**).—A mixture of **17** (1.50 g, 1.40 mmol), water (0.5 mL), and DDQ (386 mg, 1.70 mmol) in CH_2Cl_2 (5 mL) was stirred for 1 h at rt. The mixture was diluted with EtOAc, washed with satd aq $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, concentrated in vacuo, and chromatographed on a silica-gel column. Elution with 3:1 cyclohexane–EtOAc gave **18** (1.22 g, 91%) as a gum. IR $\nu_{max}(CHCl_3)$ 3434, 2928, 2856, 1740 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.002 (6 H, s), 0.82–0.90 (12 H, m), 1.25–1.67 (22 H, m), 3.65–3.87 (8 H, m, containing OH), 3,93–4.04 (2 H, m), 4.21 (1 H, dd, *J* 5.3, 12.9 Hz), 4.62 (1 H, m), 4.75 (2 H, s), 4.93 (1 H, d, *J* 3.7 Hz), 5.22–5.34 (2 H, m), 5.44 (1 H, d, *J* 9.3 Hz, NH), 5.91 (1 H, m), 7.15–7.35 (10 H, m). FABMS (positive-ion): *m/z* 974 $[M+Na]^+$; 952 $[M+H]^+$. HR-FABMS (positive-ion): *m/z* Calcd for $C_{44}H_{69}Cl_3NNaO_{11}PSi$: 974.3341; Found: 974.3345.

Allyl 6-O-*(*tert-*butyldimethylsilyl)-2-deoxy-4*-O-*(diphenylphosphono)-3*-O-*[(*R*)-3-(tetradecanoyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-*α-D-*glucopyranoside* (**19**).—To a solution of **18** (1.21 g, 1.27 mmol) in THF (6 mL) were added Et_3N (2.55 mL, 2.56 mmol), DMAP (326 mg, 2.67 mmol), and tetradecanoyl chloride (0.70 mL, 2.55 mmol) with stirring. After stirring for 24 h at rt, the mixture was diluted with EtOAc, washed with water, satd aq $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, concentrated, and chromatographed on a silica-gel column. Elution with 4:1 cyclohexane–EtOAc gave **19** (1.40 g, 95%) as an oil. IR $\nu_{max}(CHCl_3)$ 3435, 2928, 2856, 1737 cm^{-1}. ^1H NMR (270 MHz, $CDCl_3$) δ 0.01 (6 H, s), 0.86–0.92 (15 H, m), 1.26 (40 H, bs), 1.53–1.74 (4 H, m), 2.18 (2 H, t, *J* 7.3–7.7 Hz), 3.55 (1 H, m), 3.67–4.07 (7 H, m), 4.22 (1 H, dd, *J* 5.2–12.8 Hz), 4.56 (1 H, m), 4.77 (2 H, s), 4.83–4.91 (2 H, m, containing 1 H, d, *J* 3.6 Hz, at δ 4.91), 5.22–5.36 (2 H, m), 5.68 (1 H, d, *J* 9.4 Hz, NH), 5.92 (1 H, m), 7.15–7.35 (10 H, m). FABMS (positive-ion): *m/z* 1162 $[M+H]^+$; 1200 $[M+K]^+$ (on addition of KI). HR-FABMS (positive-ion): *m/z* Calcd for $C_{58}H_{95}Cl_3KNO_{12}PSi$: 1200.5064; Found: 1200.5026.

Allyl 2-deoxy-4-O-*(diphenylphosphono)-3*-O-*[(*R*)-3-(tetradecanoyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-*α-D-

glucopyranoside (**20**).—To a solution of **19** (1.35 g, 1.16 mmol) in THF (9 mL) was added aq 3 M HCl (1.2 mL) with stirring. After 2 h at rt, the reaction mixture was diluted with EtOAc, washed with satd aq $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, concentrated, and chromatographed on a silica-gel column. Elution with 7:3 cyclohexane–EtOAc gave **20** (1.11 g, 91%) as a gum. IR $\nu_{max}(CHCl_3)$ 3691, 3606, 3437, 2927, 2855, 1737 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (6 H, t, *J* 6.6 Hz), 1.19–1.73 (44 H, m), 2.23 (2 H, t, *J* 7.3–8.1 Hz), 3.52 (1 H, m), 3.60–3.70 (4 H, m), 3.89–4.03 (3 H, m), 4.17 (1 H, dd, *J* 5.1, 12.5 Hz), 4.65 (1 H, m), 4.73, 4.78 (2 H, AB-q, *J* 12.5 Hz), 4.91–4.95 (2 H, m, containing 1 H, d, *J* 3.7 Hz, at δ 4.95), 5.23–5.35 (2 H, m), 5.82 (1 H, d, *J* 9.5 Hz, NH), 5.89 (1 H, m), 7.20–7.38 (10 H, m). FABMS (positive-ion): *m*/*z* 1070 $[M + Na]^+$. HRFABMS (positive-ion): *m*/*z* Calcd for $C_{52}H_{81}Cl_3NNaO_{12}P$: 1070.4460; Found: 1070.4452. Anal. Calcd for $C_{52}H_{81}Cl_3NO_{12}P$ (1049.5): C, 59.51; H, 7.78; Cl, 10.13; N, 1.34; P, 2.95. Found: C, 59.30; H, 7.90; Cl, 10.24; N, 1.51; P, 2.94.

*Allyl 2-deoxy-4-*O*-(diphenylphosphono)-6-*O*-methyl-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-*D*-glucopyranoside* (**21**).—To a solution of **20** (1.05 g, 1.00 mmol) in CH_2Cl_2 (5 mL) were added 2,6-di-*tert*-butyl-4-methylpyridine (679 mg, 3.31 mmol) and trimethyloxonium tetrafluoroborate (446 mg, 3.02 mmol) at 0 °C. After stirring for 3 h at rt, the reaction mixture was diluted with CH_2Cl_2, washed with satd aq $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, concentrated, and chromatographed on a silica-gel column. Elution with 7:3 cyclohexane–EtOAc gave **21** (966 mg, 91%) as a gum. IR $\nu_{max}(CHCl_3)$ 3435, 2927, 2855, 1738 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (6 H, t, *J* 6.6–7.3 Hz), 1.18–1.72 (44 H, m), 2.18 (2 H, t, *J* 7.3–8.1 Hz), 3.24 (3 H, s), 3.48–3.59 (3 H, m), 3.69 (1 H, m), 3.82–3.88 (2 H, m), 3.96–4.04 (2 H, m), 4.20 (1 H, dd, *J* 5.1, 13.2 Hz), 4.64–4.80 (3 H, m), 4.88 (1 H, m), 4.94 (1 H, d, *J* 3.7 Hz), 5.22–5.35 (2 H, m), 5.69 (1 H, d, *J* 8.8 Hz, NH), 5.90 (1 H, m), 7.16–7.35 (10 H, m). FABMS (positive-ion): *m*/*z* 1084 $[M + Na]^+$; 1062 $[M + H]^+$. HRFABMS (positive-ion): *m*/*z* Calcd for $C_{53}H_{83}Cl_3NNaO_{12}P$: 1084.4616; Found: 1084.4600. Anal. Calcd for $C_{53}H_{83}Cl_3NO_{12}P$ (1063.6): C, 59.85; H, 7.87; Cl, 10.00; N, 1.32; P, 2.91. Found: C, 60.14; H, 7.59; Cl, 10.08; N, 1.42; P, 2.92.

*2-Deoxy-4-*O*-(diphenylphosphono)-6-*O*-methyl-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-*D*-glucopyranose* (**22**).—Compound **21** (478 mg, 0.450 mmol) was treated as described in the formation of **15** from **14** to give **22** (334 mg, 73%) as a solid. IR ν_{max}(KBr) 3436, 3352, 2953, 2921, 2851, 1726 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (6 H, t, *J* 6.6–7.3 Hz), 1.19–1.73 (44 H, m), 2.19 (2 H, t, *J* 7.3 Hz), 3.22 (3 H, s), 3.45–3.56 (3 H, m), 3.72–3.94 (4 H, m, containing OH), 4.13 (1 H, m), 4.56 (1 H, m), 4.71, 4.77 (2 H, AB-q, *J* 12.5 Hz), 4.90 (1 H, m), 5.29 (1 H, m), 5.88 (1 H, d, *J* 8.8 Hz, NH), 7.17–7.35 (10 H, m). FABMS (positive-ion): *m*/*z* 1060 $[M + K]^+$ (on addition of KI); 1044 $[M + Na]^+$; 1022 $[M + H]^+$. HRFABMS (positive-ion): *m*/*z* Calcd for $C_{50}H_{79}Cl_3KNO_{12}P$: 1060.4043; Found: 1060.4039. Anal. Calcd for $C_{50}H_{79}Cl_3NO_{12}P$ (1023.5): C, 58.68; H, 7.78; Cl, 10.39; N, 1.37; P, 3.03. Found: C, 58.37; H, 7.62; Cl, 10.47; N, 1.35; P, 2.95.

*Allyl 2,6-dideoxy-4-*O*-((diphenylphosphono))-6-fluoro-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-*D*-glucopyranoside* (**23**).—To a solution of **20** (938 mg, 0.894 mmol) in DME (5 mL) was gradually added a solution of DAST (0.35 mL, 2.65 mmol) in DME (1 mL) at 0 °C with stirring under N_2. After stirring for 3 h at 0 °C, water was added to the reaction mixture, and it was extracted with EtOAc. The EtOAc layer was washed with satd aq $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated to give a crude oil. The crude product was chromatographed on a silica-gel column. Elution with 7:3 cyclohexane–EtOAc gave **23** (753 mg, 80%) as a gum. IR $\nu_{max}(CHCl_3)$ 3435, 2927, 2855, 1738, 1601 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (6 H, t, *J* 6.6–7.3 Hz), 1.19–1.73 (44 H, m), 2.20 (2 H, t, *J* 7.3 Hz), 3.52 (1 H, m), 3.71 (1 H, t, *J* 9.5 Hz), 3.81–4.06 (4 H, m), 4.20 (1 H, m), 4.44–4.65 (3 H, m), 4.76 (2 H, s), 4.90 (1 H, m), 4.95 (1 H, d, *J* 3.7 Hz), 5.23–5.36 (2 H, m), 5.78 (1 H, d, *J*

9.5 Hz, NH), 5.90 (1 H, m), 7.17–7.35 (10 H, m). FABMS (positive-ion): *m/z* 1072 $[M+Na]^+$; 1050 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{52}H_{80}Cl_3FNNaO_{11}P$: 1072.4416; Found: 1072.4424.

2,6-Dideoxy-4-O-(diphenylphosphono)-6-fluoro-3-O-[(R)-3-(tetradecanoyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-D-glucopyranose (**24**).—Compound **23** (365 mg, 0.347 mmol) was treated as described in the formation of **15** from **14** to give **24** (256 mg, 73%) as a gum. IR $\nu_{max}(CHCl_3)$ 3434, 3326, 2927, 2855, 1737 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (6 H, t, *J* 6.6 Hz), 1.20–1.71 (44 H, m), 2.22 (2 H, t, *J* 7.3–8.1 Hz), 3.38 (1 H, bs, OH), 3.49 (1 H, m), 3.76–3.95 (3 H, m), 4.17 (1 H, m), 4.44–4.65 (3 H, m), 4.72, 4.77 (2 H, AB-q, *J* 12.1 Hz), 4.92 (1 H, m), 5.36 (1 H, m), 6.07 (1 H, d, *J* 8.8 Hz, NH), 7.18–7.35 (10 H, m). FABMS (positive-ion): *m/z* 1010 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{49}H_{77}Cl_3FNO_{11}P$: 1010.4284; Found: 1010.4271.

Diphenylmethyl 2,6-anhydro-7-O-[6-O-(benzyloxycarbonyl)-2-deoxy-4-O-(diphenylphosphono)-3-O-[(R)-3-(tetradecanoyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-β-D-glucopyranosyl]-3-[(R)-3-(benzyloxy)tetradecanamido]-4-O-[(R)-3-(benzyloxy)tetradecyl]-3-deoxy-D-glycero-D-ido-*heptonate* (**28**).—To a solution of **15** (116 mg, 0.102 mmol) in CH_2Cl_2 (2 mL) were added Cl_3CCN (100 mL, 0.997 mmol) and a catalytic amount of DBU (5 mg) at 0°C. After stirring for 1 h at 0 °C, the reaction mixture was concentrated in vacuo, and rapidly chromatographed to remove DBU on a short column of silica gel with 3:1 cyclohexane–EtOAc. The elution was concentrated in vacuo to give a crude imidate **25** (115 mg), which was immediately used for the next reaction without further purification. In a N_2 atmosphere, a solution of the thus-obtained imidate **25** (115 mg), diol **1** (80.6 mg, 0.081 mmol), and MS4A in CH_2Cl_2 (2 mL) was stirred at rt. After stirring for 1 h, ca. TMSOTf (5 μL) was added to the mixture at −78 °C. After stirring for 2 h at −78 °C, the mixture was quenched with satd aq $NaHCO_3$, diluted with EtOAc, washed with water and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to give a mixture, which was chromatographed on a silica-gel column. Elution with 7:3 cyclohexane–EtOAc gave **28** (152 mg, 88%) as a gum. IR $\nu_{max}(CHCl_3)$ 3432, 3354, 2927, 2855, 1739, 1670 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (12 H, t, *J* 6.5–7.1 Hz), 1.00–1.73 (86 H, m), 2.19–2.26 (4 H, m), 3.04 (1 H, bs, OH), 3.15 (1 H, m), 3.38–3.68 (12 H, m), 3.85–3.97 (2 H, m), 4.20 (1 H, dd, *J* 5.2, 11.9 Hz), 4.27–4.53 (7 H, m, containing 1 H, d, *J* 5.5 Hz, at δ 4.62), 4.78 (1 H, AB-q, *J* 12.1 Hz), 4.94–5.12 (3 H, m, containing 2 H, AB-q, *J* 12.1 Hz, at δ 5.04 and 5.10), 5.97 (1 H, m, NH), 6.80 (1 H, d, *J* 8.7 Hz, NH), 6.82 (1 H, s), 7.12–7.36 (35 H, m). FABMS (positive-ion): *m/z* 2138 $[M+Na]^+$; 2115 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{119}H_{170}Cl_3N_2NaO_{22}P$: 2138.0946; Found: 2138.0940.

Diphenylmethyl 2,6-anhydro-7-O-[2-deoxy-4-O-(diphenylphosphono)-6-O-methyl-3-O-[(R)-3-(tetradecanoyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-β-D-glucopyranosyl]-3-[(R)-3-(benzyloxy)tetradecanamido]-4-O-[(R)-3-(benzyloxy)tetradecyl]-3-deoxy-D-glycero-D-ido-*heptonate* (**29**).—Compound **22** (279 mg, 0.273 mmol) was treated as described in the formation of **28** from **15** to give **29** (261 mg, 72%) as a gum after chromatography on a silica-gel column eluted by 3:2 hexane–EtOAc. IR $\nu_{max}(CHCl_3)$ 3431, 3354, 2927, 2855, 1732, 1669 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (12 H, t, *J* 6.6 Hz), 1.25–1.76 (86 H, m), 2.20–2.25 (4 H, m), 3.10 (1 H, s, OH), 3.17–3.25 (4 H, m, containing 3 H, s, at δ 3.20), 3.40–3.74 (13 H, m), 3.82 (1 H, m), 3.98 (1 H, m), 4.27–4.37 (3 H, m, containing 2 H, AB-q, *J* 11.7 Hz, at δ 4.29 and 4.33), 4.40, 4.44 (2 H, AB-q, *J* 11.7 Hz), 4.51 (1 H, m), 4.62–4.65 (3 H, m, containing 1 H, d, *J* 5.1 Hz, at δ 4.62), 4.78 (1 H, AB-q, *J* 11.7 Hz), 4.91 (1 H, m), 5.01 (1 H, m), 5.88 (1 H, m, NH), 6.78 (1 H, d, *J* 8.1 Hz, NH), 6.82 (1 H, s), 7.17–7.35 (30 H, m). FABMS (positive-ion): *m/z* 2017 $[M+Na]^+$; 1995 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{112}H_{166}Cl_3N_2NaO_{20}P$: 2018.0735; Found: 2018.0732.

Diphenylmethyl 2,6-anhydro-7-O-[2,6-dideoxy-4-O-(diphenylphosphono)-6-fluoro-3-O-[(R)-3-(tetradecanoyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-β-D-

glucopyranosyl]-3-[(R)-3-(benzyloxy)tetradecanamido]-4-O-[(R)-3-(benzyloxy)tetradecyl]-3-deoxy-D-glycero-D-ido-heptonate (**30**).—Compound **24** (255 mg, 0.252 mmol) was treated as described in the formation of **28** from **15** to give **30** (261 mg, 72%) as a gum after chromatography on a silica-gel column eluted by 3:2 hexane–EtOAc. IR $\nu_{max}(CHCl_3)$ 2927, 2855, 1732, 1670, 1601 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (12 H, t, *J* 6.6 Hz), 1.25–1.71 (86 H, m), 2.21–2.26 (4 H, m), 2.97 (1 H, s, OH), 3.17 (1 H, m), 3.43–4.01 (14 H, m), 4.27–4.81 (11 H, m, containing 1 H, d, *J* 5.9 Hz, at δ 4.63), 5.01 (1 H, m), 5.94 (1 H, bs, NH), 6.81 (1 H, d, *J* 11.0 Hz, NH), 6.82 (1 H, s), 7.17–7.35 (30 H, m). FABMS (positive-ion): *m/z* 2005 $[M+Na]^+$; 1983 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{111}H_{163}Cl_3FN_2NaO_{19}P$: 2006.0535; Found: 2006.0531.

Diphenylmethyl 2,6-anhydro-7-O-[2-acetamido-6-O-(benzyloxycarbonyl)-2-deoxy-4-O-(diphenylphosphono)-3-O-[(R)-3-(tetradecanoyloxy)tetradecyl]-β-D-glucopyranosyl]-3-[(R)-3-(benzyloxy)tetradecanamido]-4-O-[(R)-3-(benzyloxy)tetradecyl]-3-deoxy-D-glycero-D-ido-heptonate (**31**).—To a solution of **28** (60.8 mg, 0.029 mmol) in AcOH (2 mL) was added zinc dust (40.2 mg). After stirring vigorously for 24 h at rt, the solution was filtered through Celite to remove the zinc dust, and concentrated in vacuo to give a crude product. The product was diluted with EtOAc, washed with satd aq $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Next, the crude product was dissolved in THF (0.4 mL) and water (0.8 mL), pyridine (10 mL) and Ac_2O (10 mL) were added to this solution. After stirring for 4 h at rt, the mixture was diluted with EtOAc, washed with water and brine, dried over $MgSO_4$, filtered, concentrated in vacuo, and chromatographed on a silica-gel column. Elution with 3:2 cyclohexane–EtOAc gave **31** (40.2 mg, two steps, 70%) as a gum. IR $\nu_{max}(CHCl_3)$ 3432, 3365, 2927, 2855, 1738, 1668 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (12 H, t, *J* 6.6–7.3 Hz), 1.00–1.76 (86 H, m), 1.92 (3 H, s), 2.17–2.26 (4 H, m), 3.08 (1 H, m), 3.33–3.72 (12 H, m), 3.89–4.02 (2 H, m), 4.21 (1 H, dd, *J* 5.1, 11.9 Hz), 4.28–4.52 (7 H, m), 4,63 (1 H, d, *J* 5.7 Hz), 5.02–5.10 (3 H, m, containing 2 H, AB-q, *J* 12.1 Hz, at δ 5.03 and 5.10), 5.27 (1 H, d, *J* 8.2 Hz), 6.64 (1 H, d, *J* 6.3 Hz, NH), 6.78 (1 H, d, *J* 8.9 Hz, NH), 6.81 (1 H, s), 7.12–7.37 (35 H, m). FABMS (positive-ion): *m/z* 2006 $[M+Na]^+$; 1984 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{118}H_{171}N_2NaO_{21}P$: 2006.2010; Found: 2006.2009.

Diphenylmethyl 2,6-anhydro-7-O-[2-acetamido-2-deoxy-4-O-(diphenylphosphono)-6-O-methyl-3-O-[(R)-3-(tetradecanoyloxy)tetradecyl]-β-D-glucopyranosyl]-3-[(R)-3-(benzyloxy)tetradecanamido]-4-O-[(R)-3-(benzyloxy)tetradecyl]-3-deoxy-D-glycero-D-ido-heptonate (**32**).—Compound **29** (135 mg, 0.068 mmol) was treated as described in the formation of **31** from **28** to give **32** (81.4 mg, two steps, 65%) as a gum after chromatography on a silica-gel column eluted by 1:1 hexane–EtOAc. IR $\nu_{max}(CHCl_3)$ 3433, 3369, 2927, 2855, 1720, 1669, 1600 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (12 H, t, *J* 6.6–7.3 Hz), 1.22–1.74 (86 H, m), 1.93 (3 H, s), 2.20–2.24 (4 H, m), 3.18 (1 H, m), 3.22 (3 H, s), 3.37–3.72 (14 H, m, containing OH), 3.89 (1 H, m), 4.02 (1 H, m), 4.29–4.38 (3 H, m, containing 2 H, AB-q, *J* 11.0 Hz, at δ 4.30 and 4.34), 4.42 (2 H, s), 4.50 (1 H, m), 4.63 (1 H, d, *J* 5.9 Hz), 5.07 (1 H, m), 5.21 (1 H, d, *J* 8.1 Hz), 6.56 (1 H, d, *J* 6.6 Hz, NH), 6.76 (1 H, d, *J* 8.8 Hz, NH), 6.81 (1 H, s), 7.17–7.36 (30 H, m). FABMS (positive-ion): *m/z* 1885 $[M+Na]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{111}H_{167}N_2NaO_{19}P$: 1886.1798; Found: 1886.1825.

Diphenylmethyl 2,6-anhydro-7-O-[2-acetamido-2,6-dideoxy-4-O-(diphenylphosphono)-6-fluoro-3-O-[(R)-3-(tetradecanoyloxy)tetradecyl]-β-D-glucopyranosyl]-3-[(R)-3-(benzyloxy)tetradecanamido]-4-O-[(R)-3-(benzyloxy)tetradecyl]-3-deoxy-D-glycero-D-ido-heptonate (**33**).—Compound **30** (152 mg, 0.077 mmol) was treated as described in the formation of **31** from **28** to give **33** (94.2 mg, two steps, 66%) as a gum after chromatography on a silica-gel column eluted by 3:2 hexane–EtOAc. IR $\nu_{max}(CHCl_3)$ 3432, 3364, 2927, 2855, 1718, 1668, 1600 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (12 H, t, *J* 6.6 Hz), 1.22–1.73 (86 H, m), 2.21–2.24 (4 H, m), 3.10

(1 H, m), 3.39–3.69 (12 H, m, containing OH), 3.93–4.05 (2 H, m), 4.28–4.58 (8 H, m, containing 2 H, AB-q, *J* 11.4 Hz, at δ 4.30, 4.34, and 2 H, s, at δ 4.43), 4.63 (1 H, d, *J* 5.9 Hz), 5.07 (1 H, m), 5.28 (1 H, d, *J* 8.8 Hz), 6.59 (1 H, d, *J* 6.6 Hz, NH), 6.78 (1 H, d, *J* 8.8 Hz, NH), 6.81 (1 H, s), 7.17–7.35 (30 H, m). FABMS (positive-ion): *m/z* 1873 $[M+Na]^+$; 1851 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{110}H_{164}FN_2NaO_{18}P$: 1874.1599; Found: 1874.1609.

*2,6-Anhydro-7-*O*-[2-acetamido-2-deoxy-4-*O*-(diphenylphosphono)-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecyl]-β-*D*-glucopyranosyl]-3-deoxy-3-[(*R*)-3-(hydroxy)tetradecanamido]-4-*O*-[(*R*)-3-(hydroxy)tetradecyl]-*D*-glycero-*D*-ido-heptonic acid* (**34**).—A solution of **31** (38.8 mg, 0.020 mmol) in EtOH (2 mL) containing 20% $Pd(OH)_2$–C (35.2 mg) was stirred vigorously under hydrogen for 14 h at rt. The reaction mixture was filtered and concentrated in vacuo to give a crude product. This crude product was chromatographed on a short column of silica gel. Elution with 8:1 $CHCl_3$–MeOH gave **34** (15.2 mg, 52%) as an amorphous resin. A fair amount of **34** was irreversibly absorbed on the silica-gel column. IR $\nu_{max}(CHCl_3)$ 3691, 3606, 3415, 3358, 1716, 1662, 1602 cm^{-1}. ^1H NMR (400 MHz, CD_3OD) δ 0.90 (12 H, t, *J* 6.6 Hz), 1.14–1.76 (86 H, m), 2.01 (3 H, s), 2.19 (2 H, t, *J* 7.1 Hz), 2.33–2.37 (2 H, m), 3.43 (1 H, m), 3.51–4.04 (14 H, m), 4.20 (1 H, m), 4.41 (1 H, d, *J* 4.3 Hz), 4.54 (1 H, m), 4.70 (1 H, m), 4.81–4.90 (2 H, m), 7.19–7.41 (10 H, m). FABMS (positive-ion): *m/z* 1525 $[M+Na]^+$; 1503 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{83}H_{143}N_2NaO_{19}P$: 1525.9920; Found: 1525.9941.

*2,6-Anhydro-7-*O*-[2-acetamido-2-deoxy-4-*O*-(diphenylphosphono)-6-*O*-methyl-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecyl]-β-*D*-glucopyranosyl]-3-deoxy-3-[(*R*)-3-(hydroxy)tetradecanamido]-4-*O*-[(*R*)-3-(hydroxy)tetradecyl]-*D*-glycero-*D*-ido-heptonic acid* (**35**).—Compound **32** (73.1 mg, 0.039 mmol) was treated as described in the formation of **34** from **31** to give **35** (42.7 mg, 72%) as an amorphous solid after chromatography on a silica-gel column eluted by 8:1 $CHCl_3$–MeOH. IR ν_{max}(KBr) 3321, 2924, 2854, 1731, 1651 cm^{-1}. ^1H NMR (400 MHz, CD_3OD) δ 0.90 (12 H, t, *J* 6.6–7.3 Hz), 1.28–1.76 (86 H, m), 2.00 (3 H, s), 2.19 (2 H, t, *J* 7.3 Hz), 2.34–2.37 (2 H, m), 3.21 (3 H, s), 3.43–3.48 (3 H, m), 3.57–4.01 (13 H, m), 4.21 (1 H, m), 4.47 (1 H, d, *J* 5.1 Hz), 4.55 (1 H, m), 4.64 (1 H, d, *J* 8.1 Hz), 4.83 (1 H, m), 7.20–7.41 (10 H, m). FABMS (positive-ion): *m/z* 1539 $[M+Na]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{84}H_{145}N_2NaO_{19}P$: 1540.0095; Found: 1540.0077.

*2,6-Anhydro-7-*O*-[2-acetamido-2,6-dideoxy-4-*O*-(diphenylphosphono)-6-fluoro-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecyl]-β-*D*-glucopyranosyl]-3-deoxy-3-[(*R*)-3-(hydroxy)tetradecanamido]-4-*O*-[(*R*)-3-(hydroxy)tetradecyl]-*D*-glycero-*D*-ido-heptonic acid* (**36**).—Compound **33** (90.3 mg, 0.049 mmol) was treated as described in the formation of **34** from **31** to give **36** (47.1 mg, 64%) as an amorphous solid after chromatography on a silica-gel column eluted by 8:1 $CHCl_3$–MeOH. IR $\nu_{max}(CHCl_3)$ 3606, 3416, 3357, 2927, 2855, 1713, 1663, 1602 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.90 (12 H, t, *J* 6.6 Hz), 1.23–1.75 (86 H, m), 2.00 (3 H, s), 2.20 (2 H, t, *J* 7.3 Hz), 2.34–2.37 (2 H, m), 3.45 (1 H, m), 3.58–4.04 (13 H, m), 4.20 (1 H, m), 4.38–4.58 (4 H, m, containing 1 H, d, *J* 5.1 Hz, at δ 4.47), 4.70 (1 H, d, *J* 8.1 Hz), 7.19–7.42 (10 H, m). FABMS (positive-ion): *m/z* 1527 $[M+Na]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{83}H_{142}FN_2NaO_{18}P$: 1527.9877; Found: 1527.9941.

*2,6-Anhydro-7-*O*-[2-acetamido-2-deoxy-4-*O*-phosphono-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecyl]-β-*D*-glucopyranosyl]-3-deoxy-3-[(*R*)-3-(hydroxy)tetradecanamido]-4-*O*-[(*R*)-3-(hydroxy)tetradecyl]-*D*-glycero-*D*-ido-heptonic acid* (**37**).—A solution of **34** (3.5 mg, 0.002 mmol) in THF (1 mL) containing PtO_2 (3.1 mg) was stirred vigorously under H_2 for 18 h at rt. The reaction mixture was filtered and concentrated in vacuo to give a residue. The residue was dissolved in $CHCl_3$ (4 mL), MeOH (8 mL) and aq 0.1 M HCl (3.2 mL). To this solution was added another volume of $CHCl_3$ (4 mL) and aq 0.1 M HCl (4 mL) to separate the solution into two phases. The lower $CHCl_3$ phase was collected and concentrated to give **37** (3.0 mg, 95%) as a white powder, mp 168–169 °C. $[\alpha]_D^{25}$ −4.2° (*c* 0.10, $CHCl_3$). IR $\nu_{max}(CHCl_3)$ 3353, 1713, 1657,

1604 cm^{-1}. ^1H NMR (400 MHz, 3:1 CD_3OD–$CDCl_3$) δ 0.89 (12 H, t, J 6.6–7.3 Hz), 1.28–1.75 (86 H, m), 2.01 (3 H, s), 2.28–2.42 (4 H, m), 3.31–4.53 (20 H, m), 4.99 (1 H, m). FABMS (positive-ion): m/z 1389 $[M+K]^+$ (on addition of KI); 1373 $[M+Na]^+$; 1351 $[M+H]^+$. HRFABMS (positive-ion): m/z Calcd for $C_{71}H_{136}N_2O_{19}P$: 1351.9475; Found: 1351.9468.

*2,6-Anhydro-7-*O*-[2-acetamido-2-deoxy-6-*O*-methyl-4-*O*-phosphono-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecyl]-β-*D*-glucopyranosyl]-3-deoxy-3-[(*R*)-3-(hydroxy)tetradecanamido]-4-*O*-[(*R*)-3-(hydroxy)tetradecyl]-*D*-glycero-*D*-ido-heptonic Acid* (**38**).—Compound **35** (40.8 mg, 0.027 mmol) was treated as described in the formation of **37** from **34** to give **38** (35.4 mg, 96%) as a white powder, mp 177.5–178.6 °C. $[\alpha]_D^{24}$ −44.6° (c 0.12, $CHCl_3$). IR ν_{max}(KBr) 3315, 2924, 2854, 1730, 1646 cm^{-1}. ^1H NMR (400 MHz, 1:1 CD_3OD–$CDCl_3$) δ 0.89 (12 H, t, J 6.6–7.3 Hz), 1.23–1.85 (86 H, m), 2.01 (3 H, s), 2.29–2.42 (4 H, m), 3.41 (3 H, s), 3.48–3.92 (15 H, m), 4.02–4.14 (2 H, m), 4.28 (1 H, dd, J 5.1, 9.5 Hz), 4.50 (1 H, d, J 5.1 Hz), 4.62 (1 H, d, J 8.8 Hz), 4.95 (1 H, m). FABMS (positive-ion): m/z 1387 $[M+Na]^+$; 1365 $[M+H]^+$. HRFABMS (positive-ion): m/z Calcd for $C_{72}H_{137}N_2NaO_{19}P$: 1541387.9451; Found: 1387.9464. Anal. Calcd for $C_{72}H_{137}N_2O_{19}P$ (1365.8): C, 63.32; H, 10.11; N, 2.05; P, 2.27. Found: C, 62.95; H, 9.94; N, 2.15; P, 2.27.

*2,6-Anhydro-7-*O*-[2-acetamido-2,6-dideoxy-6-fluoro-4-*O*-phosphono-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecyl]-β-*D*-glucopyranosyl]-3-deoxy-3-[(*R*)-3-(hydroxy)tetradecanamido]-4-*O*-[(*R*)-3-(hydroxy)tetradecyl]-*D*-glycero-*D*-ido-heptonic acid* (**39**).—Compound **36** (45.3 mg, 0.030 mmol) was treated as described in the formation of **37** from **34** to give **39** (40.1 mg, 98%) as a white powder, mp. 191.5–192.0 °C. $[\alpha]_D^{24}$ −30.6° (c 0.10, $CHCl_3$). IR ν_{max}(KBr) 3304, 2924, 2854, 1730, 1648 cm^{-1}. ^1H NMR (400 MHz, 1:1 CD_3OD–$CDCl_3$) δ 0.89 (12 H, t, J 6.6 Hz), 1.18–1.83 (86 H, m), 2.01 (3 H, s), 2.30–2.42 (4 H, m), 3.48–3.92 (16 H, m), 4.04–4.14 (2 H, m), 4.27 (1 H, m), 4.50 (1 H, d, J 5.1 Hz), 4.65–4.69 (2 H, m), 4.96 (1 H, m). FABMS (positive-ion): m/z 1375 $[M+Na]^+$; 1353 $[M+H]^+$. HRFABMS (positive-ion): m/z Calcd for $C_{71}H_{134}FN_2NaO_{18}P$: 1375.9251; Found: 1375.9238. Anal. Calcd for $C_{71}H_{134}FN_2O_{18}P$ (1353.8): C, 62.99; H, 9.98; F, 1.40; N, 2.07; P, 2.29. Found: C, 62.77; H, 9.72; F, 1.30; N, 2.05; P, 2.28.

*Diphenylmethyl 2,6-anhydro-7-*O*-[6-*O*-(benzyloxycarbonyl)-2-deoxy-4-*O*-(diphenylphosphono)-2-[(*R*)-3-(dodecanoyloxy)tetradecanamido]-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecyl]-β-*D*-glucopyranosyl]-3-[(*R*)-3-(benzyloxy)tetradecanamido]-4-*O*-[(*R*)-3-(benzyloxy)-tetradecyl]-3-deoxy*-*D*-glycero-*D*-ido-heptonate* (**40**).—To a solution of **28** (118.2 mg, 0.056 mmol) in AcOH (3 mL) was added zinc dust (105 mg). After stirring vigorously for 20 h at rt, the solution was filtered through Celite to remove the zinc dust and concentrated in vacuo to give a crude product. The product was diluted with EtOAc, washed with satd aq $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. Next, the crude product was dissolved in 1,2-dichloroethane, and DCC (25.5 mg, 0.124 mmol) and (*R*)-3-(dodecanoyloxy)tetradecanoic acid (48.5 mg, 0.114 mmol) were added. After stirring for 6 h at rt, the mixture was filtered, concentrated in vacuo, and chromatographed on a silica-gel column. Elution with 3:2 cyclohexane–EtOAc gave **40** (70.6 mg, two steps, 54%) as a gum. IR ν_{max}($CHCl_3$) 3692, 3435, 3364, 2928, 2855, 1732, 1660, 1601 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (18 H, t, J 6.6 Hz), 1.05–1.96 (124 H, m), 2.14 (2 H, t, J 7.3–8.1 Hz), 2.21–2.23 (2 H, m), 2.27 (2 H, t, J 7.3–8.1 Hz), 2.40–2.42 (2 H, m), 3.10 (1 H, m), 3.39–3.70 (12 H, m, containing OH), 3.90–4.05 (2 H, m), 4.17 (1 H, dd, J 5.1, 11.7 Hz), 4.31 (2 H, s), 4.34–4.37 (2 H, m), 4.41 (2 H, s), 4.48 (1 H, dd, J 8.4, 17.2 Hz), 4.62 (1 H, d, J 5.1 Hz), 5.01–5.11 (3 H, m, containing 2 H, AB-q, J 11.7 Hz, at δ 5.02 and 5.09), 5.22–5.28 (2 H, m, containing 1 H, d, J 8.1 Hz, at δ 5.23), 6.69 (1 H, d, J 5.9 Hz), 6.74 (1 H, d, J 9.5 Hz), 6.80 (1 H, s), 7.11–7.34 (35 H, m). FABMS (positive-ion): m/z 2387 $[M+K]^+$ (on addition of KI); 2371 $[M+Na]^+$. HRFABMS (positive-ion): m/z Calcd for $C_{142}H_{217}KN_2O_{23}P$: 2388.5247; Found: 2388.5266.

*Diphenylmethyl 2,6-anhydro-7-*O*-[2-deoxy-4-*O*-(diphenylphosphono)-2-[(*R*)-3-(dodecanoyloxy)tetradecanamido]-6-*O*-methyl-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecyl]-β-D-glucopyranosyl]-3-[(*R*)-3-(benzyloxy)tetradecanamido]-4-*O*-[(*R*)-3-(benzyloxy)tetradecyl]-3-deoxy*-D-glycero-D-ido-*heptonate* (**41**).—Compound **29** (110.3 mg, 0.055 mmol) was treated as described in the formation of **40** from **28** to give **41** (87.6 mg, two steps, 71%) as a gum after chromatography on a silica-gel column eluted by 3:2 hexane–EtOAc. IR ν_{max}($CHCl_3$) 3431, 3364, 2927, 2855, 1727, 1671 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (18 H, t, *J* 6.6 Hz), 1.22–1.75 (124 H, m), 2.16 (2 H, t, *J* 7.3–8.1 Hz), 2.21–2.23 (2 H, m), 2.27 (2 H, t, *J* 7.3 Hz), 2.41–2.43 (2 H, m), 3.16–3.23 (4 H, m, containing 3 H, s, at δ 3.20), 3.41–3.60 (12 H, m, containing OH), 3.69–3.75 (2 H, m), 3.87–3.99 (2 H, m), 4.31 (2 H, s), 4.35 (1 H, m), 4.42 (2 H, s), 4.47 (1 H, m), 4.62 (1 H, d, *J* 5.9 Hz), 5.10 (1 H, m), 5.17 (1 H, d, *J* 8.1 Hz), 5.27 (1 H, m), 6.66 (1 H, d, *J* 6.6 Hz), 6.74 (1 H, d, *J* 8.8 Hz), 6.81 (1 H, s), 7.17–7.34 (30 H, m). FABMS (positive-ion): *m/z* 2251 $[M + Na]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{135}H_{213}N_2NaO_{21}P$: 2252.5296; Found: 2252.5334.

*Diphenylmethyl 2,6-anhydro-7-*O*-[2,6-dideoxy-4-*O*-(diphenylphosphono)-2-[(*R*)-3-(dodecanoyloxy)tetradecanamido]-6-fluoro-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecyl]-β-D-glucopyranosyl]-3-[(*R*)-3-(benzyloxy)tetradecanamido]-4-*O*-[(*R*)-3-(benzyloxy)tetradecyl]-3-deoxy*-D-glycero-D-ido-*heptonate* (**42**).—Compound **30** (80.1 mg, 0.040 mmol) was treated as described in the formation of **40** from **28** to give **42** (51.4 mg, two steps, 58%) as a gum after chromatography on a silica-gel column eluted by 3:2 hexane–EtOAc. IR ν_{max}($CHCl_3$) 3431, 3362, 2927, 2855, 1727, 1671, 1601 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (18 H, t, *J* 6.6 Hz), 1.22–1.74 (124 H, m), 2.15 (2 H, t, *J* 7.3–8.1 Hz), 2.22–2.23 (2 H, m), 2.27 (2 H, t, *J* 7.3–8.1 Hz), 2.41–2.42 (2 H, m), 3.13 (1 H, m), 3.42–3.70 (12 H, m, containing OH), 3.93–4.01 (2 H, m), 4.31 (2 H, s), 4.36–4.55 (6 H, m, containing 2 H, s, at δ 4.42), 4.62 (1 H, d, *J* 5.1 Hz), 5.10 (1 H, m), 5.23–5.28 (2 H, m, containing 1 H, d, *J* 8.1 Hz, at δ 5.24), 6.69 (1 H, d, *J* 6.6 Hz), 6.76 (1 H, d, *J* 8.8 Hz), 6.81 (1 H, s), 7.15–7.35 (30 H, m). FABMS (positive-ion): *m/z* 2239 $[M + Na]^+$, 2217 $[M + H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{134}H_{210}FN_2NaO_{20}P$: 2240.5096; Found: 2240.5071.

*2,6-Anhydro-7-*O*-[2-deoxy-4-*O*-(diphenylphosphono)-2-[(*R*)-3-(dodecanoyloxy)tetradecanamido]-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecyl]-β-D-glucopyranosyl]-3-deoxy-3-[(*R*)-3-(hydroxy)tetradecanamido]-4-*O*-[(*R*)-3-(hydroxy)tetradecyl]-D-glycero-D-ido-heptonic acid* (**43**).—Compound **40** (70.5 mg, 0.030 mmol) was treated as described in the formation of **34** from **31** to give **43** (27.4 mg, 49%) as an amorphous solid after chromatography on a silica-gel column eluted by 9:1 $CHCl_3$–MeOH. IR ν_{max}($CHCl_3$) 3418, 2927, 2855, 1719, 1665, 1600 cm^{-1}. ^1H NMR (400 MHz, 3:1 CD_3OD–$CDCl_3$) δ 0.90 (18 H, t, *J* 6.6–7.3 Hz), 1.28–1.77 (124 H, m), 2.22 (2 H, t, *J* 7.3 Hz), 2.28–2.41 (4 H, m), 2.49–2.60 (2 H, m), 3.47–4.02 (16 H, m), 4.23 (1 H, m), 4.46 (1 H, d, *J* 5.1 Hz), 4.54 (1 H, m), 4.75 (1 H, d, *J* 8.1 Hz), 4.89 (1 H, m), 5.27 (1 H, m), 7.18–7.40 (10 H, m). FABMS (positive–ion): *m/z* 1891 $[M + Na]^+$; 1869 $[M + H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{107}H_{189}N_2NaO_{21}P$: 1892.3418; Found: 1892.3439.

*2,6-Anhydro-7-*O*-[2-deoxy-4-*O*-(diphenylphosphono)-2-[(*R*)-3-(dodecanoyloxy)tetradecanamido]-6-*O*-methyl-3-*O*-[(*R*)-3-(tetradecanoyloxy)tetradecyl]-β-D-glucopyranosyl]-3-deoxy-3-[(*R*)-3-(hydroxy)tetradecanamido]-4-*O*-[(*R*)-3-(hydroxy)tetradecyl]-D-glycero-D-ido-heptonic acid* (**44**).—Compound **41** (80.6 mg, 0.036 mmol) was treated as described in the formation of **34** from **31** to give **44** (52.5 mg, 77%) as an amorphous solid after chromatography on a silica-gel column eluted by 9:1 $CHCl_3$–MeOH. IR ν_{max}($CHCl_3$) 2927, 2855, 1716, 1666, 1601 cm^{-1}. ^1H NMR (400 MHz, 3:1 CD_3OD–$CDCl_3$) δ 0.90 (18 H, t, *J* 6.6–7.3 Hz), 1.28–1.74 (124 H, m), 2.22 (2 H, t, *J* 7.3 Hz), 2.28–2.41 (4 H, m), 2.50–2.59 (2 H, m), 3.20 (3 H, s), 3.44–3.98 (16 H, m), 4.23 (1 H, m), 4.48 (1 H, d, *J* 5.1 Hz), 4.55 (1 H, m), 4.73 (1 H, d, *J* 8.1 Hz), 4.89 (1 H, m), 5.27 (1 H, m), 7.19–7.40 (10 H, m). FABMS (positive-ion): *m/z* 1905 $[M + Na]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{108}H_{191}N_2NaO_{21}P$: 1906.3575; Found: 1906.3572.

2,6-Anhydro-7-O-[2,6-dideoxy-4-O-(diphenylphosphono)-2-[(R)-3-(dodecanoyloxy)tetradecanamido]-6-fluoro-3-O-[(R)-3-(tetradecanoyloxy)tetradecyl]-β-D-glucopyranosyl]-3-deoxy-3-[(R)-3-(hydroxy)tetradecanamido]-4-O-[(R)-3-(hydroxy)tetradecyl]-D-glycero-D-ido-heptonic acid (**45**).—Compound **42** (80.1 mg, 0.040 mmol) was treated as described in the formation of **34** from **31** to give **45** (51.4 mg, two steps, 58%) as an amorphous solid after chromatography on a silica-gel column eluted by 9:1 $CHCl_3$–MeOH IR ν_{max}($CHCl_3$) 2927, 2855, 1716, 1665, 1602 cm^{-1}. ^1H NMR (400 MHz, 3:1 CD_3OD–$CDCl_3$) δ 0.88 (18 H, t, *J* 6.6–7.3 Hz), 1.29–1.82 (124 H, m), 2.23 (2 H, t, *J* 7.3–8.1 Hz), 2.30 (2 H, t, *J* 7.3–8.1 Hz), 2.34–2.40 (2 H, m), 2.50–2.56 (2 H, m), 3.47–4.01 (14 H, m), 4.22 (1 H, m), 4.34–4.58 (4 H, m, containing 1 H, d, *J* 5.1 Hz, at δ 4.47), 4.76–4.89 (2 H, m, containing 1 H, d, *J* 8.1 Hz, at δ 4.80), 5.28 (1 H, m), 7.18–7.42 (10 H, m). FABMS (positive-ion): *m/z* 1893 $[M+Na]^+$; 1871 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{107}H_{188}FN_2NaO_{20}P$: 1894.3375; Found: 1894.3374.

2,6-Anhydro-7-O-[2-deoxy-2-[(R)-3-(dodecanoyloxy)tetradecanamido]-4-O-phosphono-3-O-[(R)-3-(tetradecanoyloxy)tetradecyl]-β-D-glucopyranosyl]-3-deoxy-3-[(R)-3-(hydroxy)tetradecanamido]-4-O-[(R)-3-(hydroxy)tetradecyl]-D-glycero-D-ido-heptonic acid (**46**).—Compound **43** (20.1 mg, 0.011 mmol) was treated as described in the formation of **37** from **34** to give **46** (18.1 mg, 98%) as a white powder, mp 185.5–186.3 °C. $[\alpha]_D^{25}$ −0.9° (*c* 0.25, $CHCl_3$). IR ν_{max}(KBr) 3400, 3310, 3085, 2957, 2923, 2853, 1730, 1650 cm^{-1}. ^1H NMR (400 MHz, 1:1 CD_3OD–$CDCl_3$) δ 0.90 (18 H, t, *J* 6.6–7.0 Hz), 1.12–1.85 (124 H, m), 2.30–2.57 (8 H, m), 3.34–4.01 (16 H, m), 4.13 (1 H, m), 4.30 (1 H, m), 4.50 (1 H, d, *J* 5.0 Hz), 4.68 (1 H, d, *J* 8.3 Hz), 5.00 (1 H, m), 5.25 (1 H, m). FABMS (positive-ion): *m/z* 1739 $[M+Na]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{95}H_{181}N_2NaO_{21}P$: 1740.2792; Found: 1740.2795.

2,6-Anhydro-7-O-[2-deoxy-2-[(R)-3-(dodecanoyloxy)tetradecanamido]-6-O-methyl-4-O-phosphono-3-O-[(R)-3-(tetradecanoyloxy)tetradecyl]-β-D-glucopyranosyl]-3-deoxy-3-[(R)-3-(hydroxy)tetradecanamido]-4-O-[(R)-3-(hydroxy)tetradecyl]-D-glycero-D-ido-heptonic acid (**47**).—Compound **44** (80.6 mg, 0.036 mmol) was treated as described in the formation of **42** from **34** to give **47** (52.5 mg, 77%) as a white powder, mp 176.5–177.0 °C. $[\alpha]_D^{24}$ −3.4° (*c* 0.18, $CHCl_3$). IR ν_{max}(KBr) 3409, 2957, 2922, 2853, 1730, 1649 cm^{-1}. ^1H NMR (400 MHz, 3:1 CD_3OD–$CDCl_3$) δ 0.89 (18 H, t, *J* 6.6 Hz), 1.28–1.85 (124 H, m), 2.29–2.42 (6 H, m), 2.49 (1 H, dd, *J* 5.9, 14.6 Hz), 2.57 (1 H, dd, *J* 7.3, 14.6 Hz), 3.40 (3 H, s), 3.53–3.63 (7 H, m), 3.69 (1 H, m), 3.79–4.00 (8 H, m), 4.09 (1 H, m), 4.27 (1 H, m), 4.51 (1 H, d, *J* 5.1 Hz), 4.66 (1 H, d, *J* 8.1 Hz), 4.98 (1 H, m), 5.26 (1 H, m). FABMS (positive-ion): *m/z* 1753 $[M+Na]^+$. FABMS (negative-ion): *m/z* 1729 $[M-H]^{-1}$. HRFABMS (positive-ion): *m/z* Calcd for $C_{96}H_{183}N_2NaO_{21}P$: 1754.2949; Found: 1754.3015. Anal. Calcd for $C_{96}H_{183}N_2O_{21}P$ (1732.5): C, 66.56; H, 10.65; N, 1.62; P, 1.79. Found: C, 66.16; H, 10.66; N, 1.54; P, 1.68.

2,6-Anhydro-7-O-[2,6-dideoxy-2-[(R)-3-(dodecanoyloxy)tetradecanamido]-6-fluoro-4-O-phosphono-3-O-[(R)-3-(tetradecanoyloxy)tetradecyl]-β-D-glucopyranosyl]-3-deoxy-3-[(R)-3-(hydroxy)tetradecanamido]-4-O-[(R)-3-(hydroxy)tetradecyl]-D-glycero-D-ido-heptonic acid (**48**).—Compound **45** (11.8 mg, 0.006 mmol) was treated as described in the formation of **37** from **34** to give **48** (9.5 mg, 88%) as a white powder, mp 195.0–196.0 °C. $[\alpha]_D^{25}$ −6.2° (*c* 0.22, $CHCl_3$). IR ν_{max}(KBr) 3423, 3312, 3085, 2957, 2923, 2853, 1731, 1649 cm^{-1}. ^1H NMR (400 MHz, 1:1 CD_3OD–$CDCl_3$) δ 0.90 (18 H, t, *J* 6.6–7.3 Hz), 1.29–1.87 (124 H, m), 2.30–2.42 (6 H, m), 2.50 (1 H, dd, *J* 5.9, 14.6 Hz), 2.57 (1 H, dd, *J* 7.3, 14.6 Hz), 3.52–4.03 (14 H, m), 4.11 (1 H, m), 4.27 (1 H, m), 4.51 (1 H, d, *J* 5.1 Hz), 4.57–4.73 (3 H, m), 4.99 (1 H, m), 5.26 (1 H, m). FABMS (positive-ion): *m/z* 1741 $[M+Na]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{95}H_{180}FN_2NaO_{20}P$: 1742.2749; Found: 1742.2716.

Allyl 2-deoxy-3-O-[(R)-3-(dodecyloxy)tetradecyl]-4,6-O-isopropylidene-2-trifluoroacetamido-α-D-glucopyranoside (**49**).—To a solution of allyl 2-deoxy-4,6-*O*-isopropylidene-2-trifluoroacetamido-α-D-glucopyranoside (**6**, 4.23 g, 11.9 mmol) in DMF (60 mL) was gradually added NaH (60% oil dispersion,

725 mg, 18.1 mmol) at 0 °C with stirring. After 30 min, (*R*)-3-(dodecyloxy)-1-(methanesulfonyloxy)tetradecane (6.80 g, 14.3 mmol) was added to this solution, which was then stirred at rt for 3 h. The reaction mixture was quenched with water, extracted with EtOAc, washed with water and brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated in vacuo to give a mixture that was chromatographed on a silica-gel column. Elution with 4:1 hexane–EtOAc gave **49** (6.60 g, 75%) as a wax. IR $\nu_{max}(CHCl_3)$ 3431, 2928, 2855, 1734 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (6 H, t, *J* 6.6 Hz), 1.21–1.67 (48 H, m, containing 3 H, s, at δ 1.41, and 3 H, s, at δ 1.51), 3.29–3.41 (3 H, m), 3.49–3.58 (2 H, m), 3.67–3.78 (3 H, m), 3.83–3.89 (2 H, m), 3.98 (1 H, dd, *J* 5.1, 12.5 Hz), 4.13–4.20 (2 H, m), 4.89 (1 H, d, *J* 3.7 Hz), 5.24–5.31 (2 H, m), 5.86 (1 H, m), 6.55 (1 H, d, *J* 9.5 Hz, NH). FABMS (positive-ion): *m/z* 736 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{40}H_{73}F_3NO_7$: 736.5339; Found: 736.5337. Anal. Calcd for $C_{40}H_{72}F_3NO_7$ (736.0): C, 65.28; H, 9.86; F, 7.74; N, 1.90. Found: C, 65.35; H, 9.89; F, 7.86; N, 1.90.

*Allyl 2-deoxy-3-*O*-[(*R*)-3-(dodecyloxy)tetradecyl]-4,6-*O*-isopropylidene-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-*D*-glucopyranoside* (**50**).—A solution of **41** (4.70 g, 6.39 mmol) in EtOH (10 mL) and aq 1 M NaOH (10 mL) was stirred at 80 °C for 4 h. The solution was concentrated in vacuo, diluted with EtOAc, washed with water and brine, dried over Na_2SO_4, filtered and concentrated to give an amine, which was dissolved in CH_2Cl_2 (10 mL). To this solution were added satd aq $NaHCO_3$ (10 mL) and chloroformic acid 2,2,2-trichloroethyl ester (1.60 g, 7.55 mmol) with stirring at rt. After 1 h, the mixture was diluted with CH_2Cl_2, washed with water and brine, dried over $MgSO_4$, filtered, concentrated in vacuo, and chromatographed on a silica-gel column. Elution with 4:1 hexane–EtOAc gave **50** (4.54 g, 87%) as a gum. IR $\nu_{max}(CHCl_3)$ 3439, 2928, 2855, 1743 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (6 H, t, *J* 6.6–7.3 Hz), 1.21–1.68 (48 H, m, containing 3 H, s, at δ 1.41, and 3 H, s, at δ 1.50), 3.30–3.48 (4 H, m), 3.57–3.77 (4 H, m), 3.82–3.92 (3 H, m), 3.98 (1 H, dd, *J* 6.6, 12.5 Hz), 4.13 (1 H, dd, *J* 5.9, 12.5 Hz), 4.74 (2 H, s), 4.87 (1 H, d, *J* 3.7 Hz), 5.22–5.32 (3 H, m, containing NH), 5.89 (1 H, m). FABMS (positive-ion): *m/z* 814 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{41}H_{75}Cl_3NO_8$: 814.4558; Found: 814.4551. Anal. Calcd for $C_{41}H_{74}Cl_3NO_8$ (815.4): C, 60.39; H, 9.15; Cl, 13.04; N, 1.72. Found: C, 59.94; H, 9.04; Cl, 12.89; N, 1.70.

*Allyl 2-deoxy-3-*O*-[(*R*)-3-(dodecyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-*D*-glucopyranoside* (**51**).—A solution of **50** (3.51 g, 4.30 mmol) in 80% aq AcOH (20 mL) was stirred at 60 °C for 4 h. The solution was diluted with EtOAc, washed with satd aq $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, concentrated in vacuo, and chromatographed on a silica-gel column. Elution with 3:2 hexane–EtOAc gave **51** (3.15 g, 95%) as a white powder. IR ν_{max}(KBr) 3335, 2923, 2853, 1709 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (6 H, t, *J* 6.6 Hz), 1.26–1.73 (42 H, m), 2.17 (1 H, t, *J* 6.6 Hz, OH), 3.36–3.50 (4 H, m), 3.60–3.91 (8 H, m, containing OH), 3.99 (1 H, dd, *J* 6.6, 13.2 Hz), 4.19 (1 H, dd, *J* 5.1, 13.2 Hz), 4.69, 4.81 (2 H, AB-q, *J* 11.7 Hz), 4.87 (1 H, d, *J* 3.7 Hz), 5.22–5.32 (3 H, m), 5.90 (1 H, m). FABMS (positive-ion): *m/z* 774 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{38}H_{71}Cl_3NO_8$: 774.4245; Found: 774.4228. Anal. Calcd for $C_{38}H_{70}Cl_3NO_8$ (775.3): C, 58.87; H, 9.10; Cl, 13.72 N, 1.81. Found: C, 58.87; H, 8.94; Cl, 14.00; N, 1.81.

*Allyl 6-*O*-benzyloxycarbonyl-2-deoxy-3-*O*-[(*R*)-3-(dodecyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-*D*-glucopyranoside* (**52**).—To a solution of **51** (526 mg, 0.678 mmol) in CH_2Cl_2 (5 mL) were added pyridine (332 mg, 4.20 mmol) and benzyloxycarbonyl chloride (0.50 mL, 3.50 mmol) at 0 °C under N_2. After stirring for 3 h at rt, the solution was diluted with EtOAc, washed with aq 1 M NH_4Cl, satd aq $NaHCO_3$, and brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated in vacuo, and chromatographed on a silica-gel column. Elution with 3:1 hexane–EtOAc gave **52** (581 mg, 94%) as a gum. IR ν_{max}(KBr) 3522, 3329, 2923, 2853, 1725, 1709 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (6 H, t, *J* 6.6 Hz),

1.59–1.21 (40 H, m), 1.71–1.74 (2 H, m), 3.33–3.48 (4 H, m), 3.56 (1 H, m), 3.64 (1 H, bs, OH), 3.69 (1 H, m), 3.79–3.84 (2 H, m), 3.88 (1 H, dt, *J* 3.7, 10.3 Hz), 3.96 (1 H, dd, *J* 6.6, 12.5 Hz), 4.15 (1 H, dd, *J* 5.1, 12.5 Hz), 4.39–4.46 (2 H, m), 4.68, 4.81 (2 H, AB-q, *J* 12.5 Hz), 4.85 (1 H, d, *J* 3.7 Hz), 5.18 (2 H, s), 5.20–5.30 (3 H, m, containing NH), 5.87 (1 H, m), 7.32–7.40 (5 H, m). FABMS (positive-ion): *m/z* 908 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{46}H_{77}Cl_3NO_{10}$: 908.4613; Found: 908.4592. Anal. Calcd for $C_{46}H_{76}Cl_3NO_{10}$ (909.5): C, 60.75; H, 8.42; Cl, 11.70; N, 1.54. Found: C, 60.44; H, 8.17; Cl, 11.63; N, 1.56.

*Allyl 6-*O*-benzyloxycarbonyl-2-deoxy-4-*O*-(diphenylphosphono)-3-*O*-[(*R*)-3-(dodecyloxy)-tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)-amino]-α-*D*-glucopyranoside* (**53**).—To a solution of **52** (553 mg, 0.608 mmol) and DMAP (111 mg, 0.911 mmol) in CH_2Cl_2 (5 mL) was added dropwise diphenyl chlorophosphate (0.19 mL, 0.917 mmol). After stirring for 2 h at rt, the reaction mixture was diluted with EtOAc, washed with satd aq $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to give a residue, which was chromatographed on a silica-gel column. Elution with 3:1 hexane–EtOAc gave **53** (663 mg, 96%) as a gum. IR $\nu_{max}(CHCl_3)$ 3436, 2928, 2855, 1747 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (6 H, t, *J* 6.6 Hz), 1.18–1.30 (38 H, m), 1.43–1.45 (2 H, m), 1.61–1.63 (2 H, m), 3.20 (1 H, m), 3.25 (2 H, t, *J* 6.6 Hz), 3.64–3.72 (2 H, m), 3.80 (1 H, m), 3.95–4.02 (3 H, m), 4.14 (1 H, dd, *J* 5.1, 13.2 Hz), 4.29 (1 H, dd, *J* 5.1, 11.7 Hz), 4.36 (1 H, dd, *J* 1.5, 11.7 Hz), 4.63 (1 H, q, *J* 9.5 Hz), 4.67, 4.79 (2 H, AB-q, *J* 12.5 Hz), 4.89 (1 H, d, *J* 3.7 Hz), 5.06, 5.11 (2 H, AB-q, *J* 12.5 Hz), 5.21–5.30 (3 H, m, containing NH), 5.87 (1 H, m), 7.12–7.36 (15 H, m). FABMS (positive-ion): *m/z* 1162 $[M+Na]^+$; 1140 $[M+H]^+$. HR-FABMS (positive-ion): *m/z* Calcd for $C_{58}H_{86}Cl_3NO_{13}P$: 1140.4902; Found: 1140.4890. Anal. Calcd for $C_{58}H_{85}Cl_3NO_{13}P$ (1141.6): C, 61.02; H, 7.51; Cl, 9.32; N, 1.23; P, 2.71. Found: C, 60.69; H, 7.61; Cl, 9.44; N, 1.19; P, 2.96.

*6-*O*-Benzyloxycarbonyl-2-deoxy-4-*O*-(diphenylphosphono)-3-*O*-[(*R*)-3-(dodecyloxy)-tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)-amino]-*D*-glucopyranose* (**54**).—To a solution of **53** (613 mg, 0.537 mmol) in THF (6 mL) was added bis(methyldiphenylphosphine)-cyclooctadieneiridium(I) hexafluorophosphate, $[C_8H_{12}Ir(PMePh_2)_2]PF_6$ (31.5 mg). The air in the reaction flask was completely replaced with N_2 and then further replaced with hydrogen to activate the iridium complex. Immediately after 1 min, when the red color solution of the iridium complex had become almost colorless, the hydrogen was completely replaced with N_2. This solution was stirred for 3 h at rt. After confirming a double bond shift to an enol ether from the 1-allyloxy group (as indicated by a slightly higher R_f value on the TLC), water (5 mL) and I_2 (276 mg) were added to this solution. After stirring for 1 h at rt, the mixture was diluted with EtOAc, washed with 10% aq $Na_2S_2O_3$, satd aq $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated to give a mixture that was chromatographed on a silica-gel column. Elution with 3:2 hexane–EtOAc gave **54** (421 mg, 71%) as a gum. IR $\nu_{max}(CHCl_3)$ 3600, 3435, 2928, 2855, 1747 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (6 H, t, *J* 6.6 Hz), 1.18–1.30 (38 H, m), 1.43–1.45 (2 H, m), 1.62–1.65 (2 H, m), 3.20–3.27 (3 H, m, containing 2 H, t, *J* 6.6 Hz at δ 3.25), 3.41 (1 H, bs, OH), 3.64–3.84 (3 H, m), 3.94 (1 H, m), 4.19–4.39 (3 H, m), 4.62 (1 H, q, *J* 9.5 Hz), 4.69, 4.76 (2 H, AB-q, *J* 12.1 Hz), 5.06, 5.11 (2 H, AB-q, *J* 11.7 Hz), 5.25 (1 H, t, *J* 3.7 Hz), 5.43 (1 H, d, *J* 9.5 Hz, NH), 7.12–7.34 (15 H, m). FABMS (positive-ion): *m/z* 1100 $[M+H]^+$. HR-FABMS (positive-ion): *m/z* Calcd for $C_{55}H_{82}Cl_3NO_{13}P$: 1100.4589; Found: 1100.4601.

*Allyl 6-*O*-(*tert*-butyldimethylsilyl)-2-deoxy-3-*O*-[(*R*)-3-(dodecyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-*D*-glucopyranoside* (**55**).—To a solution of **51** (1.32 g, 1.70 mmol) in CH_2Cl_2 (6 mL) were added DMAP (332 mg, 2.56 mmol) and *tert*-butyldimethylsilyl chloride (385 mg, 2.56 mmol). After stirring for 3 h at rt, the mixture was diluted with EtOAc, washed with water, satd aq $NaHCO_3$, and brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated in vacuo and chromatographed on a

silica-gel column. Elution with 9:1 hexane–EtOAc gave **55** (1.49 g, 99%) as a gum. IR ν_{max}($CHCl_3$) 3438, 2928, 2856, 1742 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.09 (6 H, s), 0.86–0.91 (15 H, m), 1.21–1.62 (40 H, m), 1.72 (2 H, q, *J* 5.9 Hz), 3.36–3.67 (7 H, m, containing OH), 3.76–3.89 (5 H, m), 3.98 (1 H, dd, *J* 6.6, 12.5 Hz), 4.19 (1 H, dd, *J* 5.1, 12.5 Hz), 4.70, 4.79 (2 H, AB-q, *J* 12.5 Hz), 4.86 (1 H, d, *J* 3.7 Hz), 5.20–5.31 (3 H, m, containing NH), 5.90 (1 H, m). FABMS (positive-ion): *m/z* 910 $[M + Na]^+$; 888 $[M + H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{44}H_{84}Cl_3NNaO_8Si$: 910.4930; Found: 910.4911. Anal. Calcd for $C_{44}H_{84}Cl_3NO_8Si$ (889.6): C, 59.41; H, 9.52; Cl, 11.96; N, 1.58. Found: C, 59.13; H, 9.30; Cl, 12.02; N, 1.49.

*Allyl 6-*O*-tert-butyldimethylsilyl-2-deoxy-4-*O*-(diphenylphosphono)-3-*O*-[(*R*)-3-(dodecyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-*D*-glucopyranoside* (**56**).—Compound **55** (1.45 g, 1.63 mmol) was treated as described in the formation of **53** from **52** to give **56** (1.81 g, 99%) as a gum. IR ν_{max}($CHCl_3$) 3436, 2928, 2856, 1744 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.01 (6 H, s), 0.91–0.85 (15 H, m), 1.18–1.65 (42 H, m), 3.19–3.26 (3 H, m), 3.65–3.83 (6 H, m), 3.86–4.03 (2 H, m), 4.22 (1 H, dd, *J* 5.9, 13.2 Hz), 4.55 (1 H, q, *J* 9.5 Hz), 4.69, 4.81 (2 H, AB-q, *J* 12.1 Hz), 4.90 (1 H, d, *J* 3.7 Hz), 5.23–5.33 (3 H, m, containing NH), 5.92 (1 H, m), 7.15–7.35 (10 H, m). FABMS (positive-ion): *m/z* 1120 $[M + H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{56}H_{94}Cl_3NO_{11}PSi$: 1120.5399; Found: 1120.5409. Anal. Calcd for $C_{56}H_{93}Cl_3NO_{11}PSi$ (1121.8): C, 59.96; H, 8.36; Cl, 9.48; N, 1.25; P, 2.76. Found: C, 59.59; H, 8.23; Cl, 9.66; N, 1.18; P, 2.81.

*Allyl 2-deoxy-4-*O*-(diphenylphosphono)-3-*O*-[(*R*)-3-(dodecyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-*D*-glucopyranoside* (**57**).—To a solution of **56** (1.65 g, 1.47 mmol) in THF (9 mL) was added aq 3 M HCl (1.5 mL) with stirring. After 3 h at rt, the reaction mixture was diluted with EtOAc, washed with satd aq $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, concentrated, and chromatographed on a silica-gel column. Elution with 3:2 hexane–EtOAc gave **57** (1.31 g, 89%) as an amorphous solid. IR ν_{max}(KBr) 3499, 3373, 2921, 2851, 1713, 1646 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (6 H, t, *J* 6.6 Hz), 1.18–1.47 (40 H, m), 1.65 (1 H, q, *J* 6.6 Hz), 3.21–3.29 (3 H, m), 3.59–3.70 (5 H, m), 3.88 (1 H, m), 3.97–4.03 (2 H, m), 4.17 (1 H, dd, *J* 5.9, 13.2 Hz), 4.65 (1 H, q, *J* 9.5 Hz), 4.72, 4.76 (2 H, AB-q, *J* 12.5 Hz), 4.93 (1 H, d, *J* 3.7 Hz), 5.23–5.33 (3 H, m, containing NH), 5.89 (1 H, m), 7.18–7.37 (10 H, m). FABMS (positive-ion): *m/z* 1006 $[M + H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{50}H_{80}Cl_3NO_{11}P$: 1006.4535; Found: 1006.4539. Anal. Calcd for $C_{50}H_{79}Cl_3NO_{11}P$ (1007.5): C, 59.61; H, 7.90; Cl, 10.56; N, 1.39; P, 3.07. Found: C, 59.29; H, 7.82; Cl, 10.66; N, 1.37; P, 3.09.

*Allyl 2-deoxy-4-*O*-(diphenylphosphono)-3-*O*-[(*R*)-3-(dodecyloxy)tetradecyl]-6-*O*-methyl-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-*D*-glucopyranoside* (**58**).—To a solution of **57** (385 mg, 0.382 mmol) in CH_2Cl_2 (5 mL) were added 2,6-di-*tert*-butyl-4-methylpyridine (91 mg, 0.441 mmol) and trimethyloxonium tetrafluoroborate (64 mg, 0.435 mmol) at rt. After 3 h, the reaction mixture was diluted with EtOAc, washed with satd aq $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, concentrated, and chromatographed on a silica-gel column. Elution with 7:3 hexane–EtOAc gave **58** (357 mg, 91%) as a gum. IR ν_{max}($CHCl_3$) 3436, 2928, 2855, 1744 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (6 H, t, *J* 6.6 Hz), 1.17–1.32 (38 H, m), 1.43–1.44 (2 H, m), 1.62–1.64 (2 H, m), 3.19–3.26 (6 H, m, containing 3 H, s, at δ 3.24), 3.48 (1 H, dd, *J* 2.2, 11.0 Hz), 3.54 (1 H, dd, *J* 4.4, 11.0 Hz), 3.65–3.89 (4 H, m), 3.98–4.04 (2 H, m), 4.21 (1 H, dd, *J* 5.1, 13.2 Hz), 4.67 (1 H, m), 4.69, 4.77 (2 H, AB-q, *J* 11.7 Hz), 4.93 (1 H, d, *J* 3.7 Hz), 5.23–5.33 (3 H, m, containing NH), 5.90 (1 H, m), 7.15–7.35 (10 H, m). FABMS (positive-ion): *m/z* 1020 $[M + H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{51}H_{82}Cl_3NO_{11}P$: 1020.4691; Found: 1020.4669. Anal. Calcd for $C_{51}H_{81}Cl_3NO_{11}P$ (1021.5): C, 59.97; H, 7.99; Cl, 10.41; N, 1.37; P, 3.03. Found: C, 59.50; H, 7.85; Cl, 10.51; N, 1.29; P, 3.27.

*2-Deoxy-4-*O*-(diphenylphosphono)-3-*O*-[(*R*)-3-(dodecyloxy)tetradecyl]-6-*O*-methyl-2-[(2,2,2-trichloroethoxycarbonyl)amino]-D-*

glucopyranose (**59**).—Compound **58** (695 mg, 0.681 mmol) was treated as described in the formation of **54** from **53** to give **59** (483 mg, 72%) as a gum. IR ν_{max}(KBr) 3426, 3339, 2922, 2851, 1721 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (6 H, t, *J* 6.6 Hz), 1.17–1.32 (38 H, m), 1.42–1.44 (2 H, m), 1.64–1.65 (2 H, m), 3.16–3.26 (6 H, m, containing 3 H, s, at δ 3.21 and 2 H, t, *J* 6.6 Hz, at δ 3.25), 3.43–3.51 (2 H, m), 3.65–3.85 (4 H, m, containing OH), 3.95 (1 H, m), 4.13 (1 H, m), 4.55 (1 H, q, *J* 9.5 Hz), 4.70, 4.75 (2 H, AB-q, *J* 11.7 Hz), 5.27 (1 H, t, *J* 3.7 Hz), 5.40 (1 H, d, *J* 9.5 Hz, NH), 7.16–7.35 (10 H, m). FABMS (positive-ion): *m/z* 1018 $[M+K]^+$, 1002 $[M+Na]^+$, 980 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{48}H_{78}Cl_3NO_{11}P$: 980.4360; Found: 980.4378. Anal. Calcd for $C_{48}H_{77}Cl_3NO_{11}P$ (981.5): C, 58.74; H, 7.91; Cl, 10.84; N, 1.43; P, 3.16. Found: C, 58.49; H, 8.15; Cl, 10.74; N, 1.41; P, 3.14.

*Allyl 2,6-dideoxy-4-*O*-(diphenylphosphono)-3-*O*-[(*R*)-3-(dodecyloxy)tetradecyl]-6-fluoro-2-[(2,2,2-trichloroethoxycarbonyl)amino]-α-*D*-glucopyranoside* (**60**).—To a solution of **57** (521 mg, 0.517 mmol) in DME (5 mL) was gradually added a solution of DAST (0.2 mL, 1.51 mmol) in DME (1 mL) at −40 °C with stirring under N_2. After stirring for 30 min at −40 °C, followed by 2 h at rt, water was added to the reaction mixture, and it was extracted with EtOAc. The organic layer was washed with satd aq $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated to give a crude oil. The crude product was chromatographed on a silica-gel column. Elution with 3:1 hexane–EtOAc gave **60** (432 mg, 83%). IR ν_{max}($CHCl_3$) 3691, 3436, 2928, 2855, 1744 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (6 H, t, *J* 6.6–7.3 Hz), 1.17–1.32 (38 H, m), 1.43–1.45 (2 H, m), 1.57–1.65 (2 H, m), 3.21 (1 H, m), 3.25 (2 H, t, *J* 6.6–7.3 Hz), 3.65–3.83 (3 H, m), 3.90–4.05 (3 H, m), 4.20 (1 H, dd, *J* 5.9, 13.2 Hz), 4.46 (1 H, m), 4.55–4.64 (2 H, m), 4.68, 4.79 (2 H, AB-q, *J* 11.7 Hz), 4.94 (1 H, d, *J* 3.7 Hz), 5.24–5.34 (3 H, m, containing NH), 5.89 (1 H, m), 7.16–7.34 (10 H, m). FABMS (positive-ion): *m/z* 1008 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{50}H_{79}Cl_3FNO_{10}P$: 1008.4491; Found: 1008.4485. Anal. Calcd for $C_{50}H_{78}Cl_3FNO_{10}P$ (1009.5): C, 59.49; H, 7.79; Cl, 10.54; F, 1.88; N, 1.39; P, 3.07. Found: C, 59.45; H, 7.68; Cl, 10.45; F, 2.15; N, 1.48; P, 3.24.

*2,6-Dideoxy-4-*O*-(diphenylphosphono)-3-*O*-[(*R*)-3-(dodecyloxy)tetradecyl]-6-fluoro-2-[(2,2,2-trichloroethoxycarbonyl)amino]-*D*-glucopyranose* (**61**).—Compound **60** (416 mg, 0.412 mmol) was treated as described in the formation of **54** from **53** to give **61** (329 mg, 82%) as a gum. IR ν_{max}($CHCl_3$) 3602, 3435, 2928, 2855, 1745 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (6 H, t, *J* 6.6 Hz), 1.18–1.32 (38 H, m), 1.44–1.45(2 H, m), 1.62–1.67 (2 H, m), 3.21–3.27 (3 H, m, containing 2 H, t, *J* 6.6 Hz, at δ 3.26), 3.65–3.85 (4 H, m, containing OH), 3.96 (1 H, m), 4.17 (1 H, m), 4.44 (1 H, m), 4.56 (1 H, m), 4.60 (1 H, q, *J* 9.5 Hz), 4.71, 4.76 (2 H, AB-q, *J* 11.7 Hz), 5.31 (1 H, t, *J* 3.7 Hz), 5.47 (1 H, d, *J* 9.5 Hz, NH), 7.17–7.35 (10 H, m). FABMS (positive-ion): *m/z* 968 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{47}H_{75}Cl_3FNO_{10}P$: 968.4187; Found: 968.4178. Anal. Calcd for $C_{47}H_{74}Cl_3FNO_{10}P$ (969.4): C, 58.23; H, 7.69; Cl, 10.97; F, 1.96; N, 1.45; P, 3.20. Found: C, 58.27; H, 7.76; Cl, 11.20; F, 2.04; N, 1.43; P, 3.25.

*Diphenylmethyl 2,6-anhydro-7-*O*-[6-*O*-benzyloxycarbonyl-2-deoxy-4-*O*-(diphenylphosphono)-3-*O*-[(*R*)-3-(dodecyloxy)tetradecyl]-2-[(2,2,2-trichloroethoxycarbonyl)amino]-β-*D*-glucopyranosyl]-3-[(*R*)-3-(benzyloxy)tetradecanamido]-4-*O*-[(*R*)-3-(benzyloxy)tetradecyl]-3-deoxy-*D*-glycero-*D*-ido-heptonate* (**62**).—To a solution of **54** (521 mg, 0.473 mmol) in CH_2Cl_2 (10 mL) were added Cl_3CCN (0.70 mL, 6.98 mmol) and a catalytic amount of Cs_2CO_3 (77 mg, 0.237 mmol). After stirring for 1 h at rt, the reaction mixture was quenched with satd aq $NaHCO_3$ (20 mL), and extracted with CH_2Cl_2. The extract was washed with brine and dried over Na_2SO_4. Removal of the solvent in vacuo gave a crude imidate (591 mg), which was immediately used for subsequent glycosylation without further purification. In a N_2 atmosphere, a solution of the thus-obtained imidate (591 mg), diol **1** (234 mg, 0.236 mmol), and MS4A (750 mg) in CH_2Cl_2 (10 mL) was stirred at rt. After stirring for 1 h, a catalytic amount of TMSOTf (15 mL, 0.083 mmol) was added to the mixture at −40 °C. After stirring for 2 h at

−40 °C, the mixture was quenched with satd aq $NaHCO_3$, diluted with EtOAc, washed with water and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to give a mixture, which was chromatographed on a silica-gel column. Elution with 7:3 hexane–EtOAc gave **62** (365 mg, 75%) as a gum. IR $\nu_{max}(CHCl_3)$ 3691, 3604, 3519, 3405, 2928, 2855, 1735, 1669 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (12 H, t, *J* 6.6 Hz), 1.24–1.74 (84 H, m), 2.24 (2 H, d, *J* 5.9 Hz), 3.02 (1 H, bs, OH), 3.14–3.27 (4 H, m), 3.43–3.72 (11 H, m), 3.92–4.07 (2 H, m), 4.21–4.45 (7 H, m, containing 2 H, AB-q, *J* 11.5 Hz, at δ 4.39, 4.44, and 2 H, AB-q, *J* 11.0 Hz, at δ 4.28, 4.33), 4.51 (1 H, q, *J* 9.5 Hz), 4.61 (1 H, d, *J* 5.9 Hz), 4.66, 4.71 (2 H, AB-q, *J* 11.7 Hz), 4.86 (1 H, m), 5.04, 5.10 (2 H, AB-q, *J* 11.7 Hz), 5.39 (1 H, m, NH), 6.81 (1 H, m, NH), 6.83 (1 H, s), 7.11–7.35 (35 H, m). FABMS (positive-ion): *m/z* 2095 $[M+Na]^+$. HR-FABMS (positive-ion): *m/z* Calcd for $C_{117}H_{168}Cl_3N_2O_{21}PNa$: 2096.0841; Found: 2096.0845. Anal. Calcd for $C_{117}H_{168}Cl_3N_2O_{21}P$ (2075.9): C, 67.69; H, 8.16; Cl, 5.12; N, 1.35; P, 1.49. Found: C, 67.21; H, 8.04; Cl, 5.27; N, 1.34; P, 1.37.

*Diphenylmethyl 2,6-anhydro-7-*O*-[2-deoxy-4-*O*-(diphenylphosphono)-3-*O*-[(*R*)-3-(dodecyloxy)tetradecyl]-6-*O*-methyl-2-[(2,2,2-trichloroethoxycarbonyl)amino]-β-*D*-glucopyranosyl]-3-[(*R*)-3-(benzyloxy)tetradecanamido]-4-*O*-[(*R*)-3-(benzyloxy)tetradecyl]-3-deoxy-*D*-glycero-*D*-ido-heptonate* (**63**).—Compound **59** (438 mg, 0.446 mmol) was treated as described in the formation of **62** from **54** to give **63** (298 mg, 68%) as a gum. IR $\nu_{max}(CHCl_3)$ 2928, 2855, 1735, 1668 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (12 H, t, *J* 6.6 Hz), 1.24–1.75 (84 H, m), 2.23 (2 H, d, *J* 5.9 Hz), 3.03 (1 H, bs, OH), 3.10–3.27 (7 H, m, containing 3 H, s, at δ 3.21), 3.41–3.76 (13 H, m), 3.89–4.00 (2 H, m), 4.26–4.34 (3 H, m, containing 2 H, AB-q, *J* 11.4 Hz, at δ 4.28 and 4.33), 4.40, 4.44 (2 H, AB-q, *J* 11.7 Hz), 4.54 (1 H, q, *J* 9.5 Hz), 4.61 (1 H, d, *J* 5.9 Hz), 4.67, 4.75 (2 H, AB-q, *J* 11.7 Hz), 4.84 (1 H, m), 5.33 (1 H, m, NH), 6.79 (1 H, d, *J* 9.5 Hz, NH), 6.83 (1 H, s), 7.15–7.35 (30 H, m). FABMS (positive-ion): *m/z* 1975 $[M+Na]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{110}H_{164}Cl_3N_2NaO_{19}P$: 1976.0629; Found: 1976.0585. Anal. Calcd for $C_{110}H_{164}Cl_3N_2O_{19}P$ (1955.8): C, 67.55; H, 8.45; Cl, 5.44; N, 1.43; P, 1.58. Found: C, 67.53; H, 8.25; Cl, 5.14; N, 1.43; P, 1.32.

*Diphenylmethyl 2,6-anhydro-7-*O*-[2,6-dideoxy-4-*O*-(diphenylphosphono)-3-*O*-[(*R*)-3-(dodecyloxy)tetradecyl]-6-fluoro-2-[(2,2,2-trichloroethoxycarbonyl)amino]-β-*D*-glucopyranosyl]-3-[(*R*)-3-(benzyloxy)tetradecanamido]-4-*O*-[(*R*)-3-(benzyloxy)tetradecyl]-3-deoxy-*D*-glycero-*D*-ido-heptonate* (**64**).—Compound **61** (230 mg, 0.238 mmol) was treated as described in the formation of **62** from **54** to give **64** (185 mg, 80%) as a gum. IR $\nu_{max}(CHCl_3)$ 2928, 2855, 1735, 1669 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (12 H, t, *J* 6.6 Hz), 1.25–1.74 (84 H, m), 2.25 (2 H, d, *J* 5.9 Hz), 3.03 (1 H, bs, OH), 3.15–3.27 (4 H, m), 3.43–3.75 (11 H, m), 3.92–4.02 (2 H, m), 4.26–4.57 (8 H, m, containing 2 H, AB-q, *J* 11.4 Hz, at δ 4.28, 4.33, and 2 H, AB-q, *J* 11.7 Hz, at δ 4.40 and 4.45), 4.61 (1 H, d, *J* 5.1 Hz), 4.67, 4.75 (2 H, AB-q, *J* 11.7 Hz), 4.90 (1 H, m), 5.43 (1 H, m, NH), 6.83 (1 H, s), 6.82 (1 H, m, NH), 7.17–7.35 (30 H, m). FABMS (positive-ion): *m/z* 1963 $[M+Na]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{109}H_{161}Cl_3FN_2NaO_{18}P$: 1964.0429; Found: 1964.0414. Anal. Calcd for $C_{109}H_{161}Cl_3FN_2O_{18}P$ (1943.78): C, 67.35; H, 8.35; Cl, 5.47; F, 0.98; N, 1.44; P, 1.59. Found: C, 67.34; H, 8.10; Cl, 5.39; F, 1.26; N, 1.48; P, 1.43.

*Diphenylmethyl 2,6-anhydro-7-*O*-[2-acetamido-6-*O*-(benzyloxycarbonyl)-2-deoxy-4-*O*-(diphenylphosphono)-3-*O*-[(*R*)-3-(dodecyloxy)tetradecyl]-β-*D*-glucopyranosyl]-3-[(*R*)-3-(benzyloxy)tetradecanamido]-4-*O*-[(*R*)-3-(benzyloxy)tetradecyl]-3-deoxy-*D*-glycero-*D*-ido-heptonate* (**65**).—To a solution of **62** (230 mg, 0.111 mmol) in AcOH (5 mL) was added activated zinc dust (148 mg, 2.27 mmol). After stirring vigorously for 5 h at rt, the solution was filtered to remove the zinc dust and concentrated in vacuo to give a crude product. The product was diluted with EtOAc, washed with satd aq $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was then dissolved in THF (3 mL) and water (2 mL), and pyridine (45 mL) and Ac_2O (55 mL) were added. After

stirring for 2 h at rt, the mixture was diluted with EtOAc, washed with water and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo, and chromatographed on a silica-gel column. Elution with 3:2 hexane–EtOAc gave **65** (152 mg, two steps, 71%) as a gum. IR $\nu_{max}(CHCl_3)$ 3436, 2928, 2855, 1745, 1670 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 (12 H, t, *J* 6.6 Hz), 1.26–1.73 (84 H, m), 1.91 (3 H, s), 2.25 (2 H, d, *J* 5.1 Hz), 3.03 (1 H, m), 3.27–3.72 (14 H, m, containing OH), 4.00–4.07 (2 H, m), 4.23 (1 H, dd, *J* 5.1, 11.7 Hz), 4.28–4.39 (5 H, m), 4.50 (1 H, q, *J* 9.5 Hz), 4.43 (2 H, s), 4.62 (1 H, d, *J* 5.1 Hz), 5.05, 5.11 (2 H, AB-q, *J* 11.7 Hz), 5.21 (1 H, d, *J* 8.1 Hz), 6.07 (1 H, d, *J* 6.6 Hz, NH), 6.80 (1 H, d, *J* 8.8 Hz, NH), 6.82 (1 H, s), 7.12–7.33 (35 H, m). FABMS (positive-ion): *m/z* 1963 $[M + Na]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{116}H_{169}N_2NaO_{20}P$: 1964.1904; Found: 1964.1870. Anal. Calcd for $C_{116}H_{169}N_2O_{20}P$ (1942.6): C, 71.72; H, 8.77; N, 1.44; P, 1.59. Found: C, 71.46; H, 8.60; N, 1.42; P, 1.49.

*Diphenylmethyl 2,6-anhydro-7-*O*-[2-acetamido-2-deoxy-4-*O*-(diphenylphosphono)-3-*O*-[(*R*)-3-(dodecyloxy)tetradecyl]-6-*O*-methyl-β-*D*-glucopyranosyl]-3-[(*R*)-3-(benzyloxy)tetradecanamido]-4-*O*-[(*R*)-3-(benzyloxy)tetradecyl]-3-deoxy-*D*-glycero-*D*-ido-heptonate* (**66**).—Compound **63** (229 mg, 0.117 mmol) was treated as described in the formation of **65** from **62** to give **66** (158 mg, 74%) as a gum. IR ν_{max} ($CHCl_3$) 3436, 2928, 2855, 1732, 1670 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (12 H, t, *J* 6.6 Hz), 1.25–1.74 (84 H, m), 1.91 (3 H, s), 2.23 (2 H, d, *J* 5.1 Hz), 3.11 (1 H, m), 3.22–3.30 (6 H, m, containing 3 H, s, at δ 3.22), 3.40–3.74 (14 H, m, containing OH), 3.99–4.05 (2 H, m), 4.29, 4.33 (2 H, AB-q, *J* 11.4 Hz), 4.35 (1 H, m), 4.42 (2 H, s), 4.52 (1 H, q, *J* 9.5 Hz), 4.61 (1 H, d, *J* 5.9 Hz), 5.15 (1 H, d, *J* 8.1 Hz), 5.97 (1 H, d, *J* 7.3 Hz, NH), 6.78 (1 H, d, *J* 8.8 Hz, NH), 6.81 (1 H, s), 7.15–7.33 (30 H, m). FABMS (positive-ion): *m/z* 1843 $[M + Na]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{109}H_{165}N_2NaO_{18}P$: 1844.1693; Found: 1844.1700. Anal. Calcd for $C_{109}H_{165}N_2O_{18}P$ (1822.5): C, 71.84; H, 9.13; N, 1.54; P, 1.70. Found: C, 71.38; H, 8.96; N, 1.51; P, 1.53.

*Diphenylmethyl 2,6-anhydro-7-*O*-[2-acetamido-2,6-dideoxy-4-*O*-(diphenylphosphono)-3-*O*-[(*R*)-3-(dodecyloxy)tetradecyl]-6-fluoro-β-*D*-glucopyranosyl]-3-[(*R*)-3-(benzyloxy)tetradecanamido]-4-*O*-[(*R*)-3-(benzyloxy)tetradecyl]-3-deoxy-*D*-glycero-*D*-ido-heptonate* (**67**).—Compound **64** (180 mg, 0.093 mmol) was treated as described in the formation of **65** from **62** to give **67** (115 mg, 68%) as a gum. IR $\nu_{max}(CHCl_3)$ 3529, 3335, 3064, 3032, 2924, 2854, 1733, 1646 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (12 H, t, *J* 6.6 Hz), 1.25–1.74 (84 H, m), 1.91 (3 H, s), 2.24 (2 H, d, *J* 5.9 Hz), 3.04 (1 H, m), 3.22–3.33 (4 H, m, containing OH), 3.41–3.71 (11 H, m), 4.03–4.11 (2 H, m), 4.27–4.57 (8 H, m, containing 2 H, AB-q, *J* 11.4 Hz, at δ 4.29, 4.34, and 2 H, s, at δ 4.42), 4.61 (1 H, d, *J* 5.1 Hz), 5.21 (1 H, d, *J* 8.1 Hz), 6.03 (1 H, d, *J* 6.6 Hz, NH), 6.80 (1 H, d, *J* 11.7 Hz, NH), 6.82 (1 H, s), 7.17–7.37 (30 H, m). FABMS (positive-ion): *m/z* 1831 $[M + Na]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{108}H_{162}FN_2NaO_{17}P$: 1832.1493; Found: 1832.1459. Anal. Calcd for $C_{108}H_{162}FN_2O_{17}P$ (1810.4): C, 71.65; H, 9.02; F, 1.05; N, 1.55; P, 1.71. Found: C, 71.34; H, 8.88; F, 1.18; N, 1.50; P, 1.52.

*2,6-Anhydro-7-*O*-[2-acetamido-2-deoxy-4-*O*-(diphenylphosphono)-3-*O*-[(*R*)-3-(dodecyloxy)-tetradecyl]-β-*D*-glucopyranosyl]-3-[(*R*)-3-(hydroxy)tetradecanamido]-4-*O*-[(*R*)-3-(hydroxy)tetradecyl]-3-deoxy-*D*-glycero-*D*-ido-heptonic acid* (**68**).—A solution of **65** (115 mg, 0.059 mmol) in EtOH (5 mL) containing 20% $Pd(OH)_2$–C (111 mg) was stirred vigorously under H_2 for 18 h at rt. The reaction mixture was filtered and concentrated in vacuo to give a crude product. The crude product was purified by preparative silica gel thin-layer chromatography (8:1 $CHCl_3$–MeOH) to give **68** (62.3 mg, 72%) as an amorphous solid. IR ν_{max}(KBr) 3320 (broad), 3072, 2924, 2854, 1726, 1656 cm^{-1}. ^1H NMR (400 MHz, CD_3OD) δ 0.90 (12 H, t, *J* 6.6 Hz), 1.20–1.76 (84 H, m), 2.30–2.41 (2 H, m), 2.00 (3 H, s), 3.25–3.35 (3 H, m), 3.46 (1 H, t, *J* 8.1 Hz), 3.52–3.93 (14 H, m), 4.04 (1 H, m), 4.21 (1 H, m), 4.48 (1 H, d, *J* 5.1 Hz), 4.53 (1 H, m), 4.63 (1 H, m), 7.19–7.40 (10 H, m). FABMS (positive-ion): *m/z* 1483 $[M + Na]^+$, 1461 $[M + H]^+$. HRFABMS (positive-ion): *m/z* Calcd

for $C_{81}H_{141}N_2NaO_{18}P$: 1483.9789; Found: 1483.9815.

2,6-Anhydro-7-O-[2-acetamido-2-deoxy-4-O-(diphenylphosphono)-3-O-[(R)-3-(dodecyloxy)tetradecyl]-6-O-methyl-β-D-glucopyranosyl]-3-[(R)-3-(hydroxy)tetradecanamido]-4-O-[(R)-3-(hydroxy)tetradecyl]-3-deoxy-D-glycero-D-ido-heptonic acid (**69**).—Compound **66** (136 mg, 0.074 mmol) was treated as described in the formation of **68** from **65** to give **69** (98.2 mg, 89%) as an amorphous solid. IR ν_{max}(KBr) 3318 (broad), 3072, 2924, 2854, 1729, 1656 cm^{-1}. ^1H NMR (400 MHz, CD_3OD) δ 0.90 (12 H, t, *J* 6.6 Hz), 1.21–1.75 (84 H, m), 2.03 (3 H, s), 2.33–2.40 (2 H, m), 3.20 (3 H, s), 3.22–4.00 (18 H, m), 4.19–4.22 (2 H, m), 4.29 (1 H, m), 4.56 (1 H, q, *J* 8.8 Hz), 4.75 (1 H, d, *J* 8.1 Hz), 7.19–7.40 (10 H, m). FABMS (positive-ion): *m/z* 1497 $[M+Na]^+$; 1475 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{82}H_{143}N_2NaO_{18}P$: 1497.9971; Found: 1497.9939.

2,6-Anhydro-7-O-[2-acetamido-2,6-dideoxy-4-O-(diphenylphosphono)-3-O-[(R)-3-(dodecyloxy)tetradecyl]-6-fluoro-β-D-glucopyranosyl]-3-[(R)-3-(hydroxy)tetradecanamido]-4-O-[(R)-3-(hydroxy)tetradecyl]-3-deoxy-D-glycero-D-ido-heptonic acid (**70**).—Compound **67** (75.2 mg, 0.042 mmol) was treated as described in the formation of **68** from **65** to give **70** (48.3 mg, 80%) as an amorphous solid. IR ν_{max}(KBr) 3323 (broad), 3072, 2924, 2854, 1729, 1656 cm^{-1}. ^1H NMR (400 MHz, CD_3OD) δ 0.90 (12 H, t, *J* 6.6 Hz), 1.20–1.76 (84 H, m), 2.00 (3 H, s), 2.30–2.39 (2 H, m), 3.25–3.36 (3 H, m), 3.45 (1 H, t, *J* 8.1 Hz), 3.60 (1 H, t, *J* 7.3–9.5 Hz), 3.68–3.94 (10 H, m), 4.03 (1 H, m), 4.19–4.22 (2 H, m), 4.36–4.58 (4 H, m, containing 1 H, d, *J* 5.1 Hz, at δ 4.49), 4.68 (1 H, d, *J* 8.1 Hz), 7.18–7.41 (10 H, m). FABMS (positive-ion): *m/z* 1485 $[M+Na]^+$; 1463 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{81}H_{140}FN_2NaO_{17}P$: 1485.9771; Found: 1485.9769.

2,6-Anhydro-7-O-[2-acetamido-2-deoxy-3-O-[(R)-3-(dodecyloxy)tetradecyl]-4-O-phosphono-β-D-glucopyranosyl]-3-[(R)-3-(hydroxy)tetradecanamido]-4-O-[(R)-3-(hydroxy)tetradecyl]-3-deoxy-D-glycero-D-ido-heptonic Acid (**71**).—A solution of **68** (56.4 mg, 0.039 mmol) in THF (3 mL) containing PtO_2 (55.6 mg) was stirred vigorously under H_2 for 5 h at rt. The reaction mixture was filtered and concentrated in vacuo to give a residue. The residue was dissolved in $CHCl_3$ (5 mL), MeOH (10 mL) and aq 0.1 M HCl (4 mL). To this solution was added another volume of $CHCl_3$ (5 mL) and 0.1 M HCl (5 mL) to separate the solution into two phases. The lower $CHCl_3$ phase was collected and concentrated to give **71** (48.3 mg, 96%) as a white powder, mp 179.0–181.0 °C. $[\alpha]_D^{24}$ −25.5° (*c* 0.78, $CHCl_3$). IR ν_{max}(KBr) 3294 (broad), 3040, 2924, 2854, 1723, 1627 cm^{-1}. ^1H NMR (400 MHz, 5:1 CD_3OD–$CDCl_3$) δ 0.89 (12 H, t, *J* 6.6 Hz), 1.29–1.60 (80 H, m), 1.71–1.73 (4 H, m), 2.00 (3 H, s), 2.32 (1 H, dd, *J* 8.1, 14.6 Hz), 2.38 (1 H, dd, *J* 4.4, 14.6 Hz), 3.40–3.49 (5 H, m), 3.52–3.70 (5 H, m), 3.74–3.93 (8 H, m), 4.03–4.14 (2 H, m), 4.23 (1 H, dd, *J* 5.1, 9.5 Hz), 4.49 (1 H, d, *J* 5.1 Hz), 4.59 (1 H, d, *J* 8.1 Hz). FABMS (positive-ion): *m/z* 1331 $[M+Na]^+$; 1309 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{69}H_{133}N_2NaO_{18}P$: 1331.9189; Found: 1331.9203. Anal. Calcd for $C_{69}H_{133}N_2O_{18}P$ (1309.8): C, 63.27; H, 10.24; N, 2.14; P, 2.37. Found: C, 62.92; H, 10.21; N, 2.04; P, 2.01.

2,6-Anhydro-7-O-[2-acetamido-2-deoxy-3-O-[(R)-3-(dodecyloxy)tetradecyl]-6-O-methyl-4-O-phosphono-β-D-glucopyranosyl]-3-[(R)-3-(hydroxy)tetradecanamido]-4-O-[(R)-3-(hydroxy)tetradecyl]-3-deoxy-D-glycero-D-ido-heptonic acid (**72**).—Compound **69** (95.4 mg, 0.065 mmol) was treated as described in the formation of **71** from **68** to give **72** (85.4 mg, quantitatively) as a white powder, mp 181–183 °C. $[\alpha]_D^{24}$ −28.6° (*c* 0.45, $CHCl_3$). IR ν_{max}(KBr) 3304 (broad), 3078, 2956, 2923, 2854, 1733, 1654 cm^{-1}. ^1H NMR (400 MHz, 5:1 CD_3OD–$CDCl_3$) δ 0.89 (12 H, t, *J* 6.6 Hz), 1.29–1.59 (80 H, m), 1.72–1.75 (4 H, m), 2.00 (3 H, s), 2.32 (1 H, dd, *J* 8.1, 14.6 Hz), 2.39 (1 H, dd, *J* 4.4, 14.6 Hz), 3.40 (3 H, s), 3.35–4.04 (19 H, m), 4.09 (1 H, q, *J* 9.5 Hz), 4.24 (1 H, dd, *J* 5.1, 9.5 Hz), 4.50 (1 H, d, *J* 5.1 Hz), 4.59 (1 H, d, *J* 8.1 Hz). FABMS (positive-ion): *m/z* 1345 $[M+Na]^+$; 1323 $[M+H]^+$. HRFABMS (positive-ion): *m/z* Calcd for $C_{70}H_{135}N_2NaO_{18}P$: 1345.9345; Found: 1345.9336. Anal. Calcd for $C_{70}H_{135}N_2O_{18}P$ (1323.8): C, 63.51; H, 10.28; N, 2.12; P,

2.34. Found: C, 63.23; H, 10.14; N, 1.94; P, 2.05.

2,6-Anhydro-7-O-[2-acetamido-2,6-dideoxy-3-O-[(R)-3-(dodecyloxy)tetradecyl]-6-fluoro-4-O-phosphono-β-D-glucopyranosyl]-3-[(R)-3-(hydroxy)tetradecanamido]-4-O-[(R)-3-(hydroxy)tetradecyl]-3-deoxy-D-glycero-D-ido-heptonic acid (**73**).—Compound **70** (46.5 mg, 0.032 mmol) was treated as described in the formation of **71** from **68** to give **73** (39.3 mg, 94%) as a white powder, mp 199.0–200.5 °C. $[\alpha]_D^{24}$ −34.5° (*c* 0.70, $CHCl_3$). IR ν_{max}(KBr) 3399 (broad), 3306, 3085, 2957, 2923, 2854, 1733, 1645 cm^{-1}. ^1H NMR (400 MHz, 5:1 CD_3OD–$CDCl_3$) δ 0.89 (12 H, t, *J* 6.6 Hz), 1.29–1.60 (80 H, m), 1.69–1.77 (4 H, m), 2.00 (3 H, s), 2.33 (1 H, dd, *J* 8.1, 14.6 Hz), 2.38 (1 H, dd, *J* 4.4, 14.6 Hz), 3.40–3.49 (4 H, m), 3.55–4.06 (13 H, m), 4.11 (1 H, q, *J* 9.5 Hz), 4.23 (1 H, dd, *J* 5.1, 9.5 Hz), 4.49 (1 H, d, *J* 5.1 Hz), 4.54–4.80 (3 H, m, containing 1 H, d, *J* 8.1 Hz, at δ 4.63). FABMS (positive-ion): *m/z* 1333 $[M+Na]^+$; 1311 $[M+H]^+$. HR-FABMS (positive-ion): *m/z* Calcd for $C_{69}H_{132}FN_2NaO_{17}P$: 1333.9145; Found: 1333.9158. Anal. Calcd for $C_{69}H_{132}FN_2O_{17}P$ (1311.8): C, 63.18; H, 10.14; F, 1.45; N, 2.14; P, 2.36. Found: C, 63.31; H, 10.18; F, 1.46; N, 2.06; P, 2.08.

4. Methods for measurement of biological activity

The sources of the materials used in the study are as follows: lipopolysaccharide (LPS) from *E. coli* serotype 026:B6 and 12-*O*-tetradecanoylphorbor acetate (TPA) were from Sigma, St. Louis, MO; RPMI-1640 medium, fetal bovine serum (FBS), and newborn calf serum (NBCS) were from Gibco, Grand Island, NY; and human tumor necrosis factor-α enzyme-linked immunosorbent assay (TNFα ELISA) kit was from Genzyme, Cambridge, MA.

Cell culture.—Human monoblastic U937 cells were maintained in RPMI-1640 medium supplemented with 10% FBS, 100 U/mL of penicillin and 100 μg/mL of streptomycin (growth medium).

Production of TNFα by U937 cells: U937 cells (1×10^4/200 μL/well) were plated in 96-well plates (Corning, Cambridge, MA), and were cultured in the presence of TPA (30 ng/mL) for 72 h at 37 °C. After removing the supernatant, the cells were incubated in 200 μL of fresh RPMI-1640 medium containing 10% NBCS, in the absence or the presence of 30 ng/mL of LPS with graded concentrations of the compounds in a humidified atmosphere of 5% CO_2 for 4.5 h at 37 °C. After incubation, the amount of TNFα produced in the culture supernatants was determined using the TNFα ELISA kits. As a control, the amount of TNFα produced by the U937 cells, which were stimulated with 30 ng/mL of LPS in the absence of compounds, was used. The concentrations (nM) of compounds required to inhibit the LPS-induced TNFα production by U937 cells by 50% (IC_{50}) was calculated from the control amount. All experiments were carried out at least twice, showing that the data are reproducible.

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