Synthesis and Biological Activities of Lipid A Analogs: Modification of a Glycosidically Bound Group with Chemically Stable Polar Acidic Groups and Lipophilic Groups on the Disaccharide Backbone with Tetradecanoyl or *N*-Dodecanoylglycyl Groups

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Six novel lipid A analogs were synthesized. The first two analogs, 4 and 5, have an α-glycosidically bound carboxymethyl or 1,3-dicarboxyisopropyl group on the disaccharide backbone with four tetradecanoyl groups. The next three analogs, 6, 7 and 8, have two or four *N*-dodecanoylglycyl groups on the 1-α-*O*-phosphonooxyethylated disaccharide backbone. Analog 6 bears *N*-dodecanoylglycyl groups on the hydroxyl functions at positions 3 and 3′, and tetradecanoyl groups on the amino functions at positions 2 and 2′. Analog 7 is a 2, 3, 2′ and 3′-tetrakis(*N*-dodecanoylglycyl) derivative, and analog 8 resembles compound 6, but the binding of the *N*-dodecanoylglycyl and tetradecanoyl groups at positions 2, 2′ and 3, 3′ are reversed. The third analog, 9, has the same acyl group configuration as compound 6, but has a 1,3-dicarboxyisopropyl group at position C-1.

Compounds 4 and 5 exhibited definite antitumor activity against Meth A fibrosarcoma, indicating that the phosphate group at the C-1 position in lipid A could be replaced by the carboxylic acid without reducing the antitumor activity. In rabbits, compounds 6 and 9 exhibited potent antitumor activity, but their toxicity was extremely low. On the other hand, compounds 7 and 8 showed no antitumor activity. The levels of antitumor activity of 6 and 9 were similar to those of the natural-type lipid A. The antitumor activities of analogs with a *N*-dodecanoylglycyl group on the disaccharide backbone depended on the connecting sites of the acyl groups.

Keywords lipid A analog; *N*-dodecanoylglycyl group; phosphate group; phosphonooxyethyl group; carboxymethyl group; 1,3-dicarboxyisopropyl group; antitumor activity; Meth A; toxicity; structure–activity; rabbit

The complete structure of natural *Escherichia coli* (*E. coli*) lipid A was deduced[1] and unequivocally confirmed by total synthesis.[2] This chemically synthesized *E. coli* lipid A showed biological activities identical to natural type, which possesses not only undesirable lethal toxicity but also beneficial characteristics such as its antitumor activity.[3]

However, we found that **1**, a novel synthetic analog of lipid A with an α-glycosidically bound phosphonooxyethyl group instead of the α-glycosyl phosphate group of natural lipid A, exhibited antitumor activity at the same level as synthetic *E. coli* lipid A.[4] It was proven that the α-glycosyl phosphate group is not essential for antitumor activity, and is replaceable, without loss of the activity, with other acidic groups such as chemically stable polar acidic groups.

We furthermore reported that compound **2**, which has four (*R*)-3-hydroxytetradecanoyl groups as acyl groups on the disaccharide backbone and an α-glycosidically bound phosphonooxyethyl group, exhibited distinctly less toxicity in rabbits than 1-α-*O*-phosphonooxyethylated compound **3**, which has four tetradecanoyl groups, and that, nevertheless, the difference of antitumor potency between these two compounds was not remarkable[5] (Fig. 1).

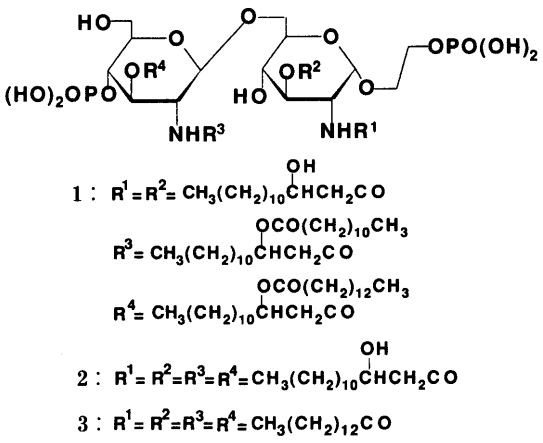


Fig. 1

The above results suggested the possibility of separating the antitumor activity from the toxicity of lipid A. Because the only structural difference between these two compounds was the presence or absence of hydroxyl groups in the fatty acid moiety, it was presumed that the effect of hydroxyl groups in decreasing the toxicity resulted from the capacity for hydrogen bond formation and an increase of polarity.

We therefore directed our effort to synthesize new antitumor compounds toward investigating the possibility of converting the phosphate group at the C-1 position into other chemically stable polar acidic groups, such as carboxylic acids. We also believed that the conversion of the hydroxyl group in (*R*)-3-hydroxytetradecanoyl groups into other functional groups, likely to have the same effect as the hydroxyl group, might lead to the separation of the beneficial antitumor activity and the lethal toxicity of lipid A.

As regards the acidic groups other than phosphoric

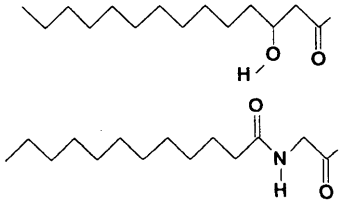


Fig. 2

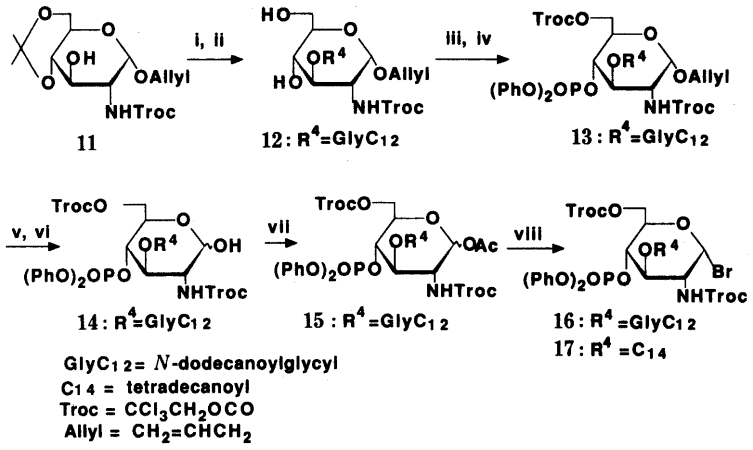


Chart 1

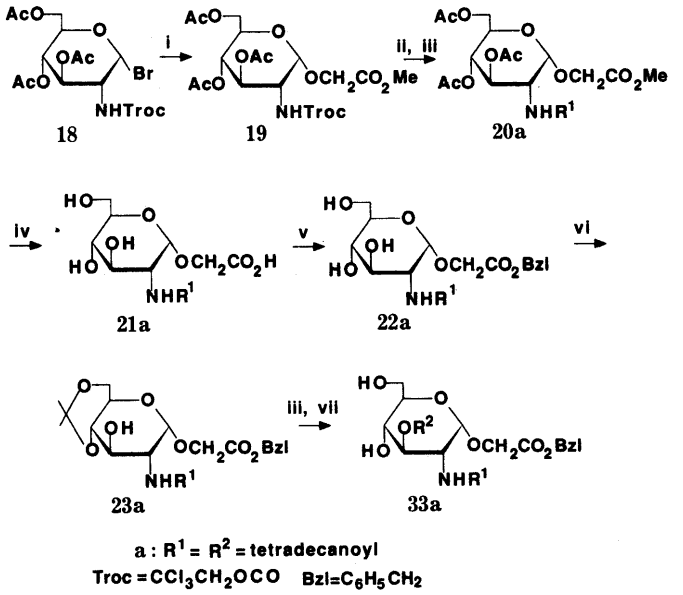


Chart 2

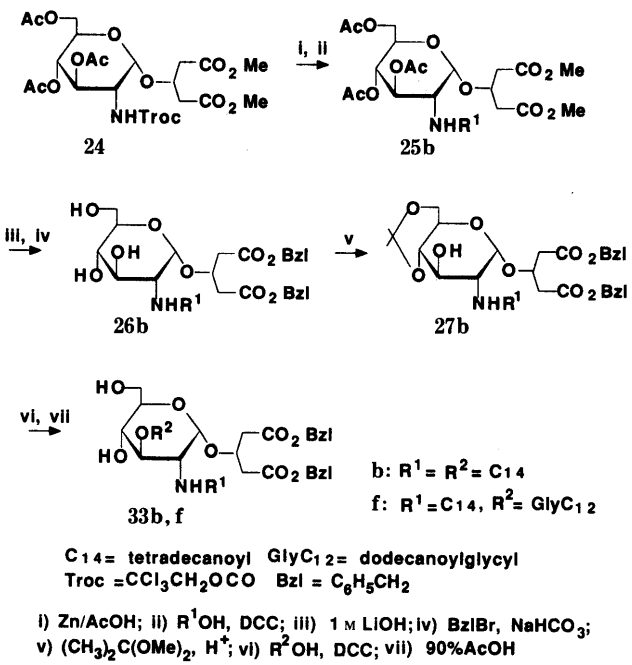


Chart 3

acid, we tried introducing carboxylic acid derivatives to the C-1 position. We chose glycolic acid as a monobasic acid and 3-hydroxyglutaric acid as a dibasic acid. Accordingly, we synthesized compounds **4** and **5** by glycosylation so that these carboxylic acid substituents were attached to the disaccharide backbone bearing four tetradecanoyl groups without a hydroxyl.

We were also interested in replacing the hydroxyl groups of the fatty acid residues of compound **2** with NH amides which can be expected to exert an effect similar to that of hydroxyl on the capacity for hydrogen bond formation and on the increase of polarity. We considered that the amide bond "CONH", which can confer properties similar to those described above without having an asymmetric carbon and without basicity, would be a suitable functional group for our purpose. Since the –CONH– sites of the acyl groups should be located at nearly the same positions as the hydroxyl groups in the (*R*)-3-hydroxytetradecanoyl group, and since the chain length should be similar to the length of the hydroxytetradecanoyl group, the *N*-dodecanoylglycyl group was chosen for introduction to the disaccaride backbone (Fig. 2).

Thus, compounds **6**, **7**, and **8**, substituted totally or partially with *N*-dodecanoylglycyl groups, were synthesized (Chart 5). The results of the biological activity evaluation of the synthesized compounds described above made it desirable to synthesize compound **9**, which has the same composition of acyl groups as compound **6**, as well as a 1,3-dicarboxyisopropyl group at the C-1 position.

This paper describes the synthesis and biological activities of compound **4**—**9**.

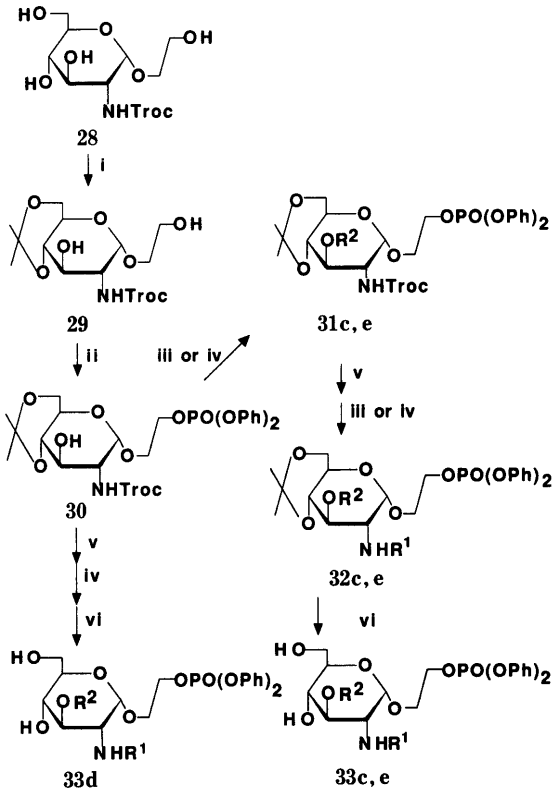
Chemistry The glycosyl donor **16** was synthesized from **11** by a method similar to that used for synthesizing the

glycosyl bromide **17** in our previous study,[5] as shown in Chart 1.

After 3-*O*-acylation of acetonide **11** with *N*-dodecanoylglycine in the presence of dicyclohexylcarbodiimide (DCC) and 4-dimethylaminopyridine (DMAP), the isopropylidene group was removed to give 3-*O*-acylated **12**. Selective *O*-trichloroethoxycarbonylation at position C-6, followed by phosphorylation with diphenyl chlorophosphate at the C-4 position, yielded the 4-*O*-diphenylphosphorylated compound **13**. After deallylation and acetylation of the C-1 position, the resulting glycosyl acetate **15** was brominated with 25% HBr–acetic acid to give the glycosyl bromide **16**.

Routes for the synthesis of glucosamine derivatives **33a**, **33b** and **33f**, glycosyl acceptors, are shown in Charts 2 and 3.

The selective glycosylation of bromide **18** with methylglycolate was employed in a similar manner, using zinc bromide, as reported for the synthesis of **24**,[6] to give α-glycoside **19**. The 2,2,2-trichloroethoxycarbonyl (Troc) group of compounds **19** and **24** were cleaved by treatment with zinc powder in acetic acid (AcOH), and a tetradecanoyl group was introduced into the resulting amino group by the acid chloride method or the DCC method to give *N*-tetradecanoyl derivatives **20a** and **25b**. Thereafter, all acetyl and methyl groups of **20a** were removed by



c: R^1= C_{14}, R^2= $GlyC_{12}$
d: R^1= R^2= $GlyC_{12}$
e: R^1= $GlyC_{12}$, R^2= C_{14}

C_{14}= tetradecanoyl $GlyC_{12}$= *N*-dodecanoylglycyl
Troc =CCl_3CH_2OCO

i) $(CH_3)_2C(OMe)_2$, H^+; ii) $(PhO)_2POCl$, DMAP; iii) $C_{14}OCl$, DMAP, pyridine; iv) $GlyC_{12}OH$, DCC, DMAP; v) Zn/AcOH; vi) 90%AcOH

Chart 4

treatment with a NaOH solution, and the resulting carboxyl group of **21a** was protected by a benzyl group to give **22a**. On the other hand, compound **25b** was deprotected by treatment with a LiOH solution, and without isolation of the deprotected compound, was immediately esterified with benzyl bromide and sodium hydrogen carbonate to give **26b**. Hydroxyl groups at the 4 and 6 positions of **22a** and **26b** were protected by isopropylidene fromation, and the residual hydroxyl groups of **23a** and **27b** were acylated with tetradecanoic acid or *N*-dodecanoylglycine (**10**) by the same method as described for **20a** and **25b**. Deprotection of isopropylidene groups with 90% AcOH afforded the glycosyl acceptors **33a**, **33b** and **33f**.

The other glucosamine components, **33c—e**, were prepared from α-glycoside **28** as shown in Chart 4.

After acetonide formation at the 4 and 6 hydroxyl groups of **28**, the remaining primary hydroxyl group was phosphorylated by treatment with diphenyl chlorophosphate to give the phosphonate **30**. Acylation of **30** with tetradecanoyl chloride or *N*-dodecanoylglycine in the presence of DCC and DMAP gave **31c** or **31e**. After removal of the Troc group of **31c** and **31e** with zinc powder in AcOH, the products were acylated as described for **31c** and **31e** to yield **32c** and **32e**, respectively. Subsequent hydrolysis with 90% AcOH produced the glycosyl acceptors **33c** and **33e**. Glycosyl acceptor **33d** was prepared from **30**. After removal of the Troc group of **30**, introduction of *N*-dodecanoylglycine to both of the resulting 2-amino and 3-hydroxyl functions, followed by hydrolysis in 90% AcOH, gave **33d**.

The basic strategy for the synthesis of compounds **4—9** was similar to that employed in our previous synthesis[5] of the 1-*O*-phosphonooxyethylated compound **3**, as shown in Chart 5.

Coupling of glycosyl bromides **16** and **17** with the acceptors **33a—f** yielded the disaccharides **34a—f**. After cleavage of the Troc groups, the resultant free amino groups were acylated with tetradecanoic acid by the 1-hydroxybenzotriazole (HOBt) active ester method to give compounds **35a—f**. Finally, hydrogenolytic deprotection of **35a—f** afforded the desired compounds **4—9**.

Antitumor Activity The antitumor activity of synthetic compounds was tested in BALB/c mice as described earlier.[5] Briefly, a group of 7 or 8 mice were inoculated intradermally with Meth A syngeneic fibrosarcoma cells (2×10^5). The triethylamine (Et_3N) salt of each compound was dissolved in an aqueous solution containing 5% glucose and 0.1% Et_3N. The resulting solution was then administered to the mice at a dose of 100 μg/mouse through the tail vein on the 7th, 12th and 17th days after implantation. The percentage antitumor effect on the growth of Meth A was determined by dividing the average tumor weight of the treated group on the 21st day by the average tumor weight of the control group, then multiplying the quotient by 100. Tables I and II show the results.

Toxicity The Et_3N salts of each of the compounds were dissolved in 5% (v/v) glucose containing 0.1% Et_3N to prepare a 100 μg/ml solution. This solution was administered through the ear vein to three NZW rabbits per group at a dose of 50 or 500 μg/kg-body weight for 3

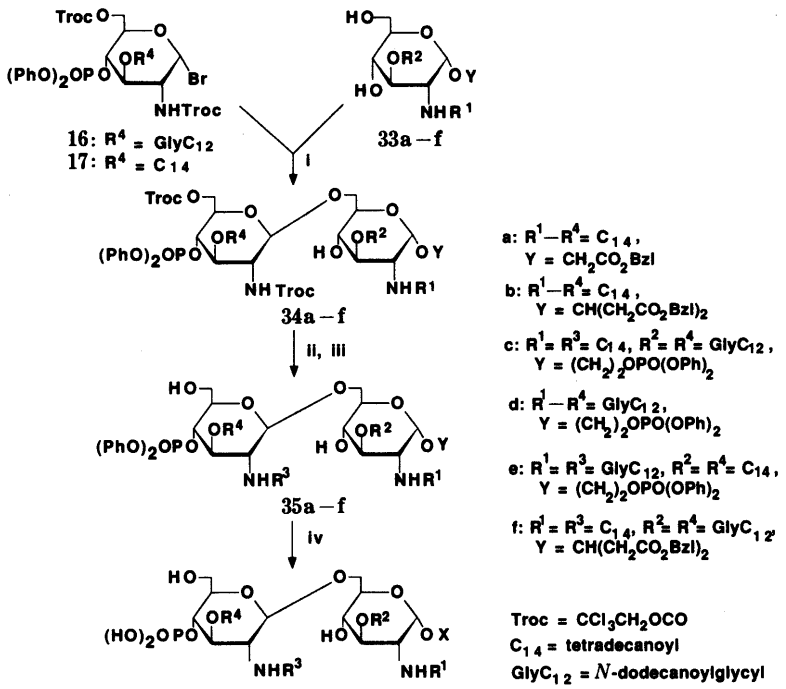


Chart 5

TABLE I. Antitumor Activity of Lipid A Analogs against Meth A Fibrosarcoma

Compound No.	Dose (μg/mouse)	T/C (%)[a]	Cured mice/ treated mice[b]
4	100 × 3	45[c]	1/7
5	100 × 3	24[d]	1/8
6	100 × 3	21[d]	1/8
7	100 × 3	80	0/7
8	100 × 3	77	0/7
9	100 × 3	20[d]	0/7
Control	—	100	0/8

a) (Mean tumor weight in tested group/that in control group) × 100. Results given are at 21 d after tumor inoculation. *b*) Number of tumor-free mice/number of mice tested. *c*) $p<0.01$ *vs.* control (Student's test). *d*) $p<0.001$ *vs.* control (Student's test).

TABLE II. Antitumor Activity of Lipid A and Compound **6** against Meth A Fibrosarcoma

Compound No.	Dose (μg/mouse)	T/C (%)[a]	Cured mice/ treated mice[b]
6	100 × 3	21[d]	1/8
Synthetic *E. coli* Lipid A[c]	100 × 3	18[d]	0/8
Control	—	100	0/8

a) (Mean tumor weight in tested group/that in control group) × 100. Results given are at 21 d after tumor inoculation. *b*) Number of tumor-free mice/number of mice tested. *c*) Synthetic *E. coli* lipid A (No. 506) was purchased from Daiichi Pure Chemicals Co., Ltd., Tokyo. *d*) $p<0.001$ *vs.* control (Student's test).

consecutive days. Toxicity was evaluated by mortality, clinical signs, decrease in body weight, decrease in platelets (%), blood chemistry and pathology (Table III).

Discussion

Compounds **4** and **5**, which have the same acyl composition and an α-glycosidically bound carboxymethyl group or 1,3-dicarboxyisopropyl group, exhibited definite antitumor activity. It becomes more clear that the conversion of substituents possessing carboxylic acid as an acidic group at the C-1 position, as well as those having glycosidically bound phosphoric acid or a phosphonooxyethyl group, retained the antitumor activity (Table I). The acidic polar moiety at the C-1 position of the dibasic acid analog **5** (which has greater acidity) demonstrated stronger antitumor activity than did monobasic acid analog **4**. On the other hand, concerning toxicity in rabbits, dicarboxylic acid analog **5** showed a tendency to be more toxic than monocarboxylic acid analog **4**, whereas the conversion of a phosphoric acid type group to a carboxylic acid type group at the C-1 position did not cause a decrease in toxicity compared with the phosphate type.

The antitumor activity of compound **6**, which has two *N*-dodecanoylglycyl groups at the C-3 and 3′ positions, was comparable to that of synthetic natural-type lipid A (Table II). However, the antitumor activity of **8**, which is

TABLE III. Toxicity of Lipid A Analogs in Rabbits

Observations	Compound							
	4	**5**	**6**	**7**	**8**	**9**	**6**	**9**
	Dose: 50	50	50	50	50	50	500	500 μg/kg
Mortality[a]	0/3	1/3	0/3	0/3	0/3	0/3	0/3	0/3
Clinical signs[b]	HE, RD	HE, AD, PT, LY	HE	NO[i]	HE	NO	HE	NO
Decrease in body weight (g)[c]	100—400	350	NO	NO	NO	NO	NO	NO
Hematological examination[d]	GPT↑, UN↑, CRE↑, CPK↑, TG↑	GPT↑, UN↑, CRE↑, TP↓, ALB↓	NO	NO	UN↑, CRE↑, CHO↑	NO	NO	NO
Pathology[a]								
Thrombus	3/3 (3+)[h]	1/3 (+)	NO	NO	NO	NO	NO	NO
Change in liver[e]	1/3 (3+)	2/3 (+)	NO	NO	NO	NO	NO	NO
Change in kidney[f]	1/3 (+)	3/3 (+)	NO	NO	1/3 (+)	NO	NO	NO
Change in heart[g]	2/3 (+, 3+)	1/3 (3+)	NO	NO	NO	NO	NO	NO

a) Mortality and pathology: number of rabbits changed/number of rabbits tested. *b*) HE, hyperemia of eye; RD, respiratory depression; AD, decrease in locomotor activity; PT, ptosis; LY, lying on side. *c*) 24 h after final injection. *d*) GPT, glutamate pyruvate transaminase; UN, urea nitrogen; CRE, creatinine; CPK, creatine phosphokinase; TG, triglyceride; TP, total protein; ALB, albumin; CHO, total cholesterol. *e*) Liver change: degeneration and necrosis of liver cells. *f*) Kidney change: degeneration and necrosis of epithelium of uriniferous tubules. *g*) Heart change: degeneration and necrosis of muscle fiber. *h*) +, slight; 2+, moderate; 3+, severe. *i*) NO: no change.

a positional isomer of compound **6** or **7** having four *N*-dodecanoylglycyl groups, was extremely weak. On the other hand, compounds **6**, **7** and **8** did not show any lipid A toxicity on treatment with 50 μg/kg-body weight dose for 3 consecutive days in rabbits.

Since compound **6** showed both strong antitumor activity and low toxicity, it was compared to the activities of compound **9** in which only the C-1 substituent was different. As a result, **9** was found to have the same strong activity and low toxicity as the original compound **6**, thus suggesting that, with the same acyl composition on the disaccharide backbone, the biological effects of the 1,3-dicarboxyisopropyl and phosphonooxyethyl groups were nearly the same. These results indicate that the structural requirements for the antitumor activities of analogs with *N*-dodecanoylglycyl groups on a disaccharide backbone are very strict, and the binding position on the disaccharide backbone of this group is very important for the expression of activity. For example, compounds **6** and **9**, having a high antitumor activity, showed almost no toxicity on treatment with a dose of 500 μg/kg-body weight (Table III), and these compounds showed a clear separation between the antitumor activity and the undesired toxicity of lipid A. Since compound **3**, which has four (*R*)-3-hydroxytetradecanoyl groups, exhibited a definite antitumor activity, as reported in previous paper,[5] and although compound **8**, with four *N*-dodecanoylglycyl groups, did not show any such activity, the influence of the –CONH– of *N*-dodecanoylglycyl groups on antitumor activity differed considerably from that of the hydroxyl of 3-hydroxytetradecanoyl groups. This difference suggested that the *N*-dodecanoylglycyl group has another relevant property in addition to its capacity for hydrogen bond formation and polarity, probably due to the restricted rotation of the amide bond in a *N*-dodecanoylglycyl group.

In conclusion, compounds **6** and **9** represent the first successful examples of separating toxicity in natural-type lipid A from its significant antitumor activity, while retaining this activity. We hope that these findings will open the way for the clinical application of lipid A derivatives, and that these compounds will be useful for the investigation of a toxicological mode of action of natural-type lipid A as an endotoxin.

Experimental

All melting points are uncorrected. ^{1}H-Nuclear magnetic resonance (^{1}H-NMR) spectra were determined on a Varian XL-200 (200 MHz) or JEOL-GSX 500 (500 MHz) spectrometer in deuteriochloroform solution unless otherwise noted. The chemical shifts are given in δ values with tetramethylsilane (TMS) as the internal standard. Optical rotations were measured with a Horiba SEDA-200 polarimeter at 25 °C. Mass spectra (MS) were obtained on a JMS-HX 110 or JMX-300 instrument. Precoated Silica gel 150 A PLK5F plates (1.0 mm thickness; Whatmann) were used for preparative thin layer chromatography (TLC). Organic solution were dried over sodium sulfate before concentration.

***N*-Dodecanoylglycine (10)** Dodecanoyl chloride (10.9 g, 50 mmol) and an aqueous solution (30 ml) of NaOH (2.00 g, 50 mmol) were added to a mixture of glycine (4.13 g, 55 mmol) and an aqueous solution (30 ml) of NaOH (2.20 g, 55 mmol) under ice-cooling maintained at pH 9. The mixture was stirred for 30 min, and then neutralized with 35% HCl with ice-cooling to about at pH 1. After the mixture was extracted with ethyl acetate (EtOAc), the organic layer was washed with H_2O, saturated aqueous NaCl, dried and concentrated. The residue was crystallized from EtOAc–hexane to give **10** (11.3 g, 88%), mp 118—119 °C (118—119 °C).[7] NMR ($CDCl_3+CD_3OD$) δ: 0.88 (3H, t, J=6 Hz, CH_3), 1.27 (16H, s, CH_2), 1.60 (2H, br, CH_2CH_2CO), 2.26 (2H, t, J=8 Hz, CH_2CON), 3.95 (2H, s, NCH_2CO_2).

Allyl 2-Deoxy-3-*O*-(*N*-dodecanoylglycyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (12) *N*-Dodecanoylglycine (**10**) (1.42 g, 5.52 mmol), DMAP 0.28 g (5.52 mmol) and DCC (1.14 g, 5.53 mmol) were added to a solution of **11** (2.00 g, 4.60 mmol) in CH_2Cl_2 (60 ml) with ice-cooling, and the mixture was stirred for 15 h at room temperature. The precipitate was filtered off, and the filtrate was concentrated *in vacuo*. The residue in 90% AcOH (50 ml) was heated at 90 °C for 20 min. Evaporation of the solvent gave a viscous oil, which was purified by silica gel column chromatography ($CHCl_3$–MeOH, 19:1) to give **12** as a colorless oil (2.60 g, 89%), $[\alpha]_D$ +54.8° (c=1.0, $CHCl_3$). NMR δ: 0.89 (3H, t, J=7 Hz, CH_3), 1.28 (16H, s, CH_2), 1.64 (2H, br, CH_2CH_2CO), 2.26 (2H, t, J=8 Hz, CH_2CON), 4.69 and 4.84 (each 1H, AB type d, J=12 Hz, CH_2CCl_3), 4.97 (1H, d, J=4 Hz, H-1), 5.2—5.5 (4H, m, H-3, $CH=CH_2$ and NHTroc), 5.96 (1H, m, $CH=CH_2$), 6.24 (1H, m, CH_2CONH). MS m/z: 633 $[(M+H)^+]$.

Allyl 2-Deoxy-4-*O*-diphenylphosphono-3-*O*-(*N*-dodecanoylglycyl)-6-*O*-(2,2,2-trichloroethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-

α-D-glucopyranoside (13) Troc-Cl (0.77 ml, 5.62 mmol) was gradually added to a solution of **12** (2.55 g, 4.02 mmol) in pyridine (20 ml) with ice-cooling. After the mixture was stirred for 1.5 h, H_2O was added and the solvent was evaporated. The residue was purified by silica gel column chromatography ($CHCl_3$–acetone, 9:1) to give a colorless oil (2.44 g, 75%). Diphenyl chlorophosphate (1.20 g, 4.47 mmol), DMAP (0.55 g, 4.47 mmol) and pyridine (0.35 ml, 4.47 mmol) were added to a solution of the above oil (2.41 g, 2.98 mmol) in CH_2Cl_2 (30 ml). After stirring for 1 h at room temperature, the mixture was diluted with $CHCl_3$, and washed successively with 1 M HCl, H_2O, 5% aqueous $NaHCO_3$ and saturated aqueous NaCl, and dried. After the solvent was evaporated, hexane was added to the residual oil to give **13** as a white powder (2.71 g, 87%), mp 80—82 °C, $[\alpha]_D$ +46.4° (c=1.1, $CHCl_3$). *Anal.* Calcd for $C_{41}H_{53}Cl_6N_2O_{14}P$: C, 47.28; H, 5.13; N, 2.69. Found: C, 47.34; H, 5.04; N, 2.74. NMR δ: 0.89 (3H, t, J=7 Hz, CH_3), 1.28 (16H, s, CH_2), 1.58 (2H, br, CH_2CH_2CO), 2.10 (2H, t, J=8 Hz, CH_2CON), 3.80 (1H, dd, J=18, 4 Hz, NCH_2CO_2), 4.00 (1H, dd, J=18, 4 Hz, NCH_2CO_2), 4.67 and 4.82 (each 1H, AB type d, J=12 Hz, CH_2CCl_3), 4.80 (3H, m, H-4 and CH_2CCl_3), 5.01 (1H, d, J=4 Hz, H-1), 5.3—5.5 (4H, m, H-3, NHTroc, $CH=CH_2$), 5.96 (1H, m, $CH=CH_2$), 6.27 (1H, m, CH_2CONH), 7.2—7.4 (10H, m, arom. H).

2-Deoxy-4-*O*-diphenylphosphono-3-*O*-(*N*-dodecanoylglycyl)-6-*O*-(2,2,2-trichloroethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-D-glucose (14) Compound **13** (2.64 g, 2.53 mmol) and 1,5-cyclooctadienebis(methyldiphenylphosphine)iridium hexafluorophosphate (50 mg) were dissolved in tetrahydrofuran (THF, 40 ml) in a nitrogen atmosphere. After activation of the catalyst with a hydrogen atmosphere for 1 min, the mixture was heated at 50 °C in the nitrogen atmosphere for 2 h. After cooling, iodine (1.28 g, 5.06 mmol) and H_2O (4 ml) were added to the solution and the mixture was stirred for 30 min. The solution was neutralized with 5% Na_2SO_3 and extracted with $CHCl_3$. The solution was washed with saturated NaCl solution, dried, and concentrated. The residue was purified by silica gel column chromatography ($CHCl_3$–acetone, 9:1) to give **14** (2.34 g, 92%) as a yellow oil, $[\alpha]_D$ +31.0° (c=1.0, $CHCl_3$). NMR δ: 0.88 (3H, t, J=7 Hz, CH_3), 1.28 (16H, s, CH_2), 1.57 (2H, br, CH_2CH_2CO), 2.12 (2H, t, J=8 Hz, CH_2CON), 3.80 (1H, dd, J=18, 4 Hz, NCH_2CO_2), 3.98 (1H, dd, J=18, 4 Hz, NCH_2CO_2), 4.50—4.90 (4H, m, CH_2CCl_3), 5.38 (1H, m, H-1), 5.58 (2H, m, H-3 and NHTroc), 6.30 (1H, m, CH_2CONH), 7.1—7.4 (10H, m, arom. H).

1-*O*-Acetyl-2-deoxy-4-*O*-diphenylphosphono-3-*O*-(*N*-dodecanoylglycyl)-6-*O*-(2,2,2-trichloroethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-D-glucopyranose (15) Acetic anhydride (1.18 g, 11.6 mmol) and pyridine (0.93 ml, 11.6 mmol) were added to a solution of **14** (2.31 g, 2.31 mmol) in CH_2Cl_2 (40 ml). After being stirred for 19 h, the mixture was diluted with $CHCl_3$. The solution was washed with 1 M HCl, H_2O and 5% $NaHCO_3$, dried, and concentrated. The residue was purified by silica gel column chromatography ($CHCl_3$–acetone, 19:1) to give **15** (2.25 g, 93%) as a pale yellow oil, $[\alpha]_D$ +43.8° (c=1.2, $CHCl_3$). NMR δ: 0.88 (3H, t, J=7 Hz, CH_3), 1.28 (16H, s, CH_2), 1.58 (2H, CH_2CH_2CO), 2.11 (2H, t, J=8 Hz, CH_2CON), 2.25 (3H, s, OAc), 3.77 (1H, dd, J=18, 4 Hz, NCH_2CO_2), 4.07 (1H, dd, J=18, 4 Hz, NCH_2CO_2), 4.57 and 4.74 (each 1H, AB type d, J=12 Hz, CH_2CCl_3), 4.86 and 4.98 (each 1H, AB type d, J=12 Hz, CH_2CCl_3), 4.92 (1H, q, J=8 Hz, H-4), 5.18 (1H, d, J=10 Hz, NHTroc), 5.50 (1H, t, J=10 Hz, H-3), 6.31 (2H, m, H-1 and CH_2CONH), 7.2—7.4 (10H, m, arom. H).

Methoxycarbonylmethyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (19) Zinc bromide (140 mg, 0.62 mmol) was added to a suspension of **18**[7] (330 mg, 0.61 mmol), methyl glycolate (65 mg, 0.73 mmol) and $CaSO_4$ (100 mg) in CH_2Cl_2 (5 ml) at room temperature, and the mixture was refluxed for 5 h, then diluted with $CHCl_3$, and filtered. The filtrate was washed with 5% aqueous $NaHCO_3$, dried, and concentrated. The residue was purified by silica gel column chromatography ($CHCl_3$–acetone, 50:1) to give **19** (204 mg, 61%) as a powder, mp 110—111 °C, $[\alpha]_D$ +85.6° (c=0.9, $CHCl_3$). *Anal.* Calcd for $C_{18}H_{24}Cl_3NO_{12}$: C, 39.11; H, 4.38; N, 2.53. Found: C, 39.13; H, 4.37; N, 2.48. NMR δ: 2.01, 2.03 and 2.10 (each 3H, s, OAc), 3.78 (3H, s, OCH_3), 4.1—4.3 (6H, m), 4.63 and 4.86 (each 1H, AB type d, J=12 Hz, CH_2CCl_3), 4.97 (1H, d, J=4 Hz, H-1), 5.13 (1H, t, J=10 Hz, H-4), 5.31 (1H, t, J=10 Hz, H-3), 5.63 (1H, d, J=10 Hz). MS m/z: 552 $[(M+H)^+]$.

Methoxycarbonylmethyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-tetradecanoylamino-α-D-glucopyranoside (20a) Zinc powder (2.0 g) was added to a solution of **19** (1.60 g, 2.89 mmol) in AcOH (20 ml), and the mixture was vigorously stirred for 3 h at room temperature. The insoluble materials were removed by filtration, and the filtrate was concentrated *in vacuo*. The resulting oily product was dissolved in EtOAc, and this solution was washed with 5% aqueous $NaHCO_3$, and dried. After evaporation of the solvent, tetradecanoyl chloride (1.07 g, 4.34 mmol) and *N*-methylmorpholine (0.48 ml, 4.34 mmol) were added to a solution of the resulting oily product in CH_2Cl_2 (20 ml). The mixture was vigorously stirred for 1 h. MeOH (5 ml) was added to the reaction mixture. After 1 h of stirring, the mixture was diluted with $CHCl_3$, washed with 1 M HCl, saturated aqueous NaCl, dried, and concentrated. The residue was purified by silica gel column chromatography ($CHCl_3$–acetone, 50:1) to give **20a** (1.68 g, 99%) as a wax, $[\alpha]_D$ +68.6° (c=1.2, $CHCl_3$). NMR δ: 0.89 (3H, t, J=7 Hz, CH_3), 1.26 (20H, s, CH_2), 1.63 (2H, br, CH_2CH_2CO), 2.02, 2.04 and 2.11 (each 3H, s, OAc), 2.20 (2H, m, CH_2CO), 3.78 (3H, s, CO_2CH_3), 4.1—4.5 (4H, m), 4.26 (2H, s, OCH_2CO_2), 4.90 (1H, d, J=4 Hz, H-1), 5.18 (1H, t, J=10 Hz, H-4), 5.32 (1H, t, J=10 Hz, H-3), 6.15 (1H, d, J=10 Hz, NH). MS m/z: 588 $[(M+H)^+]$.

Carboxymethyl 2-Deoxy-2-tetradecanoylamino-α-D-glucopyranoside (21a) A solution of 1 M NaOH (12.2 ml) was added to a solution of **20a** (1.63 g, 2.77 mmol) in THF (20 ml) with ice-cooling, and the mixture was stirred for 20 min at the same temperature, then neutralized with 10% citric acid. The insoluble material was collected by filtration, washed with H_2O and dried *in vacuo* to give **21a** (1.16 g, 93%) as a white solid, mp 153—156 °C, $[\alpha]_D$ +93.5° (c=1.0, DMF). NMR (CD_3OD–$CDCl_3$, 1:1) δ: 0.88 (3H, t, J=7 Hz, CH_3), 1.26 (20H, s, CH_2), 1.60 (2H, br, CH_2CH_2CO), 2.26 (2H, t, J=7 Hz), 4.20 (2H, d, J=5.4 Hz, OCH_2CO_2). MS m/z: 448 $[(M+H)^+]$.

Benzyloxycarbonylmethyl 2-Deoxy-2-tetradecanoylamino-α-D-glucopyranoside (22a) Benzyl bromide (0.86 g, 5.00 mmol) and Et_3N (0.70 ml, 5.00 mmol) were added to a solution of **21a** (1.12 g, 2.50 mmol) in dimethylformamide (DMF, 20 ml), and the mixture was heated at 60 °C for 2 h. The mixture was diluted with EtOAc, and washed with H_2O and 1 M HCl. The organic layer was concentrated *in vacuo*, and the residue was purified by silica gel column chromatography ($CHCl_3$–MeOH, 9:1) to give **22a** (1.18 g, 88%) as a white powder, mp 268—269 °C, $[\alpha]_D$ +82.0° (c=1.1, DMF). *Anal.* Calcd for $C_{29}H_{47}NO_8$: C, 64.78; H, 8.81; N, 2.61. Found: C, 64.63; H, 8.78; N, 2.52. NMR δ: 0.87 (3H, t, J=7 Hz, CH_3), 1.24 (20H, s, CH_2), 1.50 (2H, br, CH_2CH_2CO), 2.10 (2H, t, J=7 Hz, CH_2CO), 4.26 (2H, s, OCH_2CO_2), 4.83 (1H, d, J=4 Hz, H-1), 5.18 (2H, s, $CH_2C_6H_5$), 7.42 (5H, s, arom. H), 7.64 (1H, d, J=8 Hz, NH). MS m/z: 538 $[(M+H)^+]$.

Benzyloxycarbonylmethyl 2-Deoxy-4,6-*O*-isopropylidene-2-tetradecanoylamino-α-D-glucopyranoside (23a) Dimethoxypropane (0.45 g, 4.28 mmol) was added to a solution of **22a** (1.15 g, 2.14 mmol) in DMF (40 ml) in the presence of *p*-toluenesulfonic acid (*p*-TsOH·H_2O, 38 mg, 0.2 mmol), and the solution was stirred for 3.5 h. After evaporation of the solvent, the residue was purified by silica gel column chromatography ($CHCl_3$–acetone, 20:1) to give **23a** (1.10 g, 89%) as a white powder, mp 72—73 °C, $[\alpha]_D$ +35.0° (c=1.1, $CHCl_3$). *Anal.* Calcd for $C_{32}H_{51}NO_8$: C, 66.52; H, 8.90; N, 2.42. Found: C, 66.42; H, 8.87; N, 2.51. NMR δ: 0.88 (3H, t, J=6 Hz), 1.26 (20H, s, CH_2), 1.45 and 1.56 (each 3H, s, CCH_3), 1.66 (2H, br, CH_2CH_2CO), 2.30 (2H, t, J=8 Hz, CH_2CO), 4.28 (2H, s, OCH_2CO_2), 4.82 (1H, d, J=4 Hz, H-1), 5.25 (2H, s, $CH_2C_6H_5$), 7.42 (5H, s, arom. H). MS m/z: 578 $[(M+H)^+]$.

Benzyloxycarbonylmethyl 2-Deoxy-3-*O*-tetradecanoyl-2-tetradecanoylamino-α-D-glucopyranoside (33a) As described for **20a**, compound **23a** (1.07 g, 1.85 mmol) was reacted with tetradecanoyl chloride (640 mg, 2.60 mmol) in CH_2Cl_2 (20 ml) in the presence of pyridine (0.73 ml, 2.60 mmol) and DMAP (40 mg) with ice-cooling. After the usual work-up, the resulting oily residue was dissolved in 90% AcOH (40 ml), and the mixture was heated at 90 °C for 30 min. Evaporation of the solvent gave an oil, and the oily product was purified by silica gel column chromatography ($CHCl_3$–MeOH, 19:1) to give **33a** (1.24 g, 90%) as a colorless solid, mp 54—55 °C, $[\alpha]_D$ +46.9° (c=1.1, $CHCl_3$). *Anal.* Calcd for $C_{43}H_{73}NO_9$: C, 69.04; H, 9.84; N, 1.87. Found: C, 68.75; H, 9.67; N, 1.82. NMR δ: 0.89 (6H, t, J=7 Hz), 1.28 (40H, s, CH_2), 1.60 (4H, br, CH_2CH_2CO × 2), 2.15 and 2.35 (each 2H, m, CH_2CO), 3.8—3.9 (4H, m), 4.27 (2H, s, OCH_2CO_2), 4.33 (1H, m, H-2), 4.89 (1H, d, J=4 Hz, H-1), 5.18 (1H, m, H-3), 5.22 (2H, s, $CH_2C_6H_5$), 6.17 (1H, d, J=9 Hz, NH), 7.41 (5H, s, arom. H). MS m/z: 748 $[(M+H)^+]$.

1,3-Di(methoxycarbonyl)isopropyl 2-Deoxy-3,4,6-tri-*O*-acetyl-2-tetradecanoylamino-α-D-glucopyranoside (25b) Zinc powder (20 g) was added to a solution of **24**[6] (23.2 g, 0.04 mmol) in AcOH (100 ml), and the mixture was vigorously stirred for 1 h at room temperature. The insoluble materials were filtered off, and the filtrate was concentrated *in vacuo*. The resulting oily substance was dissolved in EtOAc, and the

solution was washed with 5% aqueous $NaHCO_3$, and dried. The solvent was distilled off at reduced pressure, and the oily product was dissolved in CH_2Cl_2 (200 ml). Tetradecanoic acid (8.2 g, 0.04 mol) and DCC (7.50 g, 0.04 mol) were added to the solution with ice-cooling, and the mixture was stirred for 1 h at room temperature. The precipitate was filtered off, and the filtrate was concentrated *in vacuo*. The oily residue was purified by silica gel column chromatography ($CHCl_3$–acetone, 20:1) to give **25b** (15.6 g, 77%) as a colorless oil, $[\alpha]_D$ +49.3° (c=1.4, $CHCl_3$). NMR δ: 0.88 (3H, t, J=7 Hz), 1.25 (20H, s, CH_2), 1.58 (2H, m, C$\underline{H}_2$CH$_2$CO), 1.99, 2.02 and 2.09 (each 3H, s, OAc), 2.56—2.67 (5H, m, C$\underline{H}_2$CON, OCH(C$\underline{H}_2$CO$_2$Me)$_2$ × 3), 2.82 (1H, dd, J=16, 6 Hz, OCH(C$\underline{H}_2$CO$_2$Me)$_2$), 3.70 and 3.72 (each 3H, s, CO_2CH_3), 4.04 (1H, m, H-5), 4.10 (1H, dd, J=12, 2 Hz, H-6), 4.20 (1H, dd, J=12, 5 Hz, H-6), 4.36 (1H, td, J=10, 4 Hz), 4.45 (1H, m, OC$\underline{H}$(CH$_2$CO$_2$Me)$_2$), 4.96 (1H, d, J=4 Hz, H-1), 5.09 (1H, t, J=10 Hz, H-4), 5.14 (1H, t, J=10 Hz, H-3), 6.28 (1H, d, J=10 Hz, NH).

1,3-Di(benzyloxycarbonyl)isopropyl 2-Deoxy-2-tetradecanoylamino-α-D-glucopyranoside (26b) Compound **25b** (500 mg, 0.74 mmol) was dissolved in MeOH–H_2O (3:1, 20 ml), and LiOH·H_2O (472 mg, 11 mmol) was added to the mixture with ice-cooling. The mixture was stirred for 12 h at room temperature. 1 M HCl was added to the mixture until the pH of the solution became acidic, then 5% $NaHCO_3$ was added until the neutral pH was achieved. After the solution was concentrated *in vacuo*, the residue was dissolved in DMF (14 ml). $NaHCO_3$ (624 mg, 7.4 mmol) and benzyl bromide (2.2 ml, 18.5 mmol) were added to this solution. After stirring for 24 h at room temperature, the solvent was removed at reduced pressure. The residue was purified by silica gel column chromatography ($CHCl_3$–MeOH, 20:1) to give **26b** (337 mg, 65%) as a colorless wax, $[\alpha]_D$ +13.2° (c=0.5, $CHCl_3$). *Anal.* Calcd for $C_{39}H_{57}NO_{10}\cdot H_2O$: C, 65.25; H, 8.30; N, 1.95. Found: C, 65.20; H, 8.21; N, 2.12. NMR (500 MHz) δ: 0.88 (3H, t, J=7.3 Hz), 1.24 (20H, s, CH_2), 1.64 (2H, m, C$\underline{H}_2$CH$_2$CO), 2.25 (2H, m, CH$_2$CO), 2.59 (1H, dd, J=16.7, 5.5 Hz, OCH(C$\underline{H}_2$CO$_2$Bzl)$_2$), 2.65 (1H, dd, J=16.7, 4.0 Hz, OCH(C$\underline{H}_2$CO$_2$Bzl)$_2$), 2.72 (1H, d, J=16.7, 8.7 Hz, OCH(C$\underline{H}_2$CO$_2$Bzl)$_2$), 2.82 (1H, dd, J=16.7, 6.4 Hz, OCH(C$\underline{H}_2$CO$_2$Bzl)$_2$), 3.49 (1H, t, J=8.7 Hz), 3.58 (1H, t, J=10.3 Hz), 3.71 (2H, m), 3.81 (1H, m), 3.94 (1H, m), 4.46 (1H, m, OC$\underline{H}$(CH$_2$CO$_2$Bzl)$_2$), 4.92 (1H, d, J=4.0 Hz, H-1), 5.14 (2H, s, C$\underline{H}_2$C$_6$H$_5$), 5.15 and 5.18 (each 1H, AB type d, J=11.9 Hz, C$\underline{H}_2$C$_6$H$_5$), 7.12 (1H, m, NH), 7.3—7.4 (10H, m, arom. H). MS m/z: 700 [(M+H)$^+$].

1,3-Di(benzyloxycarbonyl)isopropyl 2-Deoxy-4,6-*O*-isopropylidene-2-tetradecanoylamino-α-D-glucopyranoside (27b) In a manner similar to that described for **23a**, compound **26b** (640 mg, 0.91 mmol) was treated with 2,2-dimethoxypropane (0.5 ml) in the presence of *p*-TsOH·H_2O (30 mg) in acetone (10 ml) to give **27b** (540 mg, 80%) as a colorless oil, $[\alpha]_D$ +3.3° (c=0.7, $CHCl_3$). *Anal.* Calcd for $C_{42}H_{61}NO_{10}\cdot 1/4H_2O$: C, 67.75; H, 8.34; N, 1.87. Found: C, 67.53; H, 8.09; N, 1.97. NMR (500 MHz) δ: 0.88 (3H, t, J=7.3 Hz), 1.24 (20H, s, CH_2), 1.43 and 1.52 (each 3H, s, CCH_3), 1.64 (2H, m, C$\underline{H}_2$CH$_2$CO), 2.25 (2H, td, J=7.3, 2.8 Hz, CH$_2$CO), 2.57 (1H, dd, J=15.6, 6.4 Hz, OCH(C$\underline{H}_2$CO$_2$Bzl)$_2$), 2.69 (2H, m, OCH(C$\underline{H}_2$CO$_2$Bzl)$_2$ × 2), 2.78 (1H, dd, J=15.6, 6.4 Hz, OCH(C$\underline{H}_2$CO$_2$Bzl)$_2$), 3.57—3.70 (4H, m), 3.80 (1H, m), 4.05 (1H, m), 4.43 (1H, m, OC$\underline{H}$(CH$_2$CO$_2$Bzl)$_2$), 4.89 (1H, d, J=3.7 Hz, H-1), 5.10 and 5.13 (each 1H, AB type d, J=12.8 Hz, C$\underline{H}_2$C$_6$H$_5$), 5.16 (2H, s, C$\underline{H}_2$C$_6$H$_5$), 6.96 (1H, d, J=7.3 Hz, NH), 7.3—7.4 (10H, m, arom. H). MS m/z: 741 [(M+2)$^+$].

1,3-Di(benzyloxycarbonyl)isopropyl 2-Deoxy-3-*O*-tetradecanoyl-2-tetradecanoylamino-α-D-glucopyranoside (33b) Compound **27b** (480 mg, 0.65 mmol) and tetradecanoic acid (190 mg, 0.85 mmol) in CH_2Cl_2 (10 ml) were added to DMAP (100 mg, 0.85 mmol) and DCC (170 mg, 0.85 mmol) with ice-cooling, and the mixture was stirred for 2 h at room temperature. The insoluble material was filtered off, and the filtrate was concentrated at reduced pressure. The residue was dissolved in 90% AcOH (40 ml), and the mixture was heated at 90 °C for 20 min. After evaporation of the solvent, the residue was purified by silica gel column chromatography ($CHCl_3$–acetone, 10:1) to give **33b** (530 mg, 89%) as a colorless wax, $[\alpha]_D$ +32.8° (c=0.9, MeOH). *Anal.* Calcd for $C_{53}H_{83}NO_{11}$: C, 69.94; H, 9.19; N, 1.54. Found: C, 69.73; H, 9.03; N, 1.60. NMR δ: 0.88 (6H, t, CH_3), 1.26 (40H, s, CH_2), 1.60 (4H, br, C$\underline{H}_2$CH$_2$CO), 2.16 (2H, m, CH$_2$CO), 2.34 (2H, m, CH$_2$CO), 4.94 (1H, s, H-1), 5.20 (4H, s, C$\underline{H}_2$C$_6$H$_5$ × 2), 7.40 (10H, s, arom. H). MS m/z: 911 [(M+2)$^+$].

1,3-Di(benzyloxycarbonyl)isopropyl 2-Deoxy-3-*O*-(*N*-dodecanoylglycyl)-2-tetradecanoylamino-α-D-glucopyranoside (33f) As described for **33b**, compound **27b** (598 mg, 0.81 mmol) was treated with **10** (250 mg, 0.97 mmol) in the presence of DMAP (49 mg, 0.40 mmol) and DCC (200 mg, 0.97 mmol), and the resulting oil was treated with 90% AcOH to give **33f** (632 mg, 83%) as a wax, $[\alpha]_D$ +36.9° (c=1.3, $CHCl_3$). NMR (500 MHz) δ: 0.88 (6H, t, J=7.3 Hz, CH_3), 1.28 (36H, m, CH_2), 1.55—1.67 (4H, m, C$\underline{H}_2$CH$_2$CO × 2), 2.16 (2H, m, CH$_2$CO), 2.26 (2H, t, J=7.3 Hz, CH$_2$CO), 2.60 (1H, dd, J=16.5, 6.4 Hz, OCH(C$\underline{H}_2$CO$_2$Bzl)$_2$), 2.65 (1H, dd, J=16.5, 3.7 Hz, OCH(C$\underline{H}_2$CO$_2$Bzl)$_2$), 2.72 (1H, dd, J=16.5, 8.2 Hz, OCH(C$\underline{H}_2$CO$_2$Bzl)$_2$), 2.81 (1H, dd, J=16.5, 5.5 Hz, OCH(C$\underline{H}_2$CO$_2$Bzl)$_2$), 3.66 (1H, t, J=9.2 Hz), 3.74—3.83 (4H, m), 4.12 (1H, dd, J=17.4, 5.5 Hz), 4.19 (1H, td, J=9.2, 3.7 Hz), 4.46 (1H, m, OC$\underline{H}$(CH$_2$CO$_2$Bzl)$_2$), 4.92 (1H, d, J=4.6 Hz, H-1), 5.03 (1H, t, J=9.2 Hz, H-3), 5.10—5.18 (4H, m, C$\underline{H}_2$C$_6$H$_5$), 6.43 (1H, br, NH), 6.65 (1H, d, J=9.2 Hz, NH), 7.32—7.40 (10H, m, arom. H). MS m/z: 939 [(M+H)$^+$].

2-Hydroxyethyl 2-Deoxy-4,6-*O*-isopropylidene-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (29) As described for **23a**, compound **28** (3.58 g, 8.98 mmol) was treated with 2,2-dimethoxypropane (3.70 ml, 30.2 mmol) in the presence of *p*-TsOH·H_2O (170 mg, 0.89 mmol) to give **29** (2.78 g, 71%) as a white powder, mp 190—192 °C. *Anal.* Calcd for $C_{14}H_{22}Cl_3NO_8$: C, 38.33; H, 5.06; Cl, 24.25; N, 3.19. Found: C, 38.40; H, 5.02; Cl, 24.46; N, 3.59. NMR δ: 1.45 and 1.54 (each 3H, s, CCH_3), 4.75 and 4.86 (each 1H, AB type d, J=12 Hz, CH_2CCl_3), 4.95 (1H, d, J=4 Hz, H-1), 5.80 (1H, d, NH). MS m/z: 438 [(M+H)$^+$].

2-(Diphenylphosphonooxy)ethyl 2-Deoxy-4,6-*O*-isopropylidene-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (30) Diphenyl chlorophosphate (0.80 ml, 3.86 mmol), pyridine (0.4 ml) and DMAP (0.46 g, 3.77 mmol) were added to a solution of **29** (1.12 g, 2.55 mmol) in CH_2Cl_2 (20 ml) with ice cooling. After the mixture was stirred for 3 h, diphenyl chlorophosphate (0.30 ml, 1.45 mmol) and DMAP (0.19 mmol, 1.51 mmol) were added with ice cooling. After the addition of MeOH (1 ml), the mixture was stirred for 1 h and diluted with $CHCl_3$. The solution was washed with 1 M HCl, with aqueous 5% $NaHCO_3$, then with H_2O, and dried. After evaporation of the solvent, the residue was purified by silica gel column chromatography ($CHCl_3$–acetone, 30:1) to give **30** (1.23 g, 71.8%) as a white solid, mp 121—124 °C, $[\alpha]_D$ +46.4° (c=1.0, $CHCl_3$). *Anal.* Calcd for $C_{26}H_{31}Cl_3NO_{11}P$: C, 46.55; H, 4.66; N, 2.09. Found: C, 46.28; H, 4.55; N, 2.13. NMR δ: 1.45 and 1.52 (each 3H, s, CCH_3), 4.45 (2H, m, CH$_2$OP), 4.73 and 4.80 (each 1H, AB type d, J=12 Hz, CH_2CCl_3), 4.85 (1H, d, H-1), 7.10—7.50 (10H, m, arom. H). MS m/z: 671 [(M+2)$^+$].

2-(Diphenylphosphonooxy)ethyl 2-Deoxy-4,6-*O*-isopropylidene-3-*O*-(*N*-dodecanoylglycyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (31c) Compound **30** (1.89 g, 2.82 mmol) was allowed to react with *N*-dodecanoylglycine (0.83 g, 3.22 mmol) in the presence of DCC (0.67 g, 3.23 mmol) and DMAP (0.17 g, 1.40 mmol), in a manner similar to that used for **33b**, to give **31c** (2.57 g, quant.) as a colorless oil, $[\alpha]_D$ +32.2° (c=0.8, $CHCl_3$). NMR δ: 0.88 (3H, t, J=6 Hz), 1.28 (16H, br, CH_2), 1.38 and 1.48 (each 3H, s, CCH_3), 2.20—2.35 (2H, t, CH$_2$CON), 4.20 (2H, m, CH$_2$OP), 5.25 (1H, m, H-3), 7.2—7.5 (10H, m, arom. H).

2-(Diphenylphosphonooxy)ethyl 2-Deoxy-4,6-*O*-isopropylidene-3-*O*-tetradecanoyl-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (31e) As described for **33a**, compound **30** (0.50 g, 0.75 mmol) was treated with tetradecanoyl chloride (221 mg, 0.90 mmol) in the presence of pyridine (0.30 ml, 3.75 mmol) and DMAP (20 mg) in CH_2Cl_2 to give **31e** (0.49 g, 74%) as a colorless oil, $[\alpha]_D$ +36.1° (c=1.0, $CHCl_3$). *Anal.* Calcd for $C_{40}H_{57}Cl_3NO_{12}P$: C, 54.52; H, 6.52; N, 1.59. Found: C, 54.41; H, 6.81; N, 1.72. NMR δ: 0.88 (3H, t, J=7 Hz), 1.28 (16H, s, CH_2), 1.37 and 1.47 (each 3H, s, CCH_3), 1.60 (2H, br, C$\underline{H}_2$CH$_2$CO), 2.30 (2H, m), 4.42 (2H, m, CH$_2$OP), 4.58 and 4.80 (each 1H, AB type d, J=12 Hz, CH_2CCl_3), 4.86 (1H, d, J=4 Hz, H-1), 5.22 (1H, m, H-3), 5.65 (1H, d, J=10 Hz, NH), 7.2—7.5 (10H, m, arom. H). MS m/z: 881 [(M+2)$^+$].

2-(Diphenylphosphonooxy)ethyl 2-Deoxy-4,6-*O*-isopropylidene-3-*O*-(*N*-dodecanoylglycyl)-2-tetradecanoylamino-α-D-glucopyranoside (32c) As described for **20a**, compound **31c** (0.66 g, 0.73 mmol) was treated with zinc powder in AcOH (5 ml), and the resulting oil was treated with tetradecanoyl chloride (0.23 g, 0.93 mmol) in CH_2Cl_2 (5 ml) to give **32c** (0.67 g, 97%) as a colorless oil, $[\alpha]_D$ +30.1° (c=1.7, $CHCl_3$). NMR δ: 0.88 (6H, t, J=6 Hz), 1.28 (40H, br, CH_2), 1.38 and 1.48 (each 3H, s, CCH_3), 1.64 (5H, br), 2.09 (2H, m), 2.26 (2H, m), 2.35 (2H, m), 3.6—4.2 (6H, m), 4.3—4.5 (3H, m), 4.78 (1H, d, J=4 Hz, H-1), 5.21 (1H, m, H-3), 6.25 (1H, br, NH), 6.95 (1H, m, NH), 7.2—7.5 (10H, m, arom. H).

2-(Diphenylphosphonooxy)ethyl 2-Deoxy-2-(*N*-dodecanoylglycylamino)-4,6-*O*-isopropylidene-3-*O*-tetradecanoyl-α-D-glucopyranoside (32e) As described for **25b**, compound **31e** (0.47 mg, 0.53 mmol) was treated with zinc

powder (0.5 g), and the resulting oil was allowed to react with **10** (0.21 g, 0.8 mmol) to give **32e** (0.48 g, 94%) as a powder, mp 79—80 °C, $[\alpha]_D$ +28.1° (c=1.1, $CHCl_3$). NMR δ: 0.88 (6H, t, J=6 Hz), 1.28 (36H, s, CH_2), 1.37 and 1.63 (each 3H, s, CCH_3), 2.12 (2H, m, CH_2CO), 2.30 (2H, t, J=8 Hz, CH_2CO), 4.42 (2H, m, CH_2OP), 4.86 (1H, d, J=4 Hz, H-1), 5.20 (1H, t, J=10 Hz, H-3), 6.78 (1H, br, NH), 6.94 (1H, d, J=8 Hz, NH), 7.2—7.5 (10H, m, arom. H).

2-(Diphenylphosphonooxy)ethyl 2-Deoxy-3-*O*-(*N*-dodecanoylglycyl)-2-tetradecanoylamino-α-D-glucopyranoside (33c) A solution of **32c** (0.63 g, 0.67 mmol) in 90% AcOH (20 ml) was heated at 90 °C for 30 min. After evaporation of the solvent, the residue was purified by silica gel column chromatography ($CHCl_3$–acetone, 10:1) to give **33c** (0.45 g, 73%) as an oil, $[\alpha]_D$ +46.8° (c=0.9, $CHCl_3$). NMR δ: 0.88 (6H, t, J=6 Hz), 1.2—1.8 (40H, br, CH_2), 2.08 (2H, t), 2.27 (2H, t), 3.7—4.0 (8H, m), 4.05—4.50 (4H, m), 4.83 (1H, d, J=4 Hz, H-1), 5.18 (1H, m, H-3), 6.43 (1H, m, NH), 6.85 (1H, m, NH), 7.2—7.5 (10H, m, arom. H). MS m/z: 906 $[(M+2)^+]$.

2-(Diphenylphosphonooxy)ethyl 2-Deoxy-2-(*N*-dodecanoylglycylamino)-3-*O*-tetradecanoyl-α-D-glucopyranoside (33e) As described for **33c**, compound **32e** (0.46 g, 0.48 mmol) was treated with 90% AcOH (20 ml) to give **33e** (0.39 g, 90%) as a waxy solid, $[\alpha]_D$ +36.1° (c=1.1, $CHCl_3$). NMR δ: 0.90 (6H, t, J=6 Hz), 1.28 (36H, s, CH_2), 1.63 (4H, br, $CH_2CH_2CO \times 2$), 2.13 (2H, m, CH_2CO), 2.36 (2H, t, J=8 Hz, CH_2CO), 4.90 (1H, d, J=4 Hz, H-1), 5.10 (1H, m, H-3), 6.74 (1H, br, NH), 6.96 (1H, d, J=9 Hz, NH), 7.2—7.5 (10H, m, arom. H). MS m/z: 906 $[(M+2)^+]$.

2-(Diphenylphosphonooxy)ethyl 2-Deoxy-3-*O*-(*N*-dodecanoylglycyl)-2-(*N*-dodecanoylglycylamino)-α-D-glucopyranoside (33d) Compound **30** (0.60 g, 0.89 mmol) was treated with zinc powder (0.6 g) in AcOH (10 ml). After stirring for 1 h, the mixture was filtered off, and the filtrate was concentrated *in vacuo* to give an oil, which was then allowed to react with **10** (0.69 g, 2.67 mmol). The resulting oil was treated with 90% AcOH, in the same manner as described for **33f**, to give **33d** as a colorless oil (0.57 g, 93%), $[\alpha]_D$ +16.6° (c=0.8, $CHCl_3$). NMR δ: 0.90 (6H, t, J=6 Hz), 1.28 (32H, s, CH_2), 1.60 (4H, br, $CH_2CH_2CO \times 2$), 2.0—2.3 (4H, m, $CH_2CO \times 2$), 4.85 (1H, d, J=4 Hz, H-1), 5.24 (1H, t, J=10 Hz, H-3), 6.88 (1H, d, J=10 Hz, NH), 7.2—7.5 (12H, m, arom. H and NH × 2). MS m/z: 934 $[(M+H)^+]$.

Benzyloxycarbonylmethyl 2-Deoxy-6-*O*-[2-deoxy-4-*O*-diphenylphosphono-3-*O*-tetradecanoyl-6-*O*-(2,2,2-trichloroethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-3-*O*-tetradecanoyl-2-tetradecanoylamino-α-D-glucopyranoside (34a) Compounds **17** (515 mg, 0.51 mmol) and **33a** (380 mg, 0.51 mmol) were dissolved in CH_2Cl_2 (8 ml), and mercuric cyanide (253 mg, 1.0 mmol) and $CaSO_4$ (600 mg) were added to the mixture, which was then refluxed for 16 h. After the reaction mixture was diluted with $CHCl_3$, the mixture was filtered through Cerite 545, and the filtrate was washed with 5% aqueous potassium iodide and saturated aqueous NaCl, then dried. After evaporation of the solvent, the residue was purified by silica gel column chromatography ($CHCl_3$–acetone, 9:1) to give **34a** (717 mg, 83%) as a colorless oil, $[\alpha]_D$ +18.7° (c=1.1, $CHCl_3$). NMR δ: 0.89 (9H, t, J=6 Hz), 1.28 (60H, s, CH_2), 1.60 (6H, br, $CH_2CH_2O \times 3$), 2.16 (4H, m, $CH_2CO \times 2$), 2.36 (2H, t, J=8 Hz, CH_2CO), 4.64—4.86 (4H, m, $CH_2CCl_3 \times 2$), 5.13 (1H, t, J=10 Hz, H-3), 5.24 (2H, s, $CH_2C_6H_5$), 5.56 (1H, t, J=10 Hz, H-3'), 7.2—7.4 (15H, m, arom. H). MS m/z: 1698 (M^+), 1703 $[(M+5)^+]$.

1,3-Di(benzyloxycarbonyl)isopropyl 2-Deoxy-6-*O*-[2-deoxy-4-*O*-diphenylphosphono-3-*O*-tetradecanoyl-6-*O*-(2,2,2-trichloroethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-3-*O*-tetradecanoyl-2-tetradecanoylamino-α-D-glucopyranoside (34b) Similarly to the preparation of **34a**, compound **17** (500 mg, 0.49 mmol) was treated with **33b** (450 mg, 0.49 mmol) in CH_2Cl_2 (4 ml) in the presence of $CaSO_4$ (0.6 g) and mercuric cyanide (250 mg, 1.0 mmol) to give **34b** (790 mg, 86%) as a colorless oil, $[\alpha]_D$ +14.0° (c=0.8, $CHCl_3$). *Anal.* Calcd for $C_{91}H_{131}Cl_6N_2O_{23}P$: C, 58.61; H, 7.08; N, 1.50. Found: C, 58.54; H, 7.08; N, 1.47. NMR δ: 0.88 (9H, t, J=6 Hz), 1.26 (60H, s, CH_2), 4.70 (4H, m, $CH_2CCl_3 \times 2$), 5.18 (4H, d, $CH_2C_6H_5 \times 2$), 7.16—7.46 (20H, m, arom. H). MS m/z: 1860 (M^+), 1864 $[(M+4)^+]$.

2-(Diphenylphosphonooxy)ethyl 2-Deoxy-6-*O*-[2-deoxy-4-*O*-diphenylphosphono-3-*O*-(*N*-dodecanoylglycyl)-6-*O*-(2,2,2-trichloroethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-3-*O*-(*N*-dodecanoylglycyl)-2-tetradecanoylamino-α-D-glucopyranoside (34c) HBr-AcOH (25%, 16 ml) was added to a solution of **15** (2.54 g, 2.43 mmol) in CH_2Cl_2 (18 ml), and the mixture was stirred for 3 h. The reaction mixture was diluted with $CHCl_3$ and the solution was washed with ice-H_2O, 5% aqueous $NaHCO_3$ and saturated aqueous NaCl, and dried. After evaporation of the solvent, the residue (**16**) and **33c** (2.51 g, 2.77 mmol) were dissolved in CH_2Cl_2 (18 ml), then $CaSO_4$ (3.0 g) and mercuric cyanide (1.23 g, 4.86 mmol) were added to the solution. After being refluxed for 2.5 h, the reaction mixture was filtered through Celite 545, and the filtrate was washed with 5% aqueous potassium iodide and saturated aqueous NaCl, dried, and concentrated. The residue was purified by silica gel chromatography ($CHCl_3$–MeOH, 19:1) to give **34c** (4.06 g, 88%) as a colorless oil, $[\alpha]_D$ +24.0° (c=1.0, $CHCl_3$). NMR δ: 0.89 (9H, t, J=7 Hz), 1.26 (52H, s, CH_2), 1.60 (6H, br, $CH_2CH_2CO \times 3$), 2.10 (4H, m, $CH_2CO \times 2$), 2.27 (2H, t, J=8 Hz, CH_2CO), 5.00 (1H, d, J=8 Hz, H-1'), 5.11 (1H, t, J=10 Hz, H-3), 5.79 (1H, t, J=10 Hz, H-3'), 7.1—7.5 (20H, m, arom. H). MS m/z: 1884 (M^+), 1889 $[(M+5)^+]$.

2-(Diphenylphosphonooxy)ethyl 2-Deoxy-6-*O*-[2-deoxy-4-*O*-diphenylphosphono-3-*O*-(*N*-dodecanoylglycyl)-6-*O*-(2,2,2-trichloroethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-3-*O*-(*N*-dodecanoylglycyl)-2-(*N*-dodecanoylglycylamino)-α-D-glucopyranoside (34d) Compound **16**, obtained from **15** (0.28 g, 0.27 mmol) was allowed to react with **33d** (0.23 g, 0.24 mmol) in the presence of mercuric cyanide (0.14 g, 0.54 mmol), as described for **34c**, to give **34d** (0.41 g, 88%) as a colorless viscous oil, $[\alpha]_D$ +11.9° (c=1.0, $CHCl_3$). NMR δ: 0.90 (9H, t, J=6 Hz), 1.28 (48H, s, CH_2), 1.60 (6H, br, $CH_2CH_2CO \times 3$), 2.0—2.3 (6H, m, $CH_2CO \times 2$), 4.96 (1H, d, J=8 Hz, H-1'), 5.19 (1H, t, J=10 Hz, H-3), 5.58 (1H, t, J=10 Hz, H-3'), 6.1, 6.2, and 6.8 (each 1H, br, NH), 7.1—7.5 (22H, m, arom. H and NH). MS m/z: 1913 (M^+), 1916 $[(M+3)^+]$.

2-(Diphenylphosphonooxy)ethyl 2-Deoxy-6-*O*-[2-deoxy-4-*O*-diphenylphosphono-3-*O*-tetradecanoyl-6-*O*-(2,2,2-trichloroethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-3-*O*-tetradecanoyl-2-(*N*-dodecanoylglycylamino)-α-D-glucopyranoside (34e) Compound **17** was allowed to react with **33e** (0.32 g, 0.35 mmol) in the presence of mercuric cyanide (0.20 g, 0.78 mmol), as described for **34a**, to give **34e** (0.59 g, 90%) as a colorless viscous oil, $[\alpha]_D$ +14.8° (c=1.0, $CHCl_3$). NMR δ: 0.89 (9H, t, J=7 Hz), 1.28 (56H, s, CH_2), 1.60 (6H, br, $CH_2CH_2CO \times 3$), 2.14 (4H, m, $CH_2CO \times 2$), 2.35 (2H, t, J=8 Hz, CH_2CO), 5.04 (1H, d, J=10 Hz, H-3), 5.56 (2H, m, H-3' and NH), 6.66 and 6.84 (each 1H, br, NH), 7.1—7.5 (20H, m, arom. H). MS m/z: 1855 (M^+), 1859 $[(M+4)^+]$.

1,3-Di(benzyloxycarbonyl)isopropyl 2-Deoxy-6-*O*-[2-deoxy-4-*O*-diphenylphosphono-3-*O*-(*N*-dodecanoylglycyl)-6-*O*-(2,2,2-trichloroethoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-3-*O*-(*N*-dodecanoylglycyl)-2-tetradecanoylamino-α-D-glucopyranoside (34f) As described for **34c**, compound **16** obtained from **15** (416 mg, 0.40 mmol), was treated with **33f** (376 mg, 0.40 mmol) to give **34f** (531 mg, 69%) as a colorless viscous oil, $[\alpha]_D$ +19.4° (c=1.1, $CHCl_3$). NMR (500 MHz) δ: 0.88 (9H, t, J=7.3 Hz, CH_3), 1.25 (52H, s, CH_2), 1.54 (2H, m, CH_2CH_2CO), 1.63 (2H, m, CH_2CH_2CO), 2.07 (2H, t, J=7.3 Hz, CH_2CO), 2.25 (2H, m, CH_2CO), 2.26 (2H, t, J=7.3 Hz, CH_2CO), 2.64—2.74 (3H, m, $OCH(CH_2CO_2Bzl)_2 \times 3$), 2.99 (1H, m, $OCH(CH_2CO_2Bzl)_2$), 3.29 (1H, m), 3.49 (1H, m), 3.62 (1H, m), 3.78—3.91 (m), 4.09 (1H, dd, J=17.4, 5.5 Hz), 4.17 (3H, m), 4.33 (1H, dd, J=11.9, 4.6 Hz), 4.46—4.56 (m), 4.68 (2H, m), 4.80 (1H, m), 4.89 (1H, d, J=3.4 Hz, H-1), 4.99 (2H, m), 5.09—5.18 (5H, m), 5.74 (1H, t, J=9.2 Hz, H-3'), 6.06 (1H, d, J=7.3 Hz, NH), 6.17 (1H, m, NH), 6.36 (1H, m, NH), 6.54 (1H, d, J=9.2 Hz, NH), 7.10—7.37 (20H, m, arom. H). MS m/z: 1918 (M^+), 1923 $[(M+5)^+]$.

Benzyloxycarbonylmethyl 2-Deoxy-6-*O*-(2-deoxy-4-*O*-diphenylphosphono-3-*O*-tetradecanoyl-2-tetradecanoylamino-β-D-glucopyranosyl)-3-*O*-tetradecanoyl-2-tetradecanoylamino-α-D-glucopyranoside (35a) Zinc powder (0.7 g) was added to a solution of **34a** (700 mg, 0.41 mmol), and the mixture was vigorously stirred for 1 h at room temperature. The insoluble materials were removed by filtration, and the filtrate was concentrated *in vacuo*. The residue was dissolved in benzene, and washed with 5% $NaHCO_3$ aqueous solution, and then with saturated aqueous NaCl, and dried. Evaporation of the solvent gave an oil.

Separately, DCC (134 mg, 0.65 mmol) was added to a solution of tetradecanoic acid (142 mg, 0.62 mmol) and HOBt (99 mg, 0.65 mmol) in THF (3 ml) with ice-cooling. The mixture was stirred for 3 h at room temperature, and the precipitate was filtered off to give an active ester solution. This solution was added to a solution of the above oil in CH_2Cl_2 (5 ml), then *N*-methylmorpholine (71 μl, 0.65 mmol) was added to the mixture with ice cooling, and the final mixture was stirred for 18 h at room temperature. After evaporation of the solvent, the residue was purified by silica gel column chromatography ($CHCl_3$–MeOH, 50:1) to give **35a** (400 mg, 62%) as a colorless oil, $[\alpha]_D$ +8.5° (c=0.9, $CHCl_3$). NMR δ: 0.90 (12H, t, J=6 Hz), 1.26 (80H, s, CH_2), 1.58 (8H, br,

$C\underline{H}_2CH_2CO\times4$), 2.1—2.4 (8H, m, $CH_2CO\times4$), 4.75 (1H, m, H-4'), 4.84 (1H, d, J=4 Hz, H-1), 4.96 (1H, d, J=8 Hz, H-1'), 5.16 (1H, t, J=10 Hz, H-3), 5.22 (2H, s, $C\underline{H}_2C_6H_5$), 5.51 (1H, t, J=10 Hz, H-3'), 7.2—7.4 (15H, m, arom. H). MS m/z: 1562 [$(M+2)^+$].

1,3-Di(benzyloxycarbonyl)isopropyl 2-Deoxy-6-*O*-(2-deoxy-4-*O*-diphenylphosphono-3-*O*-tetradecanoyl-2-tetradecanoylamino-β-D-glucopyranosyl)-3-*O*-tetradecanoyl-2-tetradecanoylamino-α-D-glucopyranoside (35b) As described for **35a**, compound **34b** (780 mg, 0.42 mmol) was treated with zinc powder (1.2 g), and the resulting oil was allowed to react with the HOBt ester of tetradecanoic acid (140 mg, 0.63 mmol) to give **35b** (550 mg, 76%) as a white powder, mp 78—80 °C, $[\alpha]_D$ +4.4° (c=1.3, $CHCl_3$). *Anal.* Calcd for $C_{99}H_{155}N_2O_{20}P$: C, 68.96; H, 9.06; N, 1.62. Found: C, 68.72; H, 8.95; N, 1.63. NMR δ: 0.90 (12H, t, J=6 Hz), 1.26 (80H, s, CH_2), 2.1—2.4 (8H, m, $CH_2CO\times4$), 2.64—2.98 (4H, m, $OCH(CH_2CO_2Bzl)_2$), 4.75 (1H, m, H-4'), 4.94 (1H, d, J=4 Hz, H-1), 5.00 (1H, d, J=8 Hz, H-1'), 5.16 (4H, s, $C\underline{H}_2C_6H_5\times2$), 5.58 (1H, t, J=10 Hz, H-3').

2-(Diphenylphosphonooxy)ethyl 2-Deoxy-6-*O*-[2-deoxy-4-*O*-diphenylphosphono-3-*O*-(*N*-dodecanoylglycyl)-2-tetradecanoylamino-β-D-glucopyranosyl]-3-*O*-(*N*-dodecanoylglycyl)-2-tetradecanoylamino-α-D-glucopyranoside (35c) As described for **35a**, compound **34c** (4.06 g, 2.15 mmol) was treated with zinc powder, and the resulting oil was allowed to react with the HOBt ester of tetradecanoic acid (0.74 g, 3.23 mmol) in THF (15 ml) to give **34c** (3.30 g, 88%) as a colorless oil, $[\alpha]_D$ +20.9° (c=1.1, $CHCl_3$). NMR δ: 0.88 (12H, t, J=6 Hz), 1.28 (76H, s, CH_2), 1.60 (8H, br, $C\underline{H}_2CH_2CO\times4$), 2.0—2.4 (8H, m, $CH_2CON\times4$), 4.70 (1H, q, J=10 Hz, H-4'), 4.90 (1H, d, J=4 Hz, H-1), 5.16 (1H, t, J=10 Hz, H-3, 5.28 (1H, d, J=8 Hz, H-1), 5.66 (1H, t, J=10 Hz, H-3'), 7.2—7.4 (20H, m, arom. H).

2-(Diphenylphosphonooxy)ethyl 2-Deoxy-6-*O*-[2-deoxy-4-*O*-diphenylphosphono-3-*O*-(*N*-dodecanoylglycyl)-2-(*N*-dodecanoylglycylamino)-β-D-glucopyranosyl]-3-*O*-(*N*-dodecanoylglycyl)-2-(*N*-dodecanoylglycylamino)-α-D-glucopyranoside (35d) As in the preparation of **35a**, compound **34d** (0.39 g, 0.20 mmol) was treated with zinc powder, and the resulting oil was allowed to react with the HOBt ester of **10** (0.10 g, 0.40 mmol) to give **34d** (0.20 g, 54%) as a colorless oil, $[\alpha]_D$ +16.7° (c=1.0, $CHCl_3$). NMR δ: 0.9 (12H, t, J=6 Hz), 1.28 (64H, s, CH_2), 1.64 (8H, br, $C\underline{H}_2CH_2CO\times4$), 2.0—2.3 (8H, m, $CH_2CO\times4$), 4.74 (1H, m, H-4'), 4.84 (1H, d, J=4 Hz, H-1), 5.01 (1H, d, J=8 Hz, H-1'), 5.21 (1H, m, H-3), 5.60 (1H, t, J=10 Hz, H-3'), 7.2—7.5 (m, arom. H and NH). MS m/z: 1806 [$(M+2)^+$].

2-(Diphenylphosphonooxy)ethyl 2-Deoxy-6-*O*-[2-deoxy-4-*O*-diphenylphosphono-2-(*N*-dodecanoylglycylamino)-3-*O*-tetradecanoyl-β-D-glucopyranosyl]-2-(*N*-dodecanoylglycylamino)-3-*O*-tetradecanoyl-α-D-glucopyranoside (35e) As described for **35a**, compound **34e** (0.58 g, 0.31 mmol) was treated with zinc powder, and the oily product was reacted with the HOBt ester of **10** to give **35e** (0.49 g, 89%) as a colorless oil, $[\alpha]_D$ +16.4° (c=1.0, $CHCl_3$). NMR δ: 0.90 (12H, t, J=7 Hz), 1.26 (72H, s, CH_2), 2.1—2.3 (8H, m, $CH_2CO\times4$), 4.73 (1H, m, H-4'), 4.88 (1H, d, J=4 Hz, H-1), 4.93 (1H, d, J=8 Hz, H-1'), 5.41 (1H, m, H-3), 5.65 (1H, t, J=10 Hz, H-3'), 6.42 (1H, br, NH), 6.66 (2H, m, NH×2), 6.88 (1H, d, J=9 Hz, NH), 7.2—7.5 (20H, m, arom. H). MS m/z: 1748 [$(M+2)^+$].

1,3-Di(benzyloxycarbonyl)isopropyl 2-Deoxy-6-*O*-[2-deoxy-3-*O*-(*N*-dodecanoylglycyl)-2-tetradecanoylamino-4-*O*-diphenylphosphono-β-D-glucopyranosyl]-3-*O*-(*N*-dodecanoylglycyl)-2-tetradecanoylamino-α-D-glucopyranoside (35f) As described for **35a**, compound **34f** (509 mg, 0.26 mmol) was treated with zinc dust, and the resulting oil was allowed to react with the HOBt ester to tetradecanoic acid (91 mg, 0.40 mmol) to give **35f** (376 mg, 80%) as a colorless powder, mp 135—139 °C, $[\alpha]_D$ +18.8° (c=0.5, $CHCl_3$). *Anal.* Calcd for $C_{99}H_{153}N_4O_{22}P$: C, 66.62; H, 8.65; N, 3.14. Found: C, 66.81; H, 8.54; N, 3.11. NMR (500 MHz) δ: 0.89 (12H, t, J=7.3 Hz), 1.25 (72H, s, CH_2), 1.54 (2H, m, $C\underline{H}_2CH_2CO$), 1.63 (2H, m, $C\underline{H}_2CH_2CO$), 2.12 (4H, m, $CH_2CO\times2$), 2.24 (2H, t, J=7.3 Hz, CH_2CO), 2.62 (1H, dd, J=16.5, 7.3 Hz, $OCH(C\underline{H}_2CO_2Bzl)_2$), 2.67 (2H, d, J=6.4 Hz, $OCH(C\underline{H}_2CO_2Bzl)_2\times2$), 2.90 (1H, dd, J=16.5, 4.6 Hz, $OCH(C\underline{H}_2CO_2Bzl)_2$), 3.28 (1H, m), 3.56—3.67 (4H, m), 3.74—3.90 (5H, m), 4.07 (2H, m), 4.36 (1H, m), 4.66 (1H, m, $OC\underline{H}(CH_2CO_2Bzl)_2$), 4.67 (1H, q, J=9.2 Hz, H-4'), 4.90 (1H, d, J=3.7 Hz, H-1), 5.03 (1H, t, J=10.1 Hz, H-3), 5.12 (4H, m, $C\underline{H}_2C_6H_5\times2$), 5.31 (1H, d, J=8.3 Hz, H-1'), 5.67 (1H, t, J=10.1 Hz, H-3'), 6.26 (1H, t, J=5.5 Hz, NH), 6.29 (1H, t, J=5.5 Hz, NH), 6.37 (1H, d, J=6.4 Hz, NH), 6.50 (1H, d, J=9.2 Hz, NH), 7.14—7.36 (20H, m, arom. H). MS m/z: 1782 [$(M+2)^+$].

Carboxymethyl 2-Deoxy-6-*O*-(2-deoxy-4-*O*-phosphono-3-*O*-tetradecanoyl-2-tetradecanoylamino-β-D-glucopyranosyl)-3-*O*-tetradecanoyl-2-tetradecanoylamino-α-D-glucopyranoside (4) Compound **35a** (379 mg, 0.24 mmol) was dissolved in THF (30 ml) and shaken with 5% palladium–carbon (400 mg) at room temperature for 1 h in H_2 at atmospheric pressure. Then, platinum dioxide (200 mg) was added to the mixture, and the mixture was further shaken at room temperature for 1.1 h in H_2 at atmospheric pressure. The catalyst was removed by filtration and washed with $CHCl_3$–MeOH–H_2O (8:3:1, lower layer). The combined filtrate washings were concentrated at reduced pressure. The residue was purified by preparative TLC ($CHCl_3$–MeOH–H_2O, 6:4:0.2). After extraction with $CHCl_3$–MeOH–H_2O–Et_3N (6:4:1:0.02), the solvent was evaporated *in vacuo*. The residue was dissolved in $CHCl_3$–MeOH–H_2O (6:4:0.5), and the solution was desalted with Dowex 50 (H^+ type). A portion of the desalted solution was concentrated, and the residue was lyophilized from a dioxane suspension to give **4** (249 mg, 78%) as a white powder, mp 145—148 °C (dec.), $[\alpha]_D$ +14.2° (c=0.5, $CHCl_3$–MeOH, 3:1). IR (KBr): 3450, 2925, 2855, 1740, 1640 cm^{-1}. NMR ($CDCl_3$–CD_3OD) δ: 0.90 (12H, t, J=6 Hz), 1.28 (80H, s, CH_2), 1.56 (8H, br, $C\underline{H}_2CH_2CO\times4$), 2.1—2.4 (8H, m, $CH_2CO\times4$), 4.80 (1H, d, J=4 Hz, H-1), 5.24 (2H, m, H-3, H-3').

The product (220 mg) in 0.1% aqueous Et_3N was lyophilized to give 250 mg of Et_3N salt as a white powder.

1,3-Dicarboxyisopropyl 2-Deoxy-6-*O*-(2-deoxy-4-*O*-phosphono-3-*O*-tetradecanoyl-2-tetradecanylamino-β-D-glucopyranosyl)-3-*O*-tetradecanoyl-2-tetradecanoylamino-α-D-glucopyranoside (5) In a manner similar to that described for **4**, compound **35b** (280 mg, 0.20 mmol) was hydrogenolyzed with palladium-black (200 mg) in dioxane (30 ml) for 2.5 h, and then with platinum dioxide (300 mg) for 18 h to give **5** (173 mg, 77%) as a white powder, mp 142—147 °C (dec.), $[\alpha]_D$ +11.7° (c=0.7, $CHCl_3$–MeOH, 3:1). NMR δ: 0.90 (12H, t, J=6 Hz), 1.30 (80H, s, CH_2), 2.20 (m), 2.36 (m), 2.70 (m), 4.98 (1H, d, H-1).

The Et_3N salt was prepared similarly to that of **4**.

2-Phosphonooxyethyl 2-Deoxy-6-*O*-[2-deoxy-3-*O*-(*N*-dodecanoylglycyl)-4-*O*-phosphono-2-tetradecanoylamino-β-D-glucopyranosyl]-3-*O*-(*N*-dodecanoylglycyl)-2-tetradecanoylamino-α-D-glucopyranoside (6) Platinum dioxide (0.40 g) was added to a solution of **35c** (0.42 g, 0.24 mmol) in THF (80 ml). The mixture was stirred in a hydrogen atmosphere for 25 h, then a mixture of $CHCl_3$–MeOH–H_2O (8:3:1, lower layer) was added. After the catalysts had been filtered off, the filtrate was concentrated, and the resulting residue was purified by preparative TLC ($CHCl_3$–MeOH–H_2O, 6:4:0.8). The extracted solution with $CHCl_3$–MeOH–H_2O–Et_3N (6:4:1:0.02) was concentrated by evaporation. After dissolution in $CHCl_3$–MeOH–H_2O (8:3:1, lower layer), the solution was desalted with Dowex 50 (H^+). The desalting solution was concentrated and the dioxane suspension was freeze-dried to give **4** (95 mg, 27%) as a white powder, mp 140—145 °C (dec.), $[\alpha]_D$ +13.3° (c=0.6, $CHCl_3$–MeOH, 3:1). IR (KBr): 3400, 2930, 2855, 1750, 1660, 1560 cm^{-1}. NMR ($CDCl_3$–CD_3OD, 1:1) δ: 0.90 (12H, t, J=7 Hz), 1.32 (72H, s, CH_2), 1.60 (8H, br, $C\underline{H}_2CH_2CO\times4$), 2.1—2.3 (8H, m, $CH_2CO\times4$), 5.10 (1H, t, J=10 Hz, H-3), 5.38 (1H, t, J=10 Hz, H-3').

The Et_3N salt was prepared in a manner similar to that described for **4**.

2-Phosphonooxyethyl 2-Deoxy-6-[2-deoxy-3-*O*-(*N*-dodecanoylglycyl)-2-(*N*-dodecanoylglycylamino)-4-*O*-phosphono-β-D-glucopyranosyl]-3-*O*-(*N*-dodecanoylglycyl)-2-(*N*-dodecanoylglycylamino)-α-D-glucopyranoside (7) As described for **6**, compound **35d** (0.42 g, 0.23 mmol) was hydrogenolyzed in the presence of platinum dioxide, and the resulting powder was purified by preparative TLC ($CHCl_3$–MeOH–H_2O, 6:4:0.9) and desalted. The desalting solution was concentrated and the dioxane suspension was freeze-dried to give **7** (0.14 g, 39%) as a white powder, mp 145—150 °C (dec.), $[\alpha]_D$ +7.6° (c=0.8, $CHCl_3$–MeOH, 3:1). IR (KBr): 3300, 1760, 1665, 1555 cm^{-1}. NMR ($CDCl_3$–CD_3OD, 1:1) δ: 0.90 (12H, t, J=6 Hz), 1.30 (64H, s, CH_2), 1.66 (8H, br, $C\underline{H}_2CH_2CO\times4$), 2.30 (8H, m, $CH_2CO\times4$), 4.84 (1H, d, J=4 Hz, H-1), 5.19 (1H, t, J=10 Hz, H-3), 5.33 (1H, t, J=10 Hz, H-3').

The Et_3N salt was prepared similarly to that of **4**.

2-Phosphonooxyethyl 2-Deoxy-6-*O*-[2-deoxy-2-(*N*-dodecanoylglycylamino)-4-*O*-phosphono-3-*O*-tetradecanoyl-β-D-glucopyranosyl]-2-(*N*-dodecanoylglycylamino)-3-*O*-tetradecanoyl-α-D-glucopyranoside (8) In the manner described for **6**, compound **35e** (0.46 g, 0.26 mmol) was hydrogenolyzed in the presence of platinum dioxide, and the resulting powder was purified by preparative TLC ($CHCl_3$–MeOH–H_2O, 6:4:0.8) and desalted. The desalting solution was concentrated, and the dioxane suspension was freeze-dried to give **8** (0.22 g, 59%) as a white powder, mp 148—153 °C (dec.), $[\alpha]_D$ +18.4° (c=0.9, $CHCl_3$–MeOH, 3:1). IR (KBr): 3300, 1745, 1645, 1555 cm^{-1}. NMR ($CDCl_3$–CD_3OD, 1:1) δ: 0.90 (12H, t, J=6 Hz), 1.30 (72H, s, CH_2), 1.6 (8H, br, $C\underline{H}_2CH_2CO\times4$), 2.3 (8H, m, $CH_2CO\times4$), 4.86 (1H, d, J=4 Hz, H-1), 5.16 (1H, t,

$J=10$ Hz, H-3), 5.34 (1H, t, $J=10$ Hz, H-3').

The Et_3N salt was prepared in a manner similar to that for **4**.

1,3-Dicarboxyisopropyl 2-Deoxy-6-*O*-[2-deoxy-3-*O*-(*N*-dodecanoylglycyl)-4-*O*-phosphono-2-tetradecanoylamino-β-D-glucopyranosyl]-3-*O*-(*N*-dodecanoylglycyl)-2-tetradecanoylamino-α-D-glucopyranoside (9) In a manner similar to that described for **4**, compound **35f** (361 mg, 0.20 mmol) was hydrogenolyzed with 5% palladium-carbon (400 mg) in 5% aqueous THF (32 ml) for 6 h, and then with platinum dioxide for 3 h. The resulting residue was purified by preparative TLC ($CHCl_3$–MeOH–H_2O, 6:4:0.5), then desalted with Dowex 50 (H^+ type). A portion of the desalted solution was concentrated, and the residue was lyophilized from dioxane suspension to give **9** (116 mg, 39%) as a white powder, mp 158—165 °C (dec.), $[\alpha]_D$ +18.6° ($c=0.6$, $CHCl_3$–MeOH, 3:1). *Anal.* Calcd for $C_{73}H_{133}N_4O_{22}P\cdot 0.5H_2O$: C, 60.10; H, 9.26; N, 3.84. Found: C, 60.11; H, 9.55; N, 3.87. IR (KBr): 3448, 2924, 2856, 1748, 1646, 1550, 1470 cm^{-1}. NMR (500 MHz, $CDCl_3$–CD_3OD, 1:1) δ: 0.88 (12H, t, $J=7.3$ Hz), 1.26 (72H, s, CH_2), 1.56 (4H, m, $C\underline{H}_2CH_2CO\times 2$), 1.63 (4H, m, $C\underline{H}_2CH_2CO\times 2$), 2.16 (2H, t, $J=7.1$ Hz, CH_2CO), 2.21 (2H, t, $J=7.1$ Hz, CH_2CO), 2.26 (4H, t, $J=7.1$ Hz, $CH_2CO\times 2$), 2.67 (3H, m, $OCH(C\underline{H}_2CO_2H)_2\times 3$), 2.83 (1H, dd, $J=16.5$, 5.5 Hz, $OCH(C\underline{H}_2CO_2H)_2$), 3.52 (2H, m, H-4 and H-5'), 3.70 (1H, t, $J=9.5$ Hz, H-2'), 3.77 (1H, dd, $J=11.2$, 5.6 Hz, H-6), 3.84 (1H, dd, $J=12.7$, 4.8 Hz, $COCH_2N$), 3.9—4.0 (7H, m, $COCH_2N\times 3$, H-5, H-6 and H-6'$\times 2$), 4.12 (1H, m, H-2), 4.30 (1H, q, $J=9.5$ Hz, H-4'), 4.40 (1H, m, $OC\underline{H}(CH_2CO_2H)_2$), 4.84 (1H, d, $J=7.9$ Hz, H-1'), 4.95 (1H, d, $J=4.0$ Hz, H-1), 5.05 (1H, t, $J=9.5$ Hz, H-3), 5.40 (1H, t, $J=9.5$ Hz, H-3').

The Et_3N salt was prepared similarly to that of **4**.

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