Lipid A and Related Compounds. XXXVII.[1] Determination of Favorable Binding Linkages of Lipid A Analog to Antigen Moiety for Synthetic Vaccines

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For the determination of favorable binding linkages of lipid A analog as a synthetic immunoadjuvant to the antigen moiety for synthetic vaccines, new *N*-acylated L-serine-containing D-glucosamine analogs (Type A, B, C) were synthesized and their mitogenicities were examined. Among chemically synthesized compounds (6—15, 30), compound 8 for Type B exhibited the most potent mitogenicity.

Key words lipid A analog; mitogenic activity; immunoadjuvant; synthetic vaccine

Lipid A is responsible for the expression of many biological activities of the lipopolysaccharide (LPS) of gram-negative bacteria, *e.g.* endotoxicity, adjuvanticity, antitumor activity and so on.[2] Many compounds related to lipid A partial structures have been synthesized with the aim of enhancing biological activities.[3] In a series of structure–activity relationship studies on lipid A, we have already reported the synthesis and biological activities of *N*-acylated L-serine,[4a,b] L-threonine[4c] and L-homoserine[4d]-containing D-glucosamine derivatives structurally similar to the lipid A disaccharide backbone. As a result, it was found that the mitogenic activity of *N*-tetradecanoyl L-serine-linked lipid A analog (**2**) is stronger than that of L-threonine and L-homoserine linked lipid A analogs and the phosphate group was not required in lipid A analogs for mitogenicity.

Recently, the development of totally synthetic vaccines against cancers or human immunodeficiency virus (HIV) using a synthetic immunoadjuvant, such as *N*-acetylmuramyl-L-alanyl-D-isoglutamine (MDP) and lipopeptide analogs, have been attempted.[5] We plan to develop completely synthetic vaccines which consist of a lipid A analog, covalently coupled to a low-molecular-weight antigen. With the aim of determining favorable binding linkages of lipid A analog (**3**, **5**) to an antigen moiety, we designed new non-reducing *N*-acylated L-serine-containing D-glucosamine derivatives (Type A, B, C) (Fig. 2). In this paper, we describe the synthesis and mitogenic activity of new *N*-acylated L-serine-containing D-glucosamine analogs (**6**—**15**, **30**) in comparison with that of synthetic phosphorylated lipid A analog (**1**)[6] and bacterial LPS.

Synthesis First, we planned to introduce Boc-L-glycine as a spacer to the nitrogen group of the L-serine residue for **6** or **7** as Type A. Compounds **6** and **7** were synthesized from compound **16** as a starting material according to the routes shown in Charts 1 and 2, respectively. Glycosidation of **16** with **17** using *N*-bromosuccinimide (NBS), I_2, *n*-tetrabutylammonium trifluoromethanesulfonate (TBAOTf) as a promoter, and molecular sieves 4A° in CH_2Cl_2 gave the β-glycoside (**18**) in 49% yield. The β-configuration of **18** was confirmed by NMR spectroscopy; the ^{13}C-NMR showed the C-1 signal as a doublet at δ 102.5 (J=160.6 Hz).[7] Removal of the 2,2,2-trichloroethoxycarbonyl (Troc) group of **18** with activated Zn powder in acetic acid (AcOH), followed by acylation using (*R*)-3-(tetradecanoyloxy)tetradecanoic acid ($C_{14}OC_{14}OH$) in the presence of diethyl phosphorocyanidate (DEPC) and triethylamine (NEt_3) in CH_2Cl_2 afforded **19** in 81% yield in two steps. Finally, hydrogenolysis of the benzyl group using Pd-black as a catalyst in tetrahydrofuran (THF) gave the desired product **6** in 67% yield [FAB-MS *m/z*: 987 $(M+H)^+$, 1009 $(M+Na)^+$].

Synthesis of compound **7** was carried out as follows. Glycosidation of **20** with **17** in the presence of $HgBr_2$ and molecular sieves 4A° in CH_2Cl_2 gave β-glycoside (**21**) in 61% yield. The β-configuration of **21** was confirmed by NMR spectroscopy; the ^{1}H-NMR showed the H-1 signal as a doublet at δ 4.32 (J=8.9 Hz). In the same way, after removal of the Troc group of **21** with activated Zn powder in AcOH, subsequent *N*-acylation with $C_{14}OC_{14}OH$ in the presence of dicyclohexylcarbodiimide (DCC) in CH_2Cl_2 afforded **22** in 22% yield in two steps. Acylation of the remaining hydroxyl group of **22** with tetradecanoic acid ($C_{14}OH$) in the presence of DCC–*N*,*N*-dimethylaminopyridine (DMAP) in CH_2Cl_2

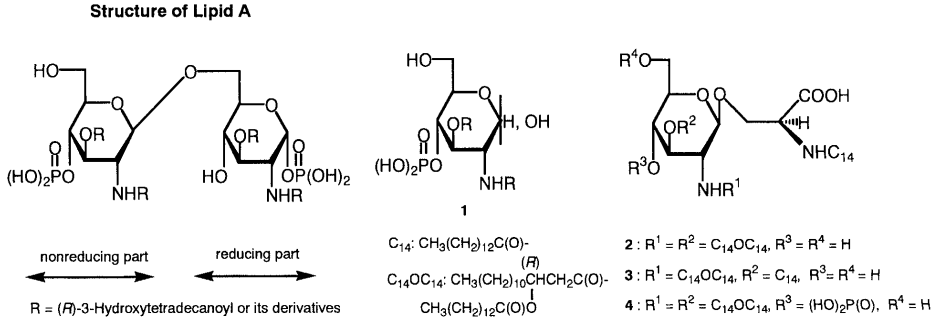

Fig. 1

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Determination of Binding Linkages of Lipid A Analog to Antigen Moiety

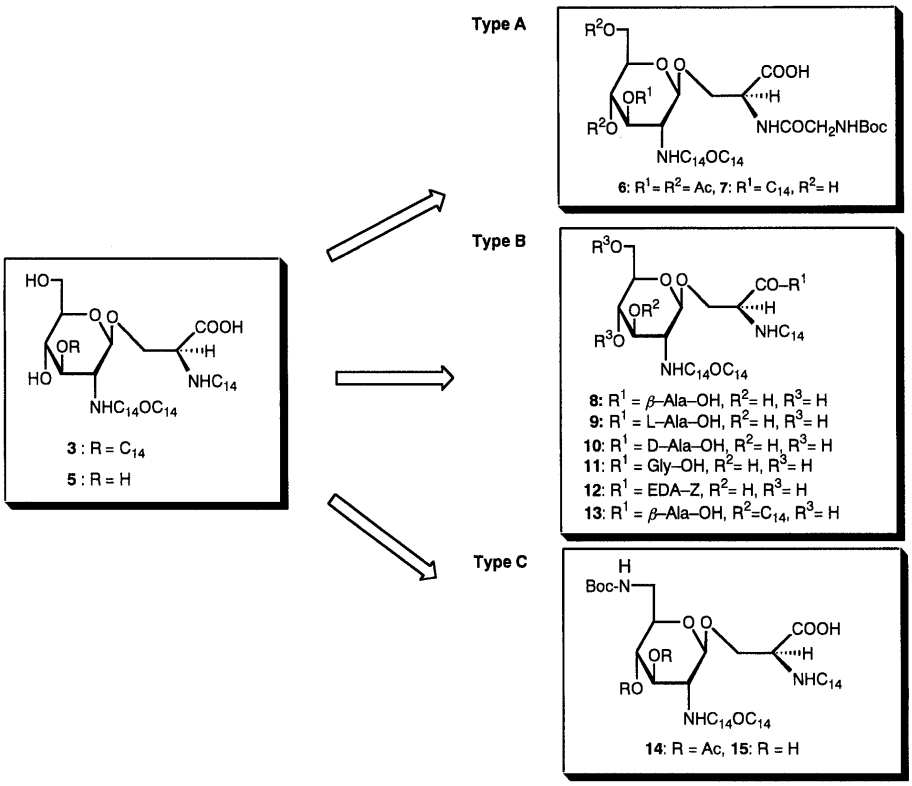

Fig. 2

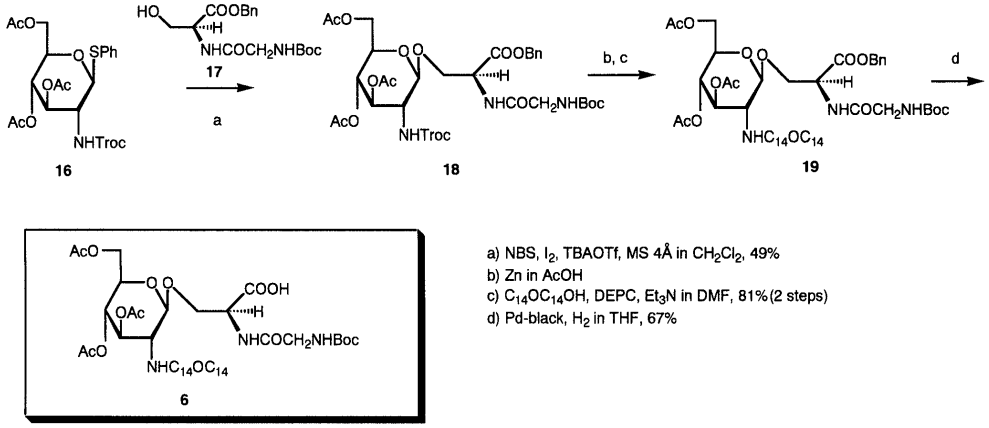

Chart 1

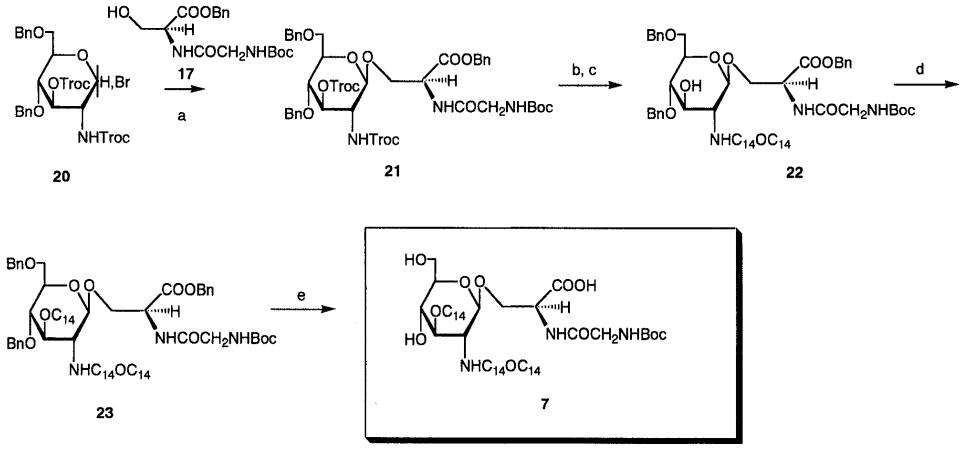

Chart 2

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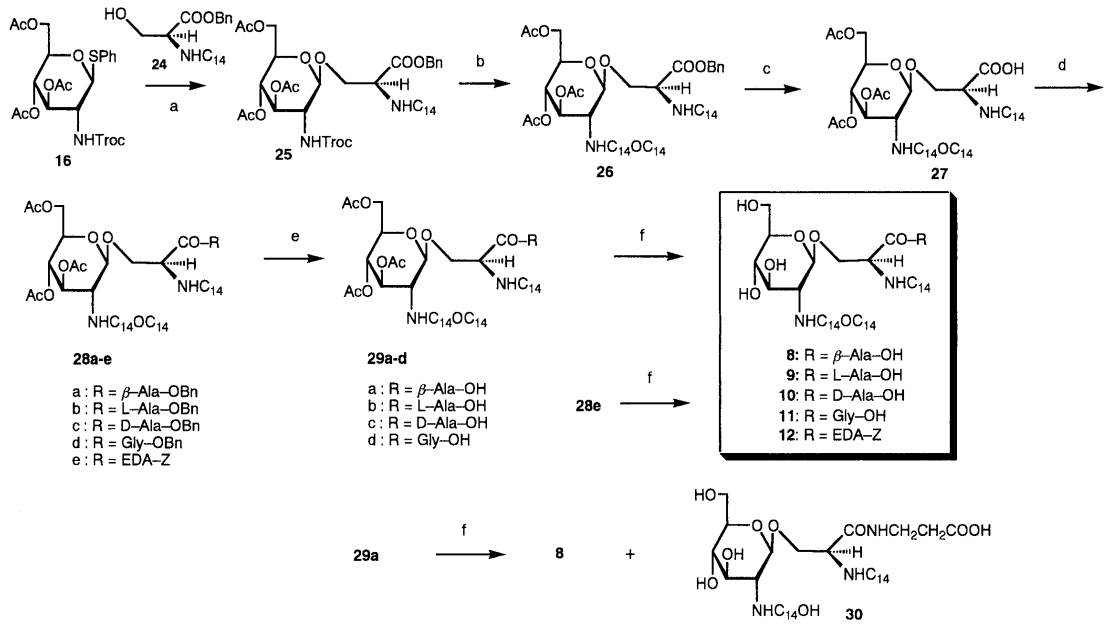

a) NBS, I_2, TBAOTf, MS 4Å in CH_2Cl_2, 83% ; b) 1)Zn in AcOH ; 2) $C_{14}OC_{14}OH$, DCC, HOBt, NMM in CH_2Cl_2-THF, 78% (2 steps);c) Pd-black, H_2 in MeOH-THF (1:1), 79% ; d) H-β-Ala-OBn•TosOH, 75% (**28a**), H-L-Ala-OBn•TosOH, 66% (**28b**), H-D-Ala-OBn•TosOH, 62% (**28c**), H-Gly-OBn•TosOH, 75% (**28d**), EDA-Z, 68% (**28e**), WSC•HCl, HOBt, NMM in DMF; e) Pd-black, H_2 in THF, 98% (**29a**), 94% (**29b**), 88% (**29c**), 94% (**29d**); f) conc. NH_4OH in MeOH-THF, 74% (**8**), 32% (**9**), 75% (**10**), 62% (**11**), 59% (**12**).

Chart 3

gave **23** in 67% yield. Finally, hydrogenolysis of the benzyl group of **23** using Pd-black as a catalyst gave the desired compound **7** in 53% yield [FAB-MS *m/z*: 1093 $(M+Na)^+$].

Next, for Type B, Charts 3 and 4 show similar synthesis of compounds **8**—**12** and **13**, respectively. Glycosidation of **16** with **24** was achieved in CH_2Cl_2 solution containing NBS, I_2 and TBAOTf as the activating agents to give **25** in 83% yield. Removal of the Troc group of **25** with activated Zn dust in AcOH, followed by *N*-acylation with $C_{14}OC_{14}OH$ in the presence of DCC and 1-hydroxybenzotriazole (HOBt) in CH_2Cl_2–THF afforded **26** in 78% yield in two steps. Hydrogenolysis of the benzyl group of **26** using Pd-black as a catalyst in MeOH–THF gave **27** in 79% yield. The treatment of **27** with β-alanine benzyl ester, L-alanine benzyl ester, D-alanine benzyl ester, glycine benzyl ester or 2-benzyloxycarbonylaminoethylamine (EDA-Z) using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (WSC·HCl), HOBt and *N*-methylmorpholine (NMM) in *N*,*N*-dimethylformamide (DMF) gave **28a**—**e** in 75, 66, 62, 75 and 68% yields, respectively. Hydrogenolysis of **28a**—**d** using Pd-black as a catalyst in THF gave **29a**—**d** in 98, 94, 88 and 94% yields, respectively. Finally, deprotection of the acetyl groups of **29a**—**d** with conc. NH_4OH in MeOH–THF afforded **8**—**11** in 74, 32, 75 and 62% yields, respectively. Compound **12** was also prepared by the treatment of **28e** with conc. NH_4OH in MeOH–THF in 59% yield.

For the preparation of compound **13**, the starting compound **31** was treated with tetradecanoyl chloride ($C_{14}Cl$) in the presence of DMAP and pyridine in CH_2Cl_2 to give **32** in 96% yield. After the treatment of **32** with 90% AcOH at room temperature, acetylation of the corresponding diol with Ac_2O–pyridine provided **33** in 93% yield. Glycosidation of **33** with **24** using NBS, I_2 and TBAOTf in CH_2Cl_2 gave **34** in 79% yield. After deprotection of the Troc group of **34**, *N*-acylation with $C_{14}OC_{14}OH$, DCC and HOBt in CH_2Cl_2–THF afforded **35** in 82% yield in two steps. Hydrogenolysis of **35** using Pd-black as a catalyst in MeOH–THF gave **36** in 99% yield. Condensation of **36** with β-alanine benzyl ester in the presence of WSC·HCl, HOBt, and NMM in DMF gave **37** in 76% yield. Finally, hydrogenolysis of the benzyl group of **37** using Pd-black as a catalyst in THF afforded **38** in 79% yield. Deacylation of **38** with conc. NH_4OH in MeOH–THF gave **13** (5% yield) [FAB-MS *m/z*: 1195 $(M+H)^+$, 1217 $(M+Na)^+$], **8** (83% yield) and **30** (6% yield) [FAB-MS *m/z*: 797 $(M+Na)^+$].

In order to synthesize a series of compounds for Type C, we used compounds **14** and **15** possessing an amino group in place of a hydroxyl group at the C-6 of D-glucosamine, then the selective tosylation of 6-OH of **39** was carried out with *p*-toluenesulfonyl chloride in pyridine–CH_2Cl_2, and acetylation of the corresponding tosylate with acetic anhydride in pyridine furnished acetate **40** in 75% in two steps. Subsequently, treatment of the tosylate **40** with sodium azide (NaN_3), 18-crown-6 in DMF gave 6-azide **41** in 61% yield. Compound **41** was treated with thiophenol, $BF_3 \cdot OEt_2$ in CH_2Cl_2 to afford the glycoside **42** in 61% yield. Hydrogenolysis of the azide group of **42** with PtO_2, followed by treatment with $(Boc)_2O$ in AcOEt gave **43** in 47% yield. The glycosidation of **43** with **24** in the presence of NBS, I_2 and TBAOTf in CH_2Cl_2 yielded β-glycoside **44** in 36% yield. Removal of the Troc group of **44** with activated Zn dust in AcOH, and subsequent *N*-acylation with $C_{14}OC_{14}OH$, DEPC and NEt_3 in DMF gave **45** in 63% yield in two steps. Hydrogenolysis of the benzyl group of **45** with Pd-black in THF afforded **14** in 93% yield [FAB-MS *m/z*: 1097 $(M+H)^+$, 1119 $(M+Na)^+$]. Finally, deprotection of **14** with conc. NH_4OH in MeOH gave the desired compound **15** in 79% yield [FAB-MS *m/z*: 1013 $(M+H)^+$, 1035 $(M+Na)^+$].

Biological Activity The mitogenicity of synthetic analogs was determined on the basis of *in vitro* [^{3}H]thymi-

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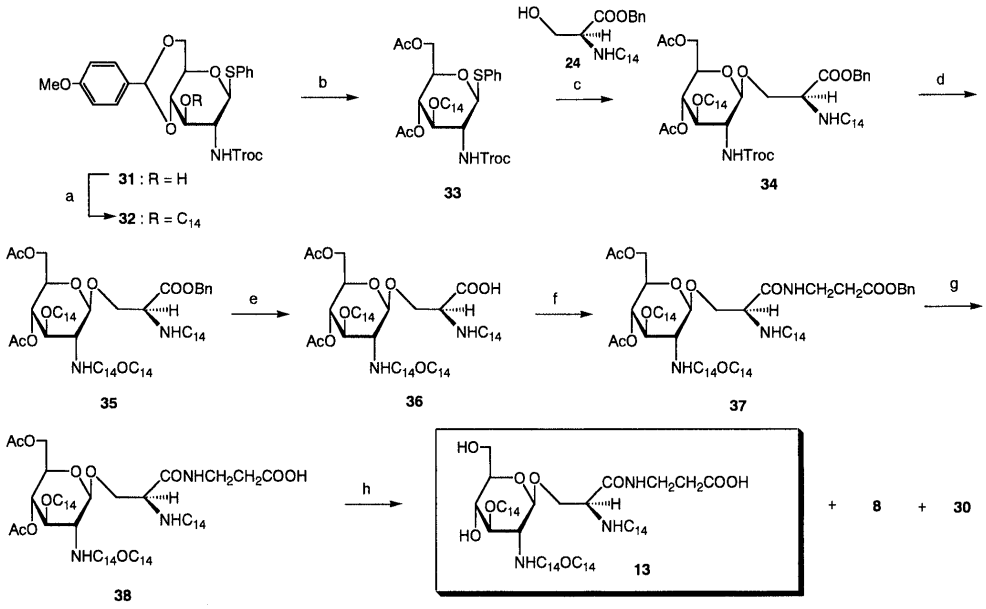
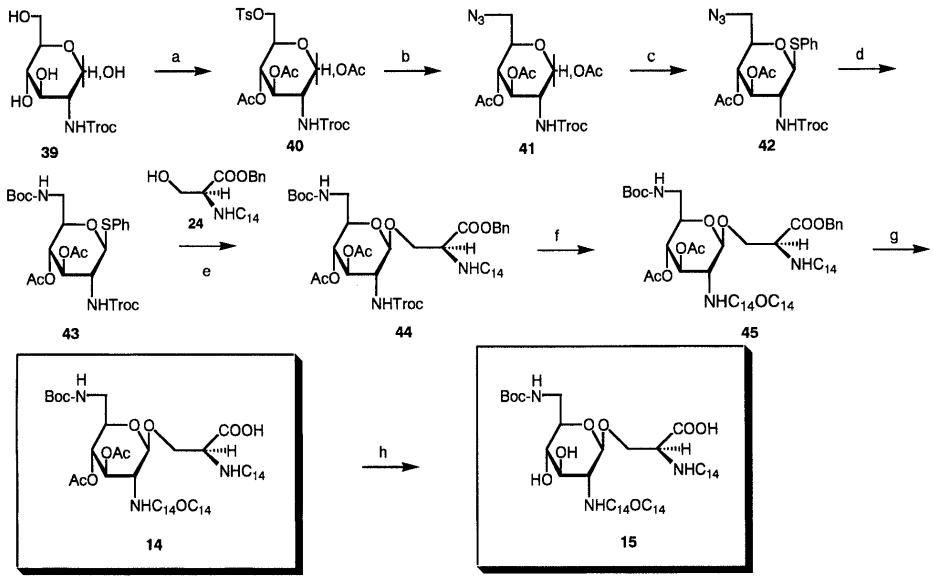


a) $C_{14}Cl$, pyridine, DMAP in CH_2Cl_2, 96%; b) 1) 90%AcOH; 2) Ac_2O in pyridine, 93% (2 steps); c) **24**, NBS, I_2, TBAOTf, MS 4Å in CH_2Cl_2, 79%; d) 1) Zn in AcOH; 2) $C_{14}OC_{14}OH$, DCC, HOBt, NMM in CH_2Cl_2-THF, 82% (2 steps); e) Pd-black, H_2 in MeOH-THF (1:1), 99% ; f) H-β-Ala-OBn•TosOH, WSC•HCl, HOBt, NMM in DMF, 76%; g) Pd-black, H_2 in THF, 79%; h) conc. NH_4OH in MeOH-THF, 83%.

Chart 4



a) 1) TsCl, pyridine, in CH_2Cl_2; 2) Ac_2O, 75% (2 steps); b) NaN_3, 18-Crown-6 in DMF, 61%; c) PhSH, $BF•Et_2O$ in CH_2Cl_2, 61%; d) PtO_2, H_2, $(Boc)_2O$ in AcOEt, 47%; e) NBS, I_2, TBAOTf, MS 4Å in CH_2Cl_2, 36%; f) 1) Zn in AcOH; 2) $C_{14}OC_{14}OH$, DEPC, Et_3N in DMF, 63% (2 steps) ; g) Pd-black, H_2 in THF, 93%; h) conc. NH_4OH in MeOH, 79%.

Chart 5

dine uptake into splenocytes from C3H/He mice.[8] As shown in Figs. 3—5, compound **8** for Type B showed the most potent mitogenicity among the analogs tested at 12.5 μM. Furthermore, the lethal toxicity of **8** in D-galactosamine-loaded C57BL/6 mice[9] was much lower than that of natural LPS. However, compounds **6** and **7** for Type A, and **14** and **15** for Type C, exhibited weaker mitogenicity than that of the lipid A analog **1** as a non-reducing unit of lipid A.

In conclusion, among these new *N*-acylated L-serine-containing D-glucosamine analogs (Type A, B, C), compound **8** for Type B exhibited the most potent mitogenicity. The mitogenicity of D-alanine derivative **10** was higher than that of L-alanine derivative **9**, suggesting that the configuration of the alanine part of **9** and **10** as a spacer affects the expression of biological activity. The reason compound **8** showed potent mitogenicity in comparison with **9** and **10** is unclear, but the difference in carbon chain length between the β-alanine residue and the L or D-alanine residue may affect the potency.

Further, the application of compound **8** as a synthetic immunoadjuvant to synthetic vaccines is in progress.

Experimental

All melting points are uncorrected. Optical rotations were measured with a JASCO DIP-140 digital polarimeter. IR spectra were recorded on a JASCO A-202 infrared spectrophotometer. FAB-MS were recorded on a JEOL JMS-

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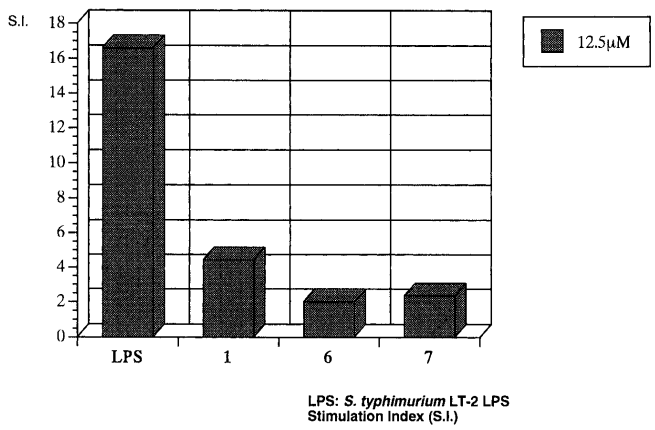

Fig. 3. Mitogenic Activity of Lipid A Analogs for Type A on Splenocytes of C3H/He Mice

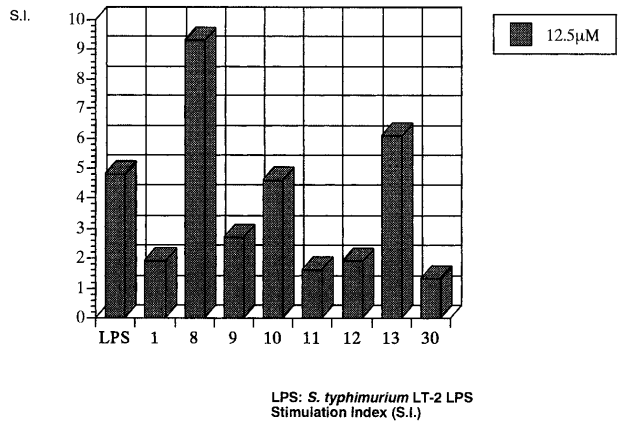

Fig. 4. Mitogenic Activity of Lipid A Analogs for Type B on Splenocytes of C3H/He Mice

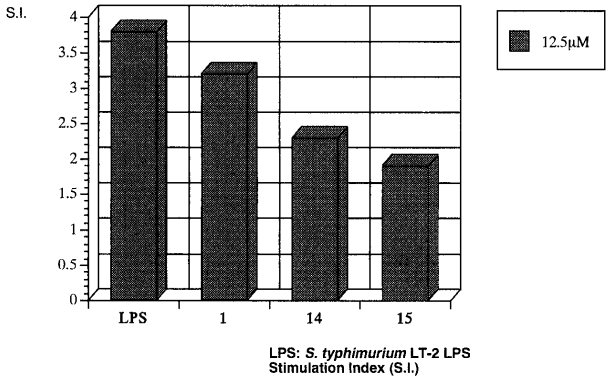

Fig. 5. Mitogenic Activity of Lipid A Analogs for Type C on Splenocytes of C3H/He Mice

SX 102 spectrometer. ^{1}H-NMR spectra were taken on a JEOL JNM-EX 270 (270 MHz) spectrometer. ^{13}C-NMR spectra were recorded with a JEOL JNM-EX 270 (67.5 MHz) spectrometer. ^{1}H and ^{13}C chemical shifts (δ) are given in ppm relative to Me_4Si (δ=0) in $CDCl_3$ or CD_3OD as an internal standard. The abbreviations of signal patterns are as follows: s, singlet; br s, broad singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Column chromatography was carried out on Silica gel 60 (70—230 mesh, Merck). Thin-layer chromatography (TLC) on Silica gel 60-F_{254} (Merck) was used to monitor the reaction and to ascertain the purity of the reaction products. The spots were visualized by spraying the plates with 5% aqueous sulfuric acid, followed by heating.

***N*-(*tert*-Butoxycarbonyl)-glycyl-*O*-[3,4,6-tri-*O*-acety-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-L-serine Benzyl Ester (18)** NBS (249 mg, 1.4 mmol), iodine (355 mg, 1.4 mmol) and TBAOTf (27 mg, 0.07 mmol) were added to a stirred mixture of **16** (200 mg, 0.35 mmol), **17** (123 mg, 0.35 mmol) and MS 4A° (400 mg) in dry CH_2Cl_2 (15 ml) at −20 °C under argon and the whole was stirred at the same temperature for 1 h. It was then diluted with CH_2Cl_2, washed with 10% aqueous $Na_2S_2O_3$ and brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (CH_2Cl_2 : CH_3COCH_3=10 : 1) to give **18** (140 mg, 49%), $[\alpha]_D$ +24.8° (c=0.9, $CHCl_3$). IR (Nujol): 3326, 1749, 1679 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.50 (9H, s, *tert*-Bu), 2.02, 2.03, 2.06 (each 3H, s, $OCOCH_3$), 3.46—3.68 (1H, m, H-2), 3.64—4.37 (8H, m, H-4, 5, 6, $NHCH_2CO$, $NHCHCH_2CO$), 4.37—4.58 (1H, m, NHCHCO), 4.71—4.85 (2H, m, CH_2CCl_3), 4.99—5.29 (6H, m, H-3, 4, NH×2, CH_2Ph), 7.32—7.51 (6H, m, Ph, NHCHCO). ^{13}C-NMR ($CDCl_3$) δ: 102.49 (d, J=160.6 Hz, C-1). FAB-MS *m/z*: 814 $(M+H)^+$, 836 $(M+Na)^+$.

***N*-(*tert*-Butoxycarbonyl)-glycyl-*O*-[3,4,6-tri-*O*-acetyl-2-deoxy-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine Benzyl Ester (19)** A mixture of **18** (140 mg, 0.172 mmol) and activated zinc powder (750 mg) in AcOH (2 ml) was stirred for 20 h at 40—50 °C. The precipitate was filtered off and the filtrate was diluted with CH_2Cl_2, washed with 10% aqueous $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue and (*R*)-3-tetradecanoyloxytetradecanoic acid (72 mg, 0.16 mmol) was dissolved in DMF (2 ml), and to the mixture, DEPC (26 mg, 0.16 mmol) and NEt_3 (16 mg, 0.16 mmol) were added at 0 °C under argon. The reaction mixture was stirred at the same temperature for 1 h, then at room temperature for 10 h. It was then diluted with CH_2Cl_2, washed with 10% aqueous $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (CH_2Cl_2 : CH_3COCH_3=10 : 1) to give **19** (92 mg, 81%), $[\alpha]_D$ +2.2° (c=0.6, $CHCl_3$). IR (Nujol): 3300, 1743, 1712 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (6H, t, J=6.9 Hz, $-CH_3$), 1.26 (38H, br s, $-CH_2-$), 1.47 (9H, s, *tert*-Bu), 1.55—1.69 (4H, m, CH_2-), 2.01, 2.02, 2.07 (each 3H, s, $OCOCH_3$), 2.21—2.46 (4H, m, $-CH_2-$), 3.50—3.75 (4H, m, H-2, 5, OCH_2CHN), 3.95—4.29 (4H, m, H-6, $NHCHCH_2O$), 4.63—4.68 (1H, m, NHCHCO), 4.73(1H, d, J=8.3 Hz, H-1), 5.02—5.15 (2H, m, H-4, $NHCOCH_2CH(OCO)-$), 5.19 (2H, br s, CH_2Ph), 5.30 (1H, dd, J=9.9 Hz, H-3), 5.68 (1H, br s, NH), 6.46 (1H, br s, NH), 7.32—7.43 (6H, m, Ph, NH). Positive FAB-MS *m/z*: 1077 $(M+H)^+$, 1099 $(M+Na)^+$.

***N*-(*tert*-Butoxycarbonyl)-glycyl-*O*-[3, 4, 6-tri-*O*-acetyl-2-deoxy-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine (6)** A mixture of **19** (53 mg, 0.049 mmol) and palladium–black (25 mg) in THF (3 ml) was hydrogenated at room temperature. The mixture was filtered, then concentrated *in vacuo*, then chromatographed. Elution with CH_2Cl_2 : MeOH=10 : 1 gave **6** (33 mg, 67%), $[\alpha]_D$ −1.5° (c=0.6, $CHCl_3$). IR (Nujol): 3386, 1747, 1712, 1644 cm^{-1}. ^{1}H-NMR ($CDCl_3$–CD_3OD) δ: 0.88 (6H, t, J=6.9 Hz, $-CH_3$), 1.25 (38H, br s, $-CH_2-$), 1.47 (9H, s, *tert*-Bu), 1.52—1.64 (4H, m, $COCH_2CH_2C_{11}H_{23}$×2), 2.01, 2.03, 2.09 (each 3H, s, $OCOCH_3$), 2.30—2.69 (4H, m, $-CH_2-$), 3.64—4.41 (9H, m, H-2, 5, 6, $NHCH_2CO$, $NHCHCH_2O$), 4.52 (1H, d, J=8.3 Hz, H-1), 5.00 (1H, t, J=9.6 Hz, H-4), 5.10 (1H, br s, $NHCH_2CO$), 5.21 (1H, t, J=9.9 Hz, H-3), 6.11 (1H, br d, $CHCH_2CONHCH$), 7.61 (1H, br d, NHCHCO). Positive FAB-MS *m/z*: 987 $(M+H)^+$, 1009 $(M+Na)^+$.

***N*-(*tert*-Butoxycarboyl)-glycyl-*O*-[4,6-di-*O*-benzyl-2-deoxy-3-*O*-(2,2,2-trichlorotoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-L-serine Benzyl Ester (21)** $HgBr_2$ (62 mg, 0.173 mmol) was added to a stirred mixture of **20** (245 mg, 0.345 mmol), **17** (122 mg, 0.345 mmol) and MS 4A° (800 mg) in dry CH_2Cl_2 (6 ml) at 0 °C under argon and the whole was stirred at the same temperature for 1 h. After stirring for 20 h at room temperature, the suspension was filtered off and the filtrate was diluted with CH_2Cl_2 and then washed with 10% KI and brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (hexane : AcOEt=2 : 1) to give **21** (201 mg, 61%), $[\alpha]_D$ +9.8° (c=1.40, $CHCl_3$). IR (Nujol): 308, 1751, 1673 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.47 (9H, s, *tert*-Bu), 3.40—4.06 (8H, m, H-2, 4, 5, 6, $NHCH_2CO$, OCH_2CHN), 4.31—4.36 (1H, m, $NHCHCH_2O$), 4.32 (1H, d, J=8.9 Hz, H-1), 4.44—4.75 (9H, m, CH_2CCl_3×2, OCH_2Ph×2, NHCHCO), 5.03—5.28 (4H, m, H-3, $COOCH_2Ph$, NH), 7.19 (1H, br s, NH), 7.24—7.39 (10H, m, Ph). Positive FAB-MS *m/z*: 1042 $(M+H)^+$, 1064 $(M+Na)^+$.

***N*-(*tert*-Butoxycarbonyl)-glycyl-*O*-[4,6-di-*O*-benzyl-2-deoxy-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine Benzyl Ester (22)** In a manner similar to that for the synthesis of **19**, **21** (124 mg, 0.12 mmol) was deprotected and acylated with (*R*)-3-tetradecanoyl-

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oxytetradecanoic acid (81 mg, 0.18 mmol) and DCC (49 mg, 0.24 mmol) to give **23** (30 mg, 22%), after purification by silica gel column chromatography (CH_2Cl_2 : CH_3COCH_3=10 : 1), $[\alpha]_D$ −4.2° (*c*=0.60, $CHCl_3$). IR (Nujol): 3332, 1729, 1537 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (6H, t, *J*=6.9 Hz, $-CH_3$), 1.25 (38H, br s, $-CH_2-$), 1.43 (9H, s, *tert*-Bu), 1.57—1.65 (4H, m, $-CH_2$), 2.28 (2H, t, *J*=7.4 Hz, CH_2CH_2CO), 2.59 (2H, t, *J*=5.8 Hz, CH_2CHCH_2CONH), 3.33—3.54 (4H, m, H-2, 3, 4, 5), 3.61—3.92 (4H, m, H-6, $NHCH_2CO$), 3.94—4.05 (1H, m, $NHCHCH_2CO$), 4.13—4.24 (1H, m, $NHCHCH_2O$), 4.46 (1H, d, *J*=8.6 Hz, H-1), 4.45—4.60 (2H, m, OCH_2Ph), 4.74 (1H, br s, NHCHCO), 4.94 (1H, d, *J*=11.1 Hz, OCH_2Ph), 5.13—5.25 (3H, m, $COOCH_2Ph$, $COCH_2CH(OCO)$), 5.53 (1H, br s, $NHCH_2CO$), 6.80 (1H, br s, NH), 7.19—7.39 (16H, m, Ph, NHCHCO). Positive FAB-MS *m/z*: 1131 $(M+H)^+$, 1153 $(M+Na)^+$.

***N*-(*tert*-Butoxycarbonyl)-glycyl-*O*-[4,6-di-*O*-benzyl-2-deoxy-3-*O*-tetradecanoyl-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine Benzyl Ester (23)** DCC (11 mg, 0.53 mmol) was added to a stirred mixture of **22** (30 mg, 0.027 mmol), tetradecanoic acid (12 mg, 0.53 mmol) and DMAP (2 mg, 0.013 mmol) in dry CH_2Cl_2 (2 ml) at 0 °C under argon. The reaction mixture was stirred at the same temperature for 1 h, then at room temperature for 20 h. The suspension was filtered off and the filtrate was concentarated under reduced pressure. It was then diluted with AcOEt, washed with 10% aqueous $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (CH_2Cl_2 : CH_3COCH_3=20 : 1) to give **23** (24 mg, 67%), $[\alpha]_D$ −3.7° (*c*=0.50, $CHCl_3$). IR (Nujol): 3280, 1734, 1652 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (9H, t, *J*=6.9 Hz, $-CH_3$), 1.25 (62H, br s, $-CH_2-$), 1.46 (9H, s, *tert*-Bu), 1.47—1.69 (6H, m, $-CH_2-$), 2.14—2.44 (6H, m, $-CH_2-$), 3.64—3.93 (7H, m, H-2, 4, 5, 6, $NHCH_2CO$), 3.61—3.92 (4H, m, H-6, $NHCH_2CO$), 3.95—4.02 (1H, m, $NHCHCH_2O$), 4.24 (1H, d, *J*=10.8 Hz, $NHCHCH_2O$), 4.50 (1H, d, *J*=8.4 Hz, H-1), 4.55—4.63 (4H, m, OCH_2Ph), 4.64—4.69 (1H, m, NHCHCO), 5.03—5.15 (2H, m, H-3, $COCH_2CH(OCO)$), 5.18 (2H, s, $COOCH_2Ph$), 5.56 (1H, br s, $NHCH_2CO$), 6.24 (1H, br s, NH), 7.12—7.38 (16H, m, Ph, NHCHCO). Positive FAB-MS *m/z*: 1341 $(M+H)^+$, 1363 $(M+Na)^+$.

***N*-(*tert*-Butoxycarbonyl)-glycyl-*O*-[2-deoxy-3-*O*-tetradecanoyl-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranoyl]-L-serine (7)** Compound **23** (24 mg, 0.018 mmol) was treated in the same manner as described above to obtain 10 mg (53%) of **7**, $[\alpha]_D$ −10.9° (*c*=0.45, $CHCl_3$: MeOH=1 : 1). IR (Nujol): 3280, 1732, 1651 cm^{-1}. Positive FAB-MS *m/z*: 1093 $(M+Na)^+$.

***N*-Tetradecanoyl-*O*-[3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-L-serine Benzyl Ester (25)** In a manner similar to that for the synthesis of **18**, **16** (573 mg, 1.0 mmol) was treated with tetradecanoyl-L-serine benzyl ester **24** (527 mg, 1.3 mmol), NBS (712 mg, 4 mmol), iodine (1.02 g, 4 mmol) and TBAOTf (76 mg, 0.2 mmol) to give **25** (720 mg, 83%), after purification by silica gel chromatography (hexane : AcOEt=2 : 1), $[\alpha]_D$ +6.3° (*c*=1.0, $CHCl_3$). IR (Nujol): 3338, 1744, 1659 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, *J*=6.9 Hz, $-CH_3$), 1.25 (20H, br s, $-CH_2-$), 1.65 (2H, br s, $CH_2CH_2C_{11}H_{23}$), 2.02, 2.03, 2.04 (each 3H, s, $OCOCH_3$), 2.25 (2H, t, *J*=8.3 Hz, $CH_2C_{12}H_{25}$), 3.55—3.63 (2H, m, H-2, H-5), 3.90 (1H, dd, *J*=3.3, 10.6 Hz, OCH_2CH), 4.03—4.17 (1H, m, H-6), 4.20—4.25 (2H, m, H-6, OCH_2CH), 4.67—4.83 (4H, m, H-1, CH_2CCl_3, OCH_2CHNH), 5.02 (1H, t, *J*=9.6 Hz, H-4), 5.08—5.31 (3H, m, H-3, OCH_2Ph), 5.62 (1H, br s, NH), 6.53 (1H, d, *J*=7.6 Hz, NH), 7.36 (5H, s, Ph). ^{13}C-NMR ($CDCl_3$) δ: 100.3 (d, C-1), 154.2, 169.3, 169.5, 170.4, 170.5, 173.4 (s, C=O). Positive FAB-MS *m/z*: 867 $(M+H)^+$.

***N*-Tetradecanoyl-*O*-[3,4,6-tri-*O*-acetyl-2-deoxy-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine Benzyl Ester (26)** In a manner similar to that for the synthesis of **19**, **25** (250 mg, 0.29 mmol) was deprotected and acylated with (*R*)-3-tetradecanoyloxytetradecanoic acid (118 mg, 0.26 mmol), HOBt (62 mg, 0.40 mmol), DCC (84 mg, 0.40 mmol), and *N*-methylmorpholine (41 mg, 0.40 mmol) to give **26** (254 mg, 78%), after purification by silica gel column chromatography (CH_2Cl_2 : CH_3COCH_3=20 : 1).

***N*-Tetradecanoyl-*O*-[3,4,6-tri-*O*-acetyl-2-deoxy-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine (27)** Compound **26** was treated in the same manner as described above to obtain 82 mg (79%) of **27**, mp 210 °C (dec.), $[\alpha]_D$ +7.2° (*c*=0.51, $CHCl_3$). IR (KBr): 3286, 2916, 1745, 1648 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (6H, t, *J*=6.9 Hz, $-CH_3$), 1.26 (58H, br s, $-CH_2-$), 1.41—1.63 (6H, m, $-CH_2-$), 2.01, 2.03, 2.09 (each 3H, s, $OCOCH_3\times3$), 2.12—2.40 (6H, m, $-CH_2-$), 2.51 (1H, dd, *J*=6.3, 14.2 Hz, $NHCOCH_2CH(OCO)$), 3.68—3.75 (1H, m, H-5), 3.82—3.90 (2H, m, H-2, 6), 4.09—4.13 (2H, m, H-6, OCH_2CHNH), 4.27—4.31 (2H, m, OCH_2CHNH), 4.61 (1H, d, *J*=8.3 Hz, H-1), 4.99 (1H, t, *J*=9.9 Hz, H-4), 5.12—5.16 (1H, m, $NHCOCH_2CH(OCO)$), 5.20 (1H, t, *J*=9.6 Hz, H-3). Positive FAB-MS *m/z*: 1040 $(M+H)^+$, 1062 $(M+Na)^+$.

***N*-Tetradecanoyl-*O*-[3,4,6-tri-*O*-acetyl-2-deoxy-2-[(*R*)-3-tetradecanoyloxy-tetradecanoylamino]-β-D-glucopyranosyl]-L-seryl-β-alanine Benzyl Ester (28a)** WSC·HCl (46 mg, 0.24 mmol) and *N*-methylmorpholine (24 mg, 0.24 mmol) was added to a stirred mixture of **27** (165 mg, 0.16 mmol), β-alanine benzyl ester *p*-TsOH (84 mg, 0.24 mmol) and HOBt (37 mg, 0.24 mmol) in DMF (6 ml) at 0 °C under argon. The reaction mixture was stirred at the same temperature for 1 h, then at room temperature for 20 h. The suspension was filtered off and the filtrate was concentarated under reduced pressure. It was then diluted with AcOEt, washed with 10% aqueous $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (hexane : AcOEt=1 : 1) to give **28a** (144 mg, 75%), $[\alpha]_D$ −2.1° (*c*=0.86, $CHCl_3$). IR (Nujol): 1745, 1648 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (9H, t, *J*=6.9Hz, $-CH_3$), 1.26 (58H, br s, $-CH_2-$), 1.40–1.63 (6H, m, $-CH_2-$), 2.00, 2.03, 2.07 (each 3H, s, $OCOCH_3\times3$), 2.08—2.36 (5H, m, $-CH_2-$), 2.46 (1H, dd, *J*=6.3, 14.5 Hz, $NHCOCH_2CH(OCO)$), 2.61 (2H, t, *J*=6.6 Hz, $NHCH_2CH_2$), 3.49—3.78 (4H, m, H-2,5, $NHCH_2CH_2$), 3.86—3.91 (1H, m, OCH_2CHNH), 3.97 (1H, dd, *J*=10.9, 5.0 Hz, OCH_2CHNH), 4.14—4.18 (2H, m, H-6), 4.30 (1H, dd, *J*=12.2, 5.3 Hz, H-6), 4.62—4.69 (1H, m, OCH_2CHNH), 4.73 (1H, d, *J*=8.3 Hz, H-1), 5.00—5.27 (5H, m, H-3, 4, CH_2Ph, $NHCOCH_2CH(OCO)$), 6.15 (1H, d, *J*=8.6 Hz, NH), 6.53 (1H, d, *J*=6.9 Hz, NH), 7.06 (1H, t, *J*=6.3 Hz, $NHCH_2$), 7.26—7.38 (5H, m, Ph). Positive FAB-MS *m/z*: 1200 $(M+H)^+$.

Compounds **28b—e** were prepared by a method similar to that described for **28a**.

28b: Yield, 66%, $[\alpha]_D$ −5.5° (*c*=1.1, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (9H, t, *J*=6.9 Hz, $-CH_3$), 1.25 (58H, br s, $-CH_2-$), 1.43 (3H, d, *J*=7.3 Hz, $CH-CH_3$), 1.47—1.63 (6H, m, $-CH_2-$), 2.00, 2.03, 2.06 (each 3H, s, $OCOCH_3\times3$), 2.10—2.34 (5H, m, $-CH_2-$), 2.41 (1H, dd, *J*=5.9, 14.2 Hz, $NHCOCH_2CH(OCO)$), 3.69—3.98 (4H, m, H-2, 5, OCH_2CHNH), 4.12—4.16 (1H, m, H-6), 4.29 (1H, dd, *J*=12.5, 5.0 Hz, H-6), 4.57—4.70 (2H, m, OCH_2CHNH, $CH-CH_3$), 4.73 (1H, d, *J*=8.3 Hz, H-1), 4.99—5.27 (5H, m, H-3, 4, CH_2Ph), 5.25—5.32 (1H, m, $NHCOCH_2CH(OCO)$), 6.38 (1H, d, *J*=8.6 Hz, NH), 6.41 (1H, d, *J*=6.9 Hz, NH), 7.28 (1H, d, *J*=6.3 Hz, NH), 7.37 (5H, s, Ph). Positive FAB-MS *m/z*: 1200 $(M+H)^+$.

28c: Yield, 62%, $[\alpha]_D$ −4.4° (*c*=0.88, $CHCl_3$).

28d: Yield, 75%, $[\alpha]_D$ −4.3° (*c*=0.92, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (9H, t, *J*=6.9 Hz, $-CH_3$), 1.25 (58H, br s, $-CH_2-$), 1.41—1.68 (6H, m, $-CH_2-$), 2.00, 2.03, 2.06 (each 3H, s, $OCOCH_3\times3$), 2.09—2.40 (6H, m, $-CH_2-$), 3.68—3.75 (2H, m, H-5, OCH_2CHNH), 3.93—4.29 (6H, m, H-2, 6, OCH_2CHNH, $NHCH_2COOBn$), 4.68—4.72 (2H, m, H-1, OCH_2CHNH), 4.96—5.12 (2H, m, H-4, $NHCOCH_2CH(OCO)$), 5.19 (2H, s, CH_2Ph), 5.22—5.27 (1H, m, H-3), 6.31 (1H, d, *J*=8.6 Hz, NH), 6.47 (1H, d, *J*=6.9 Hz, NH), 7.28 (1H, d, *J*=6.3 Hz, NH), 7.37 (5H, s, Ph). Positive FAB-MS *m/z*: 1186 $(M+H)^+$.

28e: Yield, 68%, $[\alpha]_D$ −4.6° (*c*=0.80, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (9H, t, *J*=6.9 Hz, $-CH_3$), 1.25 (58H, br s, $-CH_2-$), 1.45—1.63 (6H, m, $-CH_2-$), 1.95, 2.04, 2.07 (each 3H, s, $OCOCH_3\times3$), 2.11—2.34 (5H, m, $-CH_2-$), 2.43 (1H, dd, *J*=6.3, 14.5 Hz, $NHCOCH_2CH(OCO)$), 3.33—3.48 (4H, m, $NHCH_2CH_2NH$), 3.61—3.68 (1H, m, OCH_2CHNH), 3.68—3.73 (1H, m, H-5), 3.97—4.02 (2H, m, H-2, OCH_2CHNH), 4.12—4.18 (1H, m, H-6), 4.30 (1H, dd, *J*=12.5, 5.0 Hz, H-6), 4.57—4.62 (1H, m, OCH_2CHNH), 4.64 (1H, d, *J*=7.9 Hz, H-1), 5.0—5.27 (5H, m, H-3, 4, CH_2Ph, $NHCOCH_2CH(OCO)$), 5.92(1H, br s, NH), 6.11 (1H, d, *J*=8.6 Hz, NH), 6.55 (1H, d, *J*=6.6 Hz, NH), 6.86 (1H, br, NH), 7.36 (5H, s, Ph). Positive FAB-MS *m/z*: 1215 $(M+H)^+$.

***N*-Tetradecanoyl-*O*-[3,4,6-tri-*O*-acetyl-2-deoxy-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-seryl-β-alanine (29a)** A mixture of **28a** (110 mg, 0.092 mmol) and palladium–black (70 mg) in THF (7 ml) was hydrogenated at 40—50 °C. The catalyst was filtered off and the filtrate was concentrated under reduced pressure. The residue was chromatographed on a silica gel column (CH_2Cl_2 : MeOH=10 : 1) to give **29a** (100 mg, 98%), $[\alpha]_D$ −3.7° (*c*=0.92, $CHCl_3$: MeOH=3 : 2). ^{1}H-NMR ($CDCl_3$–CD_3OD) δ: 0.88 (9H, t, *J*=6.9 Hz, $-CH_3$), 1.25 (58H, br s, $-CH_2-$), 1.42—1.60 (6H, m, $-CH_2-$), 2.02, 2.04, 2.10 (each 3H, s, $OCOCH_3\times3$), 2.17—2.52 (8H, m, $-CH_2-$, $NHCH_2CH_2$), 3.36—4.18 (7H, m, H-2, 5, 6, $NHCH_2CH_2$, OCH_2CHNH), 4.29 (1H, dd, *J*=12.2, 5.0 Hz, H-6), 4.51—4.56 (1H, m, OCH_2CHNH), 4.65 (1H, d, *J*=8.3 Hz, H-1), 5.00—5.17 (2H, m, H-4, $NHCOCH_2CH(OCO)$), 5.20 (1H, t, *J*=9.2 Hz, H-3). Positive FAB-MS *m/z*: 1100 $(M+H)^+$.

Compounds **29b—e** were prepared by a method similar to that described for **29a**.

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29b: Yield, 94%, $[\alpha]_D$ −16.5° (c=0.42, $CHCl_3$: MeOH=4 : 1). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (9H, t, J=6.9 Hz, $-CH_3$), 1.25 (61H, br s, $-CH_2-$, $CH-CH_3$), 1.40—1.65 (6H, m, $-CH_2-$), 2.00, 2.02, 2.06 (each 3H, s, $OCOCH_3\times3$), 2.16—2.49 (6H, m, $-CH_2-$), 3.81—3.99 (4H, m, H-2, 5, OCH_2CHNH), 4.13—4.26 (3H, m, H-6, $CH-CH_3$), 4.57 (1H, m, OCH_2CHNH), 4.75 (1H, d, J=8.3 Hz, H-1), 4.99—5.12 (2H, m, H-4, $NHCOCH_2CH(OCO)$), 5.24 (1H, t, J=9.6 Hz, H-3). Positive FAB-MS m/z: 1111 $(M+H)^+$.

29c: Yield, 88%, $[\alpha]_D$ −5.6° (c=0.62, $CHCl_3$: MeOH=4 : 1).

29d: Yield, 94%, $[\alpha]_D$ −6.8° (c=0.22, $CHCl_3$: MeOH=4 : 1). ^{1}H-NMR ($CDCl_3$–CD_3OD) δ: 0.88 (9H, t, J=6.9 Hz, $-CH_3$), 1.25 (58H, br s, $-CH_2-$), 1.47—1.68 (6H, m, $-CH_2-$), 2.00, 2.03, 2.09 (each 3H, s, $OCOCH_3\times3$), 2.12—2.58 (6H, m, $-CH_2-$), 3.32—4.03 (6H, m, H-2, 5, OCH_2CHNH, $NHCH_2COOH$), 4.05—4.16 (1H, m, H-6), 4.18—4.22 (1H, m, H-6), 4.48—4.54 (1H, m, OCH_2CHNH), 4.68 (1H, d, J=8.3 Hz, H-1), 5.03—5.24 (3H, m, H-3, 4, $NHCOCH_2CH(OCO)$). Positive FAB-MS m/z: 1096 $(M+H)^+$.

***N*-Tetradecanoyl-*O*-[2-deoxy-2-[(*R*)-3-tetradecanoyloxytetradecanoyl-amino]-β-D-glucopyranosyl]-L-seryl-β-alanine (8)** A mixture of **29a** (70 mg, 0.063 mmol) and concentrated NH_4OH (2 ml) in MeOH–THF (1 : 1) (20 ml) was stirred for 20 h at room temperature. After removal of the solvent, the residue was chromatographed on a silica gel column (CH_2Cl_2 : MeOH : H_2O=12 : 8 : 1) to give **8** (46 mg, 74%) and **30** (9 mg, 18%).

8: $[\alpha]_D$ −5.2° (c=0.34, $CHCl_3$: MeOH=3 : 2). ^{1}H-NMR ($CDCl_3$–CD_3OD) δ: 0.88 (9H, t, J=6.9 Hz, $-CH_3$), 1.25 (58H, br s, $-CH_2-$), 1.52—1.60 (6H, m, $-CH_2-$), 2.07—2.57 (8H, m, $-CH_2-$, $NHCH_2CH_2$), 3.18—4.63 (12H, m, H-1, 2, 3, 4, 5, 6, $NHCH_2CH_2$, OCH_2CHNH, OCH_2CHNH), 5.23 (1H, m, $NHCOCH_2CH(OCO)$). Positive FAB-MS m/z: 985 $(M+H)^+$, 1007 $(M+Na)^+$.

30: $[\alpha]_D$ −9.9° (c=0.10, $CHCl_3$: MeOH=2 : 3). ^{1}H-NMR ($CDCl_3$–CD_3OD) δ: 0.88 (6H, t, J=6.9 Hz, $-CH_3$), 1.25 (38H, br s, $-CH_2-$), 1.45—1.61 (4H, m, $-CH_2-$), 2.24—2.50 (6H, m, $-CH_2-$, $NHCH_2CH_2$), 3.32—3.99 (11H, m,H-2, 3, 4, 5, 6, $NHCH_2CH_2$, OCH_2CHNH, $NHCOCH_2CHOH$), 4.45 (1H, d, J=9.2 Hz, H-1), 4.54—4.56 (1H, m, OCH_2CHNH). Positive FAB-MS m/z: 797 $(M+Na)^+$.

Compounds **9**, **10**, **11** and **12** were prepared by a method similar to that described for **8**.

9: Yield, 32%, $[\alpha]_D$ −14.2° (c=0.18, $CHCl_3$: MeOH=3 : 2). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (9H, t, J=6.9 Hz, $-CH_3$), 1.25 (61H, br s, $-CH_2-$, $CH-CH_3$), 1.49—1.63 (6H, m, $-CH_2-$), 2.21—2.49 (6H, m, $-CH_2-$), 3.28—4.23 (9H, m, H-2, 3, 4, 5, 6, OCH_2CHNH, $CH-CH_3$), 4.44 (1H, d, J=8.3 Hz, H-1), 4.68 (1H, m, OCH_2CHNH), 5.21—5.33 (1H, m, OCH_2CHNH), 5.21—5.33 (1H, m, $NHCOCH_2CH(OCO)$). Positive FAB-MS m/z: 985 $(M+H)^+$, 1007 $(M+Na)^+$.

10: Yield, 75 %, $[\alpha]_D$ −11.7° (c=0.36, $CHCl_3$: MeOH=3 : 2).

11: Yield, 62 %, $[\alpha]_D$ −24.4° (c=0.24, $CHCl_3$: MeOH=3 : 2). ^{1}H-NMR ($CDCl_3$–CD_3OD) δ: 0.88 (9H, t, J=6.9 Hz, $-CH_3$), 1.25 (58H, br s, $-CH_2-$), 1.59 (6H, m, $-CH_2-$), 2.24—2.49 (6H, m, $-CH_2-$), 3.29—4.10 (10H, m, H-2, 3, 4, 5, 6, OCH_2CHNH, $NHCH_2COOH$), 4.45 (1H, d, J=8.3 Hz, H-1), 4.62 (1H, m, OCH_2CHNH), 5.18—5.23 (1H, m, $NHCOCH_2CH(OCO)$). Positive FAB-MS m/z: 971 $(M+H)^+$, 993 $(M+Na)^+$.

12: Yield, 59%, $[\alpha]_D$ −12.7° (c=0.40, $CHCl_3$: MeOH=3 : 2). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (9H, t, J=6.9 Hz, $-CH_3$), 1.25 (58H, br s, $-CH_2-$), 1.47—1.65 (6H, m, $-CH_2-$), 2.18—2.30 (5H, m, $-CH_2-$), 2.40—2.47 (1H, m, $NHCOCH_2CH(OCO)$), 3.33—3.94 (12H, m, H-2, 3, 4, 5, 6, $NHCH_2CH_2NH$, OCH_2CHNH), OCH_2CHNH), 4.38 (1H, d, J=7.9 Hz, H-1), 4.51—4.55 (1H, m, OCH_2CHNH), 5.09—5.22 (3H, m, CH_2Ph, $NHCOCH_2CH(OCO)$), 7.29—7.42 (5H, m, Ph). Positive FAB-MS m/z: 1090 $(M+H)^+$, 1112 $(M+Na)^+$.

Phenyl 2-Deoxy-4,6-*O*-*p*-methoxybenzylidene-3-*O*-(tetradecanoyl)-1-thio-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (32) Tetradecanoyl chloride (3.95 g, 16 mmol) was added to a stirred mixture of **31** (5.65 g, 10.0 mmol) and DMAP (489 mg, 4.0 mmol) in pyridine–CH_2Cl_2 (2 : 1) (90 ml) at 0 °C under argon, and the whole was stirred at room temperature for 10 h. The reaction mixture was diluted with CH_2Cl_2, then washed with H_2O, saturated aqueous $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (hexane : AcOEt=3 : 1) to give **32** (7.47 g, 96%), $[\alpha]_D$ −27.2° (c=0.60, $CHCl_3$). IR (Nujol): 1745, 1713, 1542 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.9 Hz, $-CH_3$), 1.25 (20H, br s, $-CH_2-$), 1.58 (2H, br t, $-CH_2-$), 1.98—2.53 (12H, m, $-CH_2-$), 3.45—3.54 (1H, m, H-5), 3.63—3.82 (3H, m, H-2, 4, 6), 3.76 (3H, s, OCH_3), 4.32 (1H, dd, J=4.9, 10.6 Hz, H-6), 4.74, 4.83 (each 1H, d, J=11.9 Hz, CH_2CCl_3), 4.76 (1H, d, J=10.6 Hz, H-1), 5.39 (1H, t, J=9.6 Hz, H-3), 5.44 (1H, s, CHPh), 5.92 (1H, d, J=9.9 Hz, NH), 6.82 (2H, d, J=8.9 Hz, Ph), 7.27—7.48 (7H, m, Ph).

Phenyl 4,6-di-*O*-Acetyl-2-Deoxy-3-*O*-(tetradecanoyl)-1-thio-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (33) A mixture of **32** (1.37 g, 1.76 mmol) and 90% AcOH (50 ml) was stirred at room temperature for 10 h. The reaction mixture was concentrated under reduced pressure and the residue was chromatographed on a silica gel column (hexane : AcOEt=1 : 1) to give the diol (1.13 g, 98%), which was dissolved in pyridine (6 ml), and to the mixture was added Ac_2O (1.87 g, 1.8.3 mmol) at 0 °C. The mixture was then stirred at room temperature for 5 h, then concentrated under reduced pressure. The residue was diluted with CH_2Cl_2 and washed with H_2O, saturated aqueous $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (hexane : AcOEt=3 : 1) to give **33** (1.21 g, 93%). IR (Nujol): 1753, 1717, 1545 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.9 Hz, $-CH_3$), 1.25 (20H, br s, $-CH_2-$), 1.53 (2H, m, $-CH_2-$), 1.92, 2.07 (each 3H, s, $OCOCH_3$), 2.25 (2H, t, $-CH_2-$), 3.75—3.89 (2H, m, H-2, 5), 4.12—4.26 (2H, m, H-6), 4.75, 4.80 (each 1H, d, J=11.9 Hz, CH_2CCl_3), 4.84 (1H, d, J=10.6 Hz, H-1), 5.03 (1H, t, J=9.6 Hz, H-4), 5.32 (1H, t, J=9.6 Hz, H-3), 5.63 (1H, d, J=9.6 Hz, NH), 7.23—7.53 (5H, m, Ph).

***N*-Tetradecanoyl-*O*-[4,6-di-*O*-acetyl-2-deoxy-3-*O*-tetradecanoyl-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-L-serine Benzyl Ester (34)** In a manner similar to that for **18**, compound **33** (540 mg, 0.73 mmol) was treated with **24** (355 mg, 0.87 mmol), NBS (519 mg, 2.92 mmol), iodine (740 mg, 2.92 mmol) and TBAOTf (56 mg, 0.146 mmol) to give **34** (579 mg, 79%), $[\alpha]_D$ +3.8° (c=1.1 $CHCl_3$). IR (Nujol): 1762, 1642, 1587 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (6H, t, J=6.9 Hz, $-CH_3$), 1.25 (40H, br s, $-CH_2-$), 1.41—1.63 (4H, m, $COCH_2CH_2C_{11}H_{23}$), 2.01, 2.05 (each 3H, s, $OCOCH_3$), 2.22—2.28 (4H, m, $-CH_2-$), 3.18—3.29 (1H, m, H-2), 3.49—3.60 (2H, m, H-2, 5), 3.89 (1H, dd, J=2.3, 9.9 Hz, OCH_2CHNH), 4.06—4.13 (1H, m, H-6), 4.20—4.29 (2H, m, H-6, OCH_2CHNH), 4.63—4.80 (3H, H-1, CH_2CCl_3), 4.83—4.86 (1H, m, OCH_2CHNH), 5.03 (1H, t, J=9.6 Hz, H-4), 5.07—5.13 (1H, m, H-3), 5.15, 5.22 (each 1H, d, J=12.2 Hz, $COOCH_2Ph$), 5.88 (1H, d, J=9.6 Hz, NH), 6.47 (1H, d, J=7.9 Hz, NH), 7.36 (5H, s, Ph). ^{13}C-NMR ($CDCl_3$) δ: 100.3 (d, C-1), 154.2, 169.2, 169.5, 170.4, 173.2, 173.4 (s, C=O). Positive FAB-MS m/z: 1035 $(M+H)^+$.

***N*-Tetradecanoyl-*O*-[4,6-di-*O*-acetyl-2-deoxy-3-*O*-tetradecanoyl-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine Benzyl Ester (35)** In a manner similar to that for the synthesis of **19**, **34** (260 mg, 0.25 mmol) was deprotected and acylated with (*R*)-3-tetradecanoyloxytradecanoic acid (114 mg, 0.25 mmol) , HOBt (54 mg, 0.35 mmol), DCC (73 mg, 0.35 mmol) and *N*-methylmorpholine (36 mg, 0.35 mmol) to give **35** (345 mg, 82%), after purification by silica gel column chromatography (CH_2Cl_2 : CH_3COCH_3=50 : 1), $[\alpha]_D$ +1.6° (c=0.64, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (12H, t, J=6.9 Hz, $-CH_3$), 1.25 (78H, br s, $-CH_2-$), 1.48—1.77 (8H, m, $-CH_2-$), 2.00, 2.06 (each 3H, s, $OCOCH_3$), 2.10—2.38 (8H, m, $-CH_2-$), 3.56—3.60 (2H, m, H-2, 5), 3.88 (1H, dd, J=3.0, 11.2 Hz, OCH_2CHNH), 4.05—4.13 (1H, m, H-6), 4.19—4.26 (2H, m, H-6, OCH_2CHNH), 4.75—4.86 (1H, m, OCH_2CHNH), 4.80 (1H, d, J=8.2 Hz, H-1), 4.97—5.33 (5H, m, H-3, 4, $COOCH_2Ph$, $COCH_2CH(OCO)$), 5.92 (1H, d, J=7.9 Hz, NH), 6.75 (1H, d, J=7.9 Hz, NH), 7.35 (5H, s, Ph).

***N*-Tetradecanoyl-*O*-[4,6-di-*O*-acetyl-2-deoxy-3-*O*-tetradecanoyl-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine (36)** A mixture of **35** (40 mg, 0.031 mmol) and palladium–black (40 mg) in MeOH–THF (1 : 1) (5 ml) was hydrogenated at room temperature. The catalyst was filtered off and the filtrate was concentrated under reduced pressure. The residue was chromatographed on a silica gel column (CH_2Cl_2 : MeOH=10:1) to give **36** (37 mg, 99%), $[\alpha]_D$ +1.4° (c=0.56, $CHCl_3$: MeOH=3 : 2). IR (Nujol): 1732, 1671 cm^{-1}. ^{1}H-NMR ($CDCl_3$–CD_3OD) δ: 0.88 (12H, t, J=6.9 Hz, $-CH_3$), 1.25 (78H, br s, $-CH_2-$), 1.43—1.62 (8H, m, $-CH_2-$), 2.01, 2.08 (each 3H, s, $OCOCH_3$), 2.16—2.36 (7H, m, $-CH_2-$), 2.51 (1H, dd, J=14.5, 6.3 Hz, $COCH_2CH(OCO)$), 3.41—3.92 (3H, m, H-2, 5, OCH_2CHNH), 4.01—4.13 (2H, m, H-6, OCH_2CHNH), 4.25—4.31 (2H, m, H-6, OCH_2CHNH), 4.57 (1H, d, J=8.3 Hz, H-1), 5.00 (1H, t, J=9.9, 9.6 Hz, H-4), 5.08—5.16 (1H, m, $COCH_2CH(OCO)$), 5.20 (1H, t, J=9.6 Hz, H-3). Positive FAB-MS m/z: 1208 $(M+H)^+$.

***N*-Tetradecanoyl-*O*-[4,6-di-*O*-acetyl-2-deoxy-3-*O*-tetradecanoyl-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-seryl-β-alanine Benzyl Ester (37)** WSC·HCl (25 mg, 0.13 mmol) and *N*-methylmorpholine (13 mg, 0.13 mmol) were added to a stirred mixture of **36** (120 mg, 0.099 mmol), β-alanine benzyl ester *p*-TsOH (46 mg, 0.13 mmol), *N*-methylmorpholine (13 mg, 0.13 mmol) and HOBt (20 mg, 0.13 mmol) in DMF (6 ml) at 0 °C under argon. The reaction mixture was stirred at the same temperature for 1 h, then at room temperature for 18 h. The reaction

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mixture was poured into ice-cooled water and extracted with AcOEt and the organic layer was washed with brine, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (hexane : AcOEt=1 : 1) to give **37** (104 mg, 76%), $[\alpha]_D$ −5.5° (*c*=0.16, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (12H, t, *J*=6.9 Hz, $-CH_3$), 1.25 (78H, br s, $-CH_2-$), 1.42—1.68 (8H, m, $-CH_2-$), 2.02, 2.08 (each 3H, s, $OCOCH_3$), 2.11—2.35 (7H, m, $-CH_2-$), 2.42 (1H, dd, *J*=14.5, 6.3 Hz, $COCH_2CH(OCO)$), 2.61 (2H, m, $NHCH_2CH_2$), 3.54—3.68 (3H, m, OCH_2CHNH, $NHCH_2CH_2$), 3.69—3.75 (1H, m, H-5), 3.82—3.98 (2H, m, H-2, OCH_2CHNH), 4.10—4.18 (1H, m, H-6), 4.30 (1H, dd, *J*=5.3, 12.2 Hz, H-6), 4.62—4.67 (1H, m, OCH_2CHNH), 4.70 (1H, d, *J*=8.6 Hz, H-1), 5.03—5.26 (5H, m, H-3, 4, CH_2Ph, $COCH_2CH(OCO)$), 6.13 (1H,d, *J*=8.6 Hz, NH), 6.53 (1H, d, *J*=6.6 Hz, NH), 7.05—7.09 (1H, m, NH), 7.36 (5H, br s, Ph). Positive FAB-MS *m/z*: 1369 $(M+H)^+$.

***N*-Tetradecanoyl-*O*-[4,6-di-*O*-acetyl-2-deoxy-3-*O*-tetradecanoyl-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-seryl-β-alanine (38)** A mixture of **37** (100 mg, 0.073 mmol) and palladium–black (100 mg) in THF (7 ml) was hydrogenated at room temperature. The catalyst was filtered off and the filtrate was concentrated under reduced pressure. The residue was chromatographed on a silica gel column (CH_2Cl_2 : MeOH=10:1) to give **38** (74 mg, 79%), $[\alpha]_D$ −4.4° (*c*=0.6, $CHCl_3$: MeOH=3 : 2). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (12H, t, *J*=6.9 Hz, $-CH_3$), 1.25 (78H, br s, $-CH_2-$), 1.44—1.73 (8H, m, $-CH_2-$), 2.02, 2.09 (each 3H, s, $OCOCH_3$), 2.17—2.57 (10H, m, $-CH_2-$, $NHCH_2CH_2$), 3.28—3.39 (2H, m, $NHCH_2CH_2$), 3.45—3.98 (4H, m, H-2, 5, OCH_2CHNH), 4.06—4.17(1H, m, H-6), 4.22—4.36 (1H, m, H-6), 4.42—4.57 (1H, m, OCH_2CHNH), 4.67 (1H, d, *J*=8.3 Hz, H-1), 5.00—5.09 (2H, m, H-4, $COCH_2CH(OCO)$), 5.23 (1H, d, *J*=9.6 Hz, H-3). Positive FAB-MS *m/z*: 1279 $(M+H)^+$.

***N*-Tetradecanoyl-*O*-[2-deoxy-3-*O*-tetradecanyl-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-seryl-β-alanine (13)** A mixture of **38** (25 mg, 0.0195 mmol) and concentrated NH_4OH (1 ml) in MeOH–THF (1:1) (20 ml) was stirred for 20 h at room temperature. After removal of the solvent, the residue was chromatographed on a silica gel column (CH_2Cl_2 : MeOH : H_2O=12 : 8 : 1) to give **13** (1.1 mg, 5%), **8** (16 mg, 83%) and **30** (9 mg, 6%). **13**: $[\alpha]_D$ −8.2° (*c*=0.16, $CHCl_3$: MeOH=3 : 2). Positive FAB-MS *m/z*: 1195 $(M+H)^+$, 1217 $(M+Na)^+$.

1,3,4-Tri-*O*-acetyl-2-deoxy-6-*O*-tosyl-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (40) A solution of *p*-toluenesulfonyl chloride (9.68 g, 50.8 mmol) in CH_2Cl_2 (50 ml) was added to a stirred mixture of **39** (10.0 g, 28.2 mmol) in pyridine (25 ml) at 0 °C. After stirring at room temperature for 2 h, Ac_2O (43.2 g, 423 mmol) was added to the reaction mixture at 0 °C and the whole was stirred at room temperature for 5 h and concentarated under reduced pressure. The residue was chromatographed on a silica gel column (hexane : AcOEt=2 : 1) to give **40** (13.5 g, 75%). ^{1}H-NMR ($CDCl_3$) δ: 2.01, 2.04, 2.16 (each 3H, s, $OCOCH_3$), 2.45 (3H, s, CH_3), 4.62, 4.80 (each 1H, d, *J*=11.9 Hz, CH_2CCl_3), 7.35 (2H, d, *J*=7.9 Hz, Ts), 7.76 (2H, d, *J*=8.3 Hz, Ts).

1,3,4-Tri-*O*-acetyl-6-azido-2,6-dideoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (41) A mixture of **40** (127 mg, 0.20 mmol), NaN_3 (65 mg,1.0 mmol) and 18-crown-6 (18 mg, 0.067 mmol) in DMF (5 ml) was stirred at 40—50 °C for 40 h. The precipitate was filtered off and the filtrate was concentrated under reduced pressure. The residue was chromatographed on a silica gel column (hexane : AcOEt=2 : 1) to give **41** (62 mg, 61%). IR (Nujol): 2095, 1757, 1662 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.05, 2.07, 2.21 (each 3H, s, $OCOCH_3$), 4.63, 4.82 (each 1H, d, *J*=11.9 Hz, CH_2CCl_3).

Phenyl 3,4-Di-*O*-acetyl-6-azido-2,6-dideoxy-1-thio-2-(2,2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (42) $BF_3 \cdot OEt_2$ (1.61 g, 11.4 mmol) was added to a stirred mixture of **41** (2.11 g, 4.55 mmol) and PhSH (598 mg, 5.92 mmol) in CH_2Cl_2 (25 ml) at 0 °C under argon and the mixture was stirred at room temperature for 24 h. The reaction mixture was washed with saturated aqueous $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on a silica gel column (hexane : AcOEt=4 : 1) to give **42** (1.43 g, 61%). IR (neat): 2100, 1745 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.99, 2.01 (each 3H, s, $OCOCH_3$), 3.33—3.45 (2H, m, -6), 3.64—3.75 (2H, m, H-2, 5), 4.73, 4.89 (each 1H, d, *J*=11.9 Hz, CH_2CCl_3), 4.96 (1H, d, *J*=9.9 Hz, H-4), 5.30 (1H, t, *J*=9.9 Hz, H-3).

Phenyl 3,4-Di-*O*-acetyl-6-(*tert*-buthoxycarbonylamino)-2,6-dideoxy-1-thio-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside (43) A mixture of **42** (204 mg, 0.40 mmol), PtO_2 (100 mg), and $(Boc)_2O$ (156 mg, 0.72 mmol) in AcOEt (5 ml) at 40—50 °C for 18 h under hydrogen. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The residue was chromatograped on a silica gel column (CH_2Cl_2 : CH_3COCH_3=20 : 1) to give **43** (117 mg, 47%), $[\alpha]_D$ +9.6° (*c*= 0.84, $CHCl_3$). IR (neat): 1765, 1662 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ:1.44 (9H, s, Boc), 1.99, 2.01 (each 3H, s, $OCOCH_3$), 3.19—3.75 (4H, m, H-2, 5, 6), 4.72—4.99 (4H, m, H-1, 4, CH_2CCl_3), 5.25 (1H, t, *J*=9.6 Hz, H-3), 5.52 (1H, d, *J*=9.2 Hz, NH), 7.24—7.99 (5H, m, Ph). Positive FAB-MS *m/z*: 631 $(M+3)^+$.

***N*-Tetradecanoyl-*O*-[3,4-di-*O*-acetyl-6-(*tert*-buthoxycarbonylamino)-2,6-dideoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-L-serine Benzyl Ester (44)** In a manner similar to that for **18**, **43** (110 mg, 0.175 mmol) was treated with **24** (85 mg, 0.21 mmol), NBS (125 mg, 0.70 mmol), iodine (177 mg, 0.70 mmol) and TBAOTf (13 mg, 0.035 mmol) to give **44** (116 mg, 36%), after purification by silica gel column chromatography (CH_2Cl_2 : CH_3COCH_3=10 : 1), $[\alpha]_D$ +8.2° (*c*=0.76, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, *J*=6.9 Hz, $-CH_3$), 1.25 (20H, br s, $-CH_2-$), 1.44 (9H, s, Boc), 1.61—1.71 (2H, m, $COCH_2CH_2C11H_{23}$), 2.01, 2.04 (each 3H, s, $OCOCH_3$), 2.22 (2H, t, $-CH_2-$), 3.23—3.59 (4H, m, H-2, 5, 6), 3.81—3.89 (1H, m, OCH_2CHNH), 4.20—4.25 (1H, m, OCH_2CHNH), 4.40—4.91 (5H, H-1, 4, CH_2CCl_3, OCH_2CHNH), 5.11—5.30 (4H, m, H-3, CH_2Ph, NH), 6.48 (1H, br s, NH), 7.37 (5H, s, Ph). Positive FAB-MS *m/z*: 927 $(M+3)^+$.

***N*-Tetradecanoyl-*O*-[3,4-di-*O*-acetyl-6-(*tert*-buthoxycarbonylamino)-2,6-dideoxy-2-[(*R*)-3-tetradecanoyloxytetraecanoylamino]-β-D-glucopyranosyl]-L-serine Benzyl Ester (45)** In a manner similar that for **19**, **44** (66 mg, 0.071 mmol) was deprotected and acylated with (*R*)-3-tetradecanoyloxytradecanoic acid (32 mg, 0.071 mmol), DEPC (12 mg, 0.071 mmol) and TEA (7 mg, 0.071 mmol) to give **45** (53 mg, 63%), after purification by silica gel column chromatography (CH_2Cl_2 : CH_3COCH_3=50 : 1), $[\alpha]_D$ −6.5° (c=0.40, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (9H, t, *J*=6.9 Hz, $-CH_3$), 1.25 (58H, br s, $-CH_2-$), 1.44 (9H, s, Boc), 1.47—1.78 (6H, m, $-CH_2-$), 2.01, 2.03 (each 3H, s, $OCOCH_3$), 2.11—2.36 (8H, m, $-CH_2-$), 3.16—3.29 (1H, m, H-6), 3.30—3.47 (2H, m, H-5, 6), 3.56—3.68 (1H, m, H-2), 3.85 (1H, dd, *J*=3.0, 10.9 Hz, OCH_2CHNH), 4.22 (1H, dd, *J*=3.3, 10.9 Hz, OCH_2CHNH), 4.70 (1H, d, *J*=7.9 Hz, H-1), 4.77—5.26 (6H, m, H-3, 4, CH_2Ph, $COCH_2CH(OCO)$), 5.92 (1H, d, *J*=7.9 Hz, NH), 6.76 (1H, d, *J*=7.9 Hz, NH), 7.44 (5H, s, Ph). Positive FAB-MS *m/z*: 1187 $(M+H)^+$.

***N*-Tetradecanoyl-*O*-[3,4-di-*O*-acetyl-6-(*tert*-buthoxycarbonylamino)-2,6-dideoxy-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine (14)** A mixture of **45** (21 mg, 0.018 mmol) and palladium–black (20 mg) in THF (5 ml) was hydrogenated at room temperature for 20 h. The catalyst was filtered off and the filtrate was concentrated under reduced pressure. The residue was chromatographed on a silica gel column (CH_2Cl_2 : MeOH=10 : 1) to give **14** (18 mg, 93%), $[\alpha]_D$ +5.4° (*c*=0.34, $CHCl_3$: MeOH=3 : 2). IR(Nujol): 1751, 1648 cm^{-1}. ^{1}H-NMR ($CDCl_3$–CD_3OD) δ: 0.88 (9H, t, *J*=6.9Hz, $-CH_3$), 1.25 (58H, br s, $-CH_2-$), 1.44 (9H, s, Boc), 1.51–1.77 (6H, m, $-CH_2-$), 2.01, 2.05 (each 3H, s, $OCOCH_3$), 2.16—2.31 (7H, m, $-CH_2-$), 2.51 (1H, dd, *J*=14.5, 5.6 Hz, $COCH_2CH(OCO)$), 3.24—4.12 (6H, m, H-2, 5, 6, OCH_2CHNH), 4.35 (1H, m, OCH_2CHNH), 4.47 (1H, d, *J*=8.3 Hz, H-1), 4.88 (1H, t, *J* =9.6 Hz, H-4), 5.08—5.14 (2H, m, H-3, $COCH_2CH(OCO)$). ^{13}C-NMR ($CDCl_3$–CD_3OD) δ: 101.3 (d, C-1), 156.7, 170.3, 171.0, 171.4, 174.1, 174.4, 175.9 (s, C=O). Positive FAB-MS *m/z*: 1097 $(M+H)^+$, 1119 $(M+Na)^+$.

***N*-Tetradecanoyl-*O*-[6-(*tert*-buthoxycarbonylamino)-2,6-dideoxy-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine (15)** A mixture of **14** (11 mg, 0.01 mmol) and concentrated NH_4OH (0.3 ml) in MeOH–THF (1 : 4) (5 ml) was stirred for 20 h at room temperature. After removal of the solvent, the residue was chromatographed on a silica gel column (CH_2Cl_2 : MeOH : H_2O=12 : 8 : 1) to give **15** (8 mg, 79%), $[\alpha]_D$ −9.4° (*c*=0.1, $CHCl_3$: MeOH=3 : 2). ^{1}H-NMR ($CDCl_3$–CD_3OD) δ: 0.88 (9H, t, *J*=6.9 Hz, $-CH_3$), 1.26 (58H, br s, $-CH_2-$), 1.45 (9H, s, Boc), 1.53—1.67 (6H, m, $-CH_2-$), 2.18—2.35 (7H, m, $-CH_2-$), 2.49—2.55 (1H, m, $COCH_2CH(OCO)$), 3.25—4.19 (9H, m, H-2, 3, 4, 5, 6, OCH_2CHNH, OCH_2CHNH), 4.32 (1H, d, *J*=8.6 Hz, H-1), 5.20—5.34 (1H, m, $COCH_2CH(OCO)$). ^{13}C-NMR ($CDCl_3$–CD_3OD) δ: 100.8 (d, C-1), 157.4, 172.2, 174.0, 174.2, 175.7 (s, C=O). Positive FAB-MS *m/z*: 1013 $(M+H)^+$, 1035 $(M+Na)^+$.

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