Lipid A and Related Compounds. XXXI.[1] Synthesis of Biologically Active *N*-Acylated L-Serine-Containing D-Glucosamine 4-Phosphate Derivatives of Lipid A

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New *N*-acylated L-serine-containing non-phosphorylated and phosphorylated D-glucosamine derivatives structurally corresponding to the lipid A disaccharide backbone were synthesized. Compounds 2, 4 and 5 exhibited potent mitogenic activity. Further, compound 5 showed nitric oxide (NO) productivity.

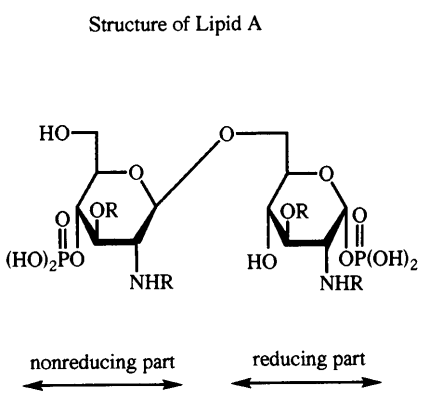
Key words *N*-acylated L-serine; D-glucosamine 4-phosphate; lipid A analog; lipoamino acid; mitogenic activity; nitric oxide productivity

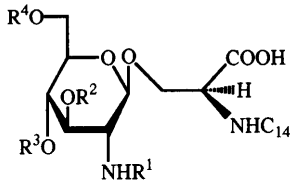
Lipid A is well known for being responsible for the expression of many of the biological activities, such as endotoxicity, adjuvanticity, antitumor activity and so on, of lipopolysaccharide (LPS) of gram-negative bacteria.[2] Lipid A consists of a D-glucosaminyl-β(1→6)-D-glucosamine disaccharide carrying two phosphates and several fatty acids residues,[3] as indicated in Chart 1. Among the various synthetic lipid A analogs, D-glucosamine-4-phosphate analogs of the non-reducing unit of lipid A showed many of the biological activities of LPS.[4] Recently, various novel acyclic analogs related to lipid A partial structure have been synthesized.[5] We have already reported the synthesis of *N*-acylated L-serine-containing non-phosphorylated D-glucosamine derivatives (**1**—**5**) and a phosphorylated D-glucosamine derivative (**6**) structurally similar to the lipid A disaccharide backbone, with the aim of clarifying the structure–activity relationships between the molecular structure and the biological activity of lipid A.[6] In this paper, we describe the details of the synthesis of *N*-acylated L-serine-containing D-glucosamine analogs (**1**—**6**), and their biological effects.

First, we synthesized the non-phosphorylated D-glucosamine-derived lipid A analogs (**1**—**5**) to examine whether or not the phosphate group is required in lipid A analogs for biological activity. Compounds **1**, **2** and **3** were easily prepared from a D-glucosamine derivative (**7**) and lipoamino acid (**8**) as indicated in Chart 2.

Condensation of **7** with **8** in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) and molecular sieves 4 Å in CH_2Cl_2 gave the β-glycoside **9** in 87% yield. The β-configuration of **9** was determined from the coupling constant value (8.3 Hz) of the signal due to the anomeric proton in the proton magnetic resonance (^{1}H-NMR) spectrum of **9**. After cleavage of the chloroacetyl group of **9** with thiourea, diisopropylethylamine (DIPEA) and molecular sieves 4 Å in tetrahydrofuran (THF), acylation of the resulting product with tetradecanoic acid or optically active (*R*)-3-tetradecanoyloxytetradecanoic acid[7] in the presence of diethylphosphorocyanidate (DEPC) and triethylamine (TEA) in dimethylformamide (DMF) gave **11a** and **11b** in two steps in yields of 70% and 71%, respectively. The benzyl groups of **11a** and **11b** were removed by hydrogenolysis over palladium-black at room temperature in MeOH to afford the desired compounds **1** and **2** in yields of 86% and 79%, respectively. Removal of acetyl groups in **1** by treatment with concentrated NH_4OH in MeOH gave the alcohol **3** in 57% yield.

Next, compounds **4** and **5** were synthesized *via* the route shown in Chart 3. The diol **12**[8] was benzylated with benzyl trichloroacetoimidate in the presence of a catalytic amount





1 : $R^1 = C_{14}$, $R^2 = R^3 = R^4 = Ac$

2 : $R^1 = C_{14}OC_{14}$, $R^2 = R^3 = R^4 = Ac$

3 : $R^1 = C_{14}$, $R^2 = R^3 = R^4 = H$

4 : $R^1 = R^2 = C_{14}OC_{14}$, $R^3 = R^4 = H$

5 : $R^1 = C_{14}OC_{14}$, $R^2 = C_{14}$, $R^3 = R^4 = H$

6 : $R^1 = R^2 = C_{14}OC_{14}$, $R^3 = (HO)_2P(O)$, $R^4 = H$

C_{14}: $CH_3(CH_2)_{12}C(O)$-

$C_{14}OC_{14}$: $CH_3(CH_2)_{10}\underset{(R)}{C}HCH_2C(O)$-
$CH_3(CH_2)_{12}C(O)O$

Chart 1

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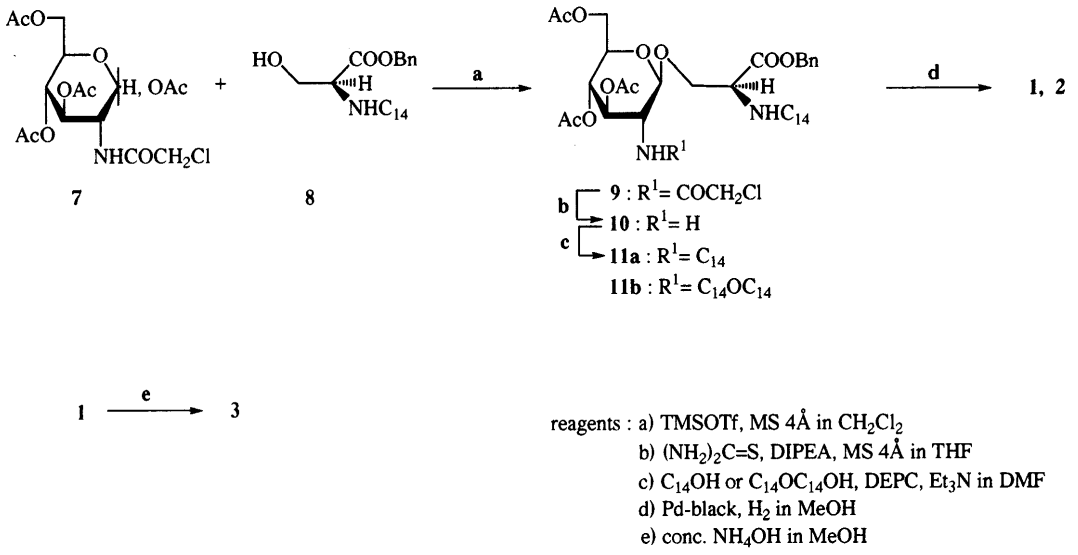
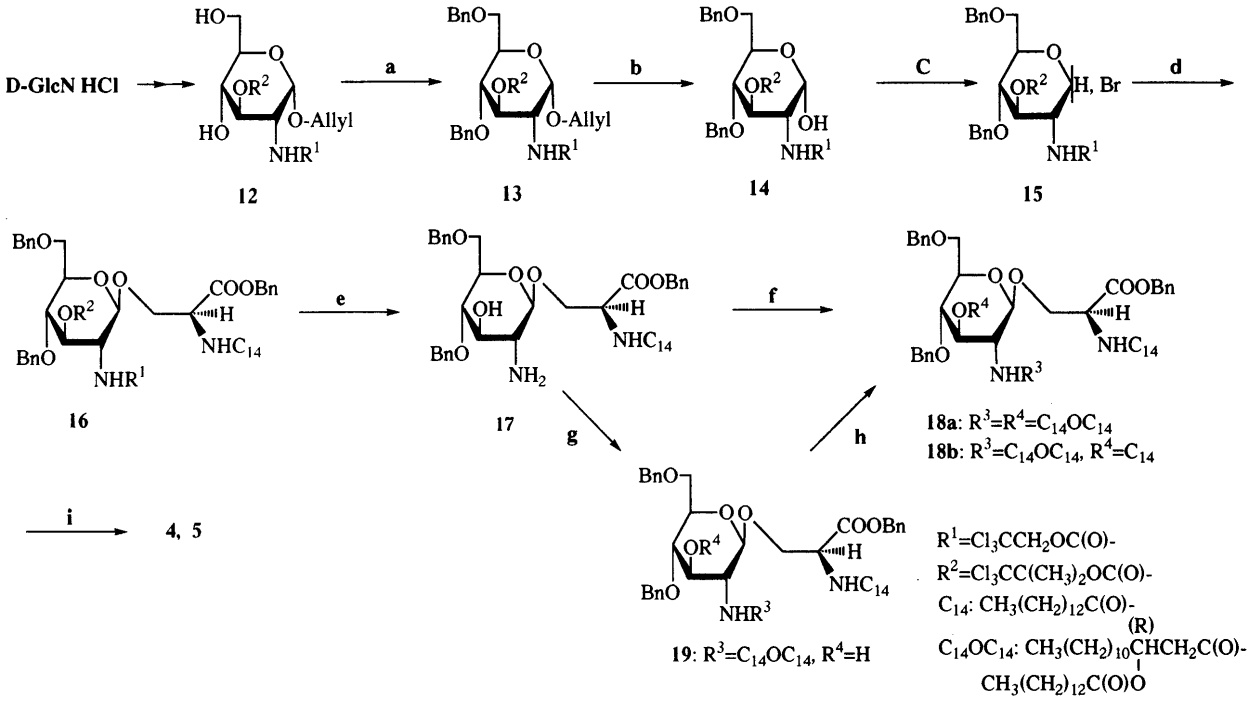


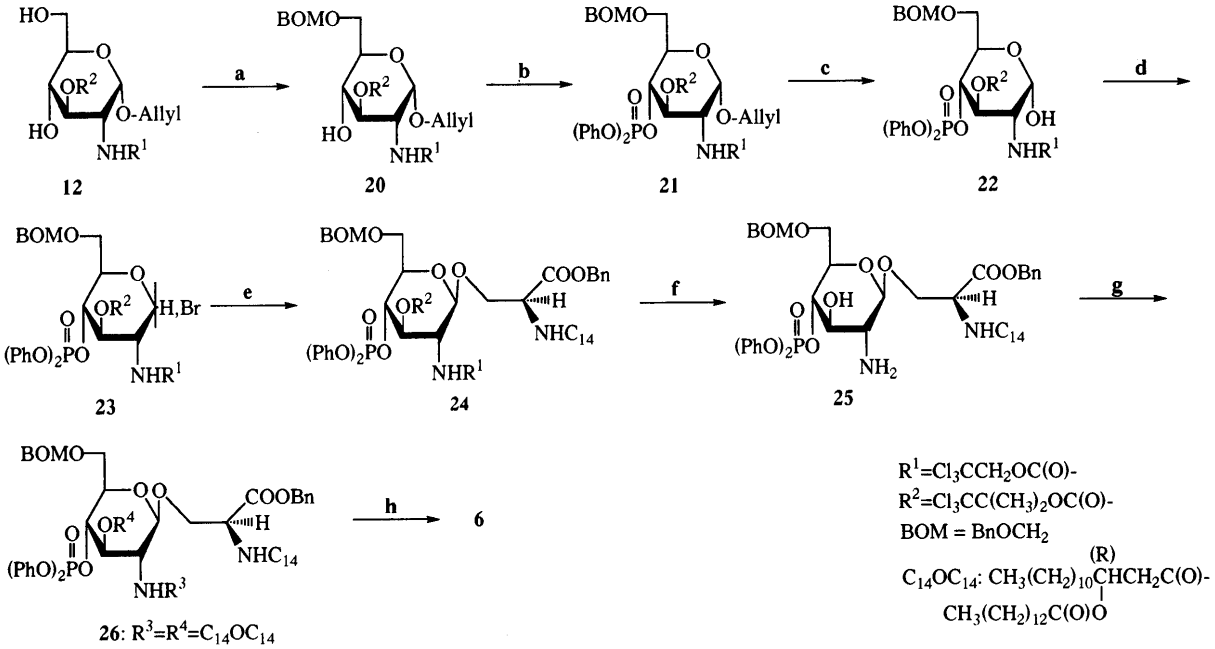
Chart 2



reagents : a) $Cl_3CC(OBn)=NH$, CF_3SO_3H in CH_2Cl_2-cyclohexane (1:2) ; b) 1) $[CODIr(PMePh_2)_2]PF_6$ in THF ; 2) I_2, pyridine in THF-H_2O ; c) $SOBr_2$ in CH_2Cl_2-DMF (10:1) ; d) 8, $HgBr_2$, MS 4Å in CH_2Cl_2 ; e) Zn in HOAc ; f) $C_{14}OC_{14}OH$, DCC-DMAP in CH_2Cl_2 ; g) $C_{14}OC_{14}OH$, DCC in CH_2Cl_2 ; h) $C_{14}Cl$, pyridine-DMAP in CH_2Cl_2 ; i) Pd-black, H_2 in MeOH-THF (2:1).

Chart 3

of trifluoromethanesulfonic acid in CH_2Cl_2–cyclohexane to give the dibenzyl ether **13** in 62% yield. Removal of the allyl group with iridium catalyst, followed by hydrolysis with I_2–H_2O–pyridine gave the alcohol **14** in 60% yield. Bromination of **14** with the Vilsmeier reagent, generated *in situ* by use of thionyl bromide and DMF,[9] gave the bromide **15** in quantitative yield. Condensation of **15** and lipoamino acid **8** with $HgBr_2$ as a promoter and molecular sieves 4 Å in CH_2Cl_2 gave the β-glycoside **16** in 48% yield; the configuration of the glycosidic linkage was assigned as β form on the basis of the ^{1}H-NMR data ($J_{1,2}=8.1$ Hz), as in the case of **9**. Treatment of **16** with activated zinc powder in acetic acid gave the crude amino alcohol **17** in quantitative yield. The key intermediate **17** thus obtained was acylated with optically active (*R*)-3-tetradecanoyloxytetradecanoic acid in the presence of dicyclohexylcarbodiimide (DCC) and 4-dimethylaminopyridine (DMAP) to give **18a** in 48% yield. Finally, catalytic hydrogenolysis using palladium-black in MeOH–THF gave the desired compound **4** in 66% yield after purification followed by lyophilization from dioxane. Similarly, compound **5**, bearing the (*R*)-3-tetradecanoyloxytetradecanoyl group at *N*-2 and the tetradecanoyl group at *O*-3 of the D-glucosamine skeleton of the GLA-27



reagents : a) BOMCl, TMU in CH_2Cl_2 ; b) $(PhO)_2P(O)Cl$, pyridine-DMAP in CH_2Cl_2 ; c) 1) $[CODIr(PMePh_2)_2]PF_6$ in THF ; 2) I_2, pyridine in THF-H_2O ; d) $SOBr_2$ in CH_2Cl_2-DMF (10:1) ; e) **8**, $HgBr_2$, MS 4Å in CH_2Cl_2 ; f) Zn in HOAc ; g) $C_{14}OC_{14}OH$, DCC-DMAP in CH_2Cl_2 ; h) 1) Pd-black, H_2 in MeOH ; 2) PtO_2, H_2 in MeOH.

Chart 4

type,[10] was synthesized stepwise by successive acylation of the amino and hydroxy groups of **17**. Compound **17** was first acylated at the amino group with (*R*)-3-tetradecanoyloxytetradecanoic acid and DCC to give **19** in 59% yield. The remaining hydroxy group of **19** was acylated with tetradecanoyl chloride, pyridine–DMAP to give **18b** in 57% yield. Finally, deprotection of **18b** as described for the preparation of **4** gave the desired product **5** in 68% yield after purification followed by lyophilization from dioxane.

Next, the synthesis of the phosphorylated D-glucosamine-derived lipid A analog **6** was carried out as follows (Chart 4). The 6-hydroxy group of **12** was selectively protected with benzyloxymethyl chloride and 1,1,3,3-tetramethylurea (TMU) in CH_2Cl_2 to give **20** in 66% yield. The phosphorylation of **20** with diphenyl phosphorochloridate in the presence of pyridine–DMAP in CH_2Cl_2 gave compound **21** in 89% yield. Deprotection of the allyl group of **21** as described for the preparation of **14** gave compound **22** in 81% yield. Condensation of **8** and the bromide **23**, freshly prepared from **22** and Vilsmeier reagent ($SOBr_2$–DMF), in the presence of $HgBr_2$ afforded the coupling compound **24** in 33% yield. Deprotection of 2,2,2-trichloroethoxycarbonyl (TCEC) and 2,2,2-trichloro-*tert*-butoxycarbonyl (TCBOC) groups of **24** with activated zinc powder in acetic acid gave the crude amino alcohol **25** in almost quantitative yield. The simultaneous acylation of the amino and hydroxy groups of **25** with (*R*)-3-tetradecanoyloxytetradecanoic acid and DCC–DMAP gave **26** in 56% yield. Finally, the protective benzyl and phenyl groups of **26** were removed by stepwise hydrogenolysis catalyzed by palladium-black and then platinum oxide in MeOH to give the expected compound **6** in 44% yield after purification followed by lyophilization from dioxane.

The structures of all compounds were characterized by ^{1}H-NMR spectroscopy, as well as infrared (IR) spectroscopy, elemental analyses, and fast-atom bombardment (FAB) mass spectroscopy.

In a preliminary examination of the biological activities, compound **5** was about twice as mitogenic towards the splenocytes of C3H/He mice, while **2**, **4** exhibited the same level, in comparison with the original acyl derivatives of D-glucosamine 4-phosphate.[11] Further, compound **5** showed about twice the NO-inducing activity of the above original compound.[12]

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-SX 102 spectrometer. ^{1}H-NMR spectra were taken on a JEOL JNM-GX 270 (270 MHz) spectrometer. 1H chemical shifts (δ) are given in ppm relative to that of Me_4Si ($\delta=0$) 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 and then heating.

***N*-Tetradecanoyl-*O*-(3,4,6-tri-*O*-acetyl-2-chloroacetylamino-2-deoxy-β-D-glucopyranosyl)-L-serine Benzyl Ester (9)** A solution of **7** (635 mg, 1.5 mmol) and *N*-tetradecanoyl-L-serine benzyl ester **8** (730 mg, 1.80 mmol) in anhydrous CH_2Cl_2 (20 ml) was stirred for 1 h at room temperature under argon in the presence of 4 Å powdered molecular sieves (1.0 g). The mixture was cooled to 0 °C, then TMSOTf (170 mg, 0.75 mmol) was added. Stirring was continued at room temperature for 16h. After removal of the insoluble materials by filtration, the filtrate was washed successively with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated *in vacuo*. The residue was purified by silica gel column chromatography using CH_2Cl_2–CH_3COCH_3 (20 : 1) to

give **9** (1.0 g, 87%) as a white powder, mp 144—147 °C, $[\alpha]_D$ + 8.7° (c = 1.17, $CHCl_3$). IR (KBr): 3410, 2924, 1748, 1674, 738 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, J = 6.9 Hz, $-CH_3$), 1.26 (20H, br s, $-CH_2-$), 1.64 (2H, br s, $CH_2CH_2C_{11}H_{23}$), 2.02, 2.03, 2.06 (each 3H, s, $OCOCH_3 \times 3$), 2.21—2.36 (2H, m, $CH_2C_{12}H_{25}$), 3.56—3.64 (2H, m, H-2, H-5), 3.90 (1H, dd, J = 2.6, 10.9 Hz, OCH_2CHN), 4.02 (2H, s, $COCH_2Cl$), 4.10 (1H, dd, J = 2.3, 10.2 Hz, H-6), 4.25 (2H, m, H-6, OCH_2CHN), 4.80 (1H, m, OCH_2CHN), 4.87 (1H, d, J = 8.3 Hz, H-1), 5.03 (1H, t, J = 9.6 Hz, H-4), 5.15, 5.22 (each 1H, d, J = 12.2 Hz, OCH_2Ph), 5.32 (1H, t, J = 10.1 Hz, H-3), 6.50 (1H, d, J = 7.9 Hz, NH), 6.57 (1H, d, J = 7.9 Hz, NH), 7.36 (5H, m, Ph). Positive FAB-MS m/z: 769 $(M+H)^+$.

***N*-Tetradecanoyl-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-tetradecanoylamino-β-D-glucopyranosyl)-L-serine Benzyl Ester (11a)** Thiourea (114 mg, 1.5 mmol) was added to a solution of **9** (230 mg, 0.3 mmol), diisopropylethylamine (194 mg, 1.5 mmol), and 4 Å powdered molecular sieves (300 mg) in THF (10 ml) at 40—50 °C. The mixture was stirred at the same temperature for 16 h. The insoluble materials were filtered off, and the filtrate was evaporated *in vacuo*. The resulting powder and myristic acid (64 mg, 0.28 mmol) were dissolved in DMF (10 ml), and DEPC (46 mg, 0.28 mmol) and TEA (28 mg, 0.28 mmol) were added to the solution with ice cooling under argon. The reaction mixture was stirred for 16 h, diluted with CH_2Cl_2, and then washed successively with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated *in vacuo*. The residue was purified by silica gel column chromatography using CH_2Cl_2–CH_3COCH_3 (20 : 1) to give **11a** (190 mg, 70%) as a white powder, mp 164—166 °C, $[\alpha]_D$ −0.9° (c = 1.03, $CHCl_3$). IR (KBr): 3344, 2920, 1743, 1639, 757 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (6H, t, J = 6.9 Hz, $-CH_3$), 1.25 (40H, br s, $-CH_2-$), 1.55 (4H, br s, $CH_2CH_2C_{11}H_{23} \times 2$), 2.02, 2.05, 2.07 (each 3H, s, $OCOCH_3 \times 3$), 2.19—2.34 (4H, m, $CH_2C_{12}H_{25} \times 2$), 3.58—3.64 (2H, m, H-2, H-5), 3.87 (1H, dd, J = 3.3, 10.9 Hz, OCH_2CHN), 4.09 (1H, dd, J = 2.0, 12.2 Hz, H-6), 4.20—4.27 (2H, m, H-6, OCH_2CHN), 4.79—4.83 (1H, m, OCH_2CHN), 4.81 (1H, d, J = 8.2 Hz, H-1), 5.02 (1H, t, J = 9.6 Hz, H-4), 5.14, 5.21 (each 1H, d, J = 12.2 Hz, CH_2Ph), 5.32 (1H, t, J = 10.1 Hz, H-3), 5.52 (1H, d, J = 7.9 Hz, NH), 6.62 (1H, d, J = 8.2 Hz, NH), 7.54 (5H, m, Ph). Positive FAB-MS m/z: 904 $(M+H)^+$.

***N*-Tetradecanoyl-*O*-[3,4,6-tri-*O*-acetyl-2-deoxy-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine Benzyl Ester (11b)** As described for **11a**, compound **9** (184 mg, 0.24 mmol) was treated with thiourea (91 mg, 1.2 mmol), diisopropylethylamine (155 mg, 1.2 mmol) and 4 Å powdered molecular sieves (300 mg), and the resulting powder was treated with (*R*)-3-tetradecanoyloxytetradecanoic acid (109 mg, 0.24 mmol) in the presence of DEPC (39 mg, 0.24 mmol) and TEA (24 mg, 0.24 mmol). This product was purified by silica gel column chromatography using CH_2Cl_2–CH_3COCH_3 (20 : 1) to give **11b** (192 mg, 71%) as a white powder, mp 148—150 °C, $[\alpha]_D$ −0.3° (c = 0.91, $CHCl_3$). IR (KBr): 3286, 2916, 1745, 1648 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (9H, t, J = 6.9 Hz, $-CH_3$), 1.24 (58H, br s, $-CH_2-$), 1.61 (6H, br s, $-CH_2-$), 2.02, 2.05, 2.07 (each 3H, s, $OCOCH_3 \times 3$), 2.18—2.38 (6H, m, $CH_2C_{12}H_{25}$, $NHCOCH_2CH(OCOCH_2)$), 3.54—3.61 (2H, m, H-2, 5), 3.90 (1H, dd, J = 3.0, 11.2 Hz, OCH_2CHN), 4.08 (1H, dd, J = 2.0, 12.2 Hz, H-6), 4.20—4.26 (2H, m, H-6, OCH_2CHN), 4.84 (1H, m, OCH_2CHN), 4.87 (1H, d, J = 8.3 Hz, H-1), 4.97—5.03 (2H, m, H-3, $NHCOCH_2CH(OCO)$), 5.13, 5.21 (each 1H, d, J = 12.0 Hz, CH_2Ph), 5.23 (1H, t, J = 10.6 Hz, H-3), 5.95 (1H, d, J = 7.9 Hz, NH), 6.76 (1H, d, J = 8.2 Hz, NH), 7.35 (5H, m, Ph). Positive FAB-MS m/z: 1130 $(M+H)^+$.

***N*-Tetradecanoyl-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-tetradecanoylamino-β-D-glucopyranosyl)-L-serine (1)** Palladium-black (150 mg) was added to a solution of **11a** (172 mg, 0.19 mmol) in MeOH (15 ml), and the mixture was stirred under a hydrogen atmosphere for 16 h at room temperature. The catalyst was filtered off and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography using CH_2Cl_2–MeOH (3 : 1) to give **1** (133 mg, 86%) as a white powder, $[\alpha]_D$ + 7.9° (c = 1.0, CH_2Cl_2 : MeOH = 5 : 1). 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 (40H, br s, $-CH_2-$), 1.57 (4H, br s, $CH_2CH_2C_{11}H_{23} \times 2$), 2.01, 2.05, 2.09 (each 3H, s, $OCOCH_3 \times 3$), 2.13—2.24 (4H, m, $CH_2C_{12}H_{25} \times 2$), 3.62—3.69 (1H, m, H-5), 3.86—3.97 (2H, m, H-2, OCH_2CHNH), 4.09—4.14 (2H, m, H-6, OCH_2CHNH), 4.27—4.35 (2H, m, H-6, OCH_2CHNH), 4.59 (1H, d, J = 8.3 Hz, H-1), 5.01 (1H, t, J = 9.6 Hz, H-4), 5.18 (1H, t, J = 9.6 Hz, H-3). Positive FAB-MS m/z: 814 $(M+H)^+$, 836 $(M+Na)^+$.

***N*-Tetradecanoyl-*O*-[3,4,6-tri-*O*-acetyl-2-deoxy-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine (2)** As described for **1**, compound **11b** (113 mg, 0.1 mmol) was subjected to hydrogenolysis over palladium-black (100 mg) to give **2** (82 mg, 79%) as a white solid, 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, $OCOCH_3 \times 3$), 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*-(2-deoxy-2-tetradecanoylamino-β-D-glucopyranosyl)-L-serine (3)** Compound **1** (98 mg, 0.12 mmol) was dissolved in a solution of concentrated NH_4OH (5 ml) in MeOH (10 ml). The mixture was stirred for 7 h, and the solvent was removed by evaporation. The residue was purified by silica gel column chromatography using CH_2Cl_2–MeOH (3 : 1) to give **3** (47 mg, 57%) as a white solid, mp 158—162 °C, $[\alpha]_D$ −1.4° (c = 0.52, $CHCl_3$: MeOH = 1 : 1). IR (KBr): 3282, 2921, 1748, 1648 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 0.88 (6H, t, J = 6.9 Hz, $-CH_3$), 1.24 (40H, br s, $-CH_2-$), 1.58 (4H, br s, $CH_2CH_2C_{11}H_{23} \times 2$), 2.03—2.21 (4H, m, $CH_2C_{12}H_{25} \times 2$). Positive FAB-MS m/z: 688 $(M+H)^+$, 710 $(M+Na)^+$.

Allyl 4,6-Di-*O*-benzyl-2-deoxy-3-*O*-(2,2,2-trichloro-*tert*-butoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (13) Trifluoromethanesulfonic acid (80 mg, 0.53 mmol) was added to a solution of **12** (1.60 g, 2.68 mmol) and benzyl 2,2,2-trichloroacetoimidate (203 mg, 8.04 mmol) in CH_2Cl_2–cyclohexane (1 : 2) (30 ml) at 0 °C under argon, and the mixture was stirred for 20 h at room temperature. MeOH was added and the insoluble materials were removed by filtration. The filtrate was washed with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated *in vacuo*. The residue was purified by silica gel column chromatography using hexane–AcOEt (10 : 1) to give **13** (1.30 g, 62%) as a white powder, mp 97—100 °C, $[\alpha]_D$ +40.2° (c = 2.30, $CHCl_3$). IR (KBr): 1752, 1731, 719, 695 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.88, 1.89 (each 3H, s, TCBOC), 3.68 (1H, dd, J = 11.0, 1.5 Hz, H-6), 3.78 (1H, dd, J = 11.0, 3.5 Hz, H-6), 3.87 (1H, t, J = 10.5 Hz, H-4), 3.99 (1H, dd, J = 12.5, 5.5 Hz, $OCH_2CH=CH_2$), 4.09 (1H, m, H-2), 4.18 (1H, dd, J = 12.5, 5.5 Hz, $OCH_2CH=CH_2$), 4.47, 4.69 (each 1H, d, J = 11.0 Hz, CH_2CCl_3), 4.50, 4.66 (each 1H, d, J = 12.0 Hz, OCH_2Ph), 4.62, 4.77 (each 1H, d, J = 12.0 Hz, OCH_2Ph), 4.95 (1H, d, J = 3.5 Hz, H-1), 5.19—5.30 (2H, m, $OCH_2CH=CH_2$), 5.39 (1H, d, J = 10.5 Hz, NH), 5.83—5.90 (1H, m, $OCH_2CH=CH_2$), 7.25—7.36 (10H, m, Ph). *Anal.* Calcd for $C_{31}H_{35}Cl_6NO_9$: C, 47.84; H, 4.53; N, 1.80. Found: C, 48.25; H, 4.20; N, 2.27.

4,6-Di-*O*-benzyl-2-deoxy-3-*O*-(2,2,2-trichloro-*tert*-butoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranose (14) Compound **13** (540 mg, 0.7 mmol) was dissolved in THF (30 ml) and treated with 1,5-cyclooctadienebis(methyldiphenylphosphine)iridium hexafluorophosphate (30 mg, 0.035 mmol) under an argon atmosphere at 50 °C for 2 h after activation of the iridium catalyst with hydrogen. After cooling, iodine (360 mg, 1.42 mmol), pyridine (220 mg, 2.8 mmol) and H_2O (3.0 ml) were added to the solution, and the mixture was stirred for 15 min at room temperature. The solution was concentrated by evaporation. The residue was dissolved in CH_2Cl_2 and the solution was washed with 5% aqueous Na_2SO_3 and brine, dried ($MgSO_4$), and evaporated *in vacuo*. The residue was purified by silica gel column chromatography using CH_2Cl_2–CH_3COCH_3 (50 : 1) to give **14** (310 mg, 60%) as a white powder, mp 66—68 °C. $[\alpha]_D$ +22.7° (c = 1.40, $CHCl_3$). IR (KBr): 1743, 718, 693 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.87, 1.89 (each 3H, s, TCBOC), 3.65—3.66 (2H, m, H-6), 3.71 (1H, dd, J = 10.0 Hz, H-4), 4.03 (1H, m, H-2), 4.08—4.10 (1H, m, H-5), 4.46, 4.69 (each 1H, d, J = 11.0 Hz, CH_2CCl_3), 4.49, 4.59 (each 1H, d, J = 12.0 Hz, OCH_2Ph), 4.58, 4.82 (each 1H, d, J = 12.0 Hz, OCH_2Ph), 5.15 (1H, dd, J = 10.5 Hz, H-3), 5.28 (1H, d, J = 3.5 Hz, H-1), 5.50 (1H, d, J = 10.5 Hz, NH), 7.25—7.40 (10H, m, Ph). Positive FAB-MS m/z: 738 $(M+3)^+$.

***N*-Tetradecanoyl-*O*-[4,6-di-*O*-benzyl-2-deoxy-3-*O*-(2,2,2-trichloro-*tert*-butoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-L-serine Benzyl Ester (16)** Thionyl bromide (1.0 M solution in CH_2Cl_2) (0.54 ml, 0.54 mmol) was added to a solution of **14** (133 mg, 0.18 mmol) in CH_2Cl_2–DMF (10 : 1) (3.3 ml) at 0 °C under argon, and the mixture was stirred at room temperature for 5 h. The mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$ and brine, and dried ($MgSO_4$). Evaporation of the solvent gave **15** as a syrup. A

solution of this syrup and **8** (69 mg, 0.12 mmol) in anhydrous CH_2Cl_2 (3 ml) was stirred for 1 h at room temperature under argon in the presence of 4 Å powdered molecular sieves (100 mg). The mixture was cooled to 0 °C for 1 h, then $HgBr_2$ (7 mg, 0.02 mmol) was added. Stirring was continued at room temperature for 20 h. The insoluble materials were filtered off, and the filtrate was washed successively with 10% aqueous KI, saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated *in vacuo*. The residue was chromatographed on silica gel using CH_2Cl_2–CH_3COCH_3 (10 : 1) to give **16** (550 mg, 48%) as an amorphous powder, $[\alpha]_D$ +4.2° (c = 2.27, $CHCl_3$). IR (KBr): 1742, 1727, 1658, 1540 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, J = 6.7 Hz, –CH_3), 1.25 (20H, br s, –CH_2–), 1.64 (2H, m, $CH_2C\underline{H}_2C_{11}H_{23}$), 1.84, 1.89 (each 3H, s, TCBOC), 2.19—2.28 (2H, m, $C\underline{H}_2C_{12}H_{25}$), 3.41—3.46 (2H, m, $OC\underline{H}_2CHN$), 3.70 (2H, m, H-6), 3.78 (1H, dd, J = 10.0 Hz, H-4), 3.89 (1H, dt, J = 3.5, 9.5 Hz, H-2), 4.28 (1H, dd, J = 11.0, 3.2 Hz, $OC\underline{H}_2CHNH$), 4.46, 4.60 (each 2H, d, J = 11.9 Hz, $OC\underline{H}_2Ph$), 4.50, 4.66 (each 1H, d, J = 10.5 Hz, CH_2CCl_3), 4.78 (1H, d, J = 8.1 Hz, H-1), 5.02 (1H, m, H-3), 5.14, 5.20 (each 1H, d, J = 12.5 Hz, $COOC\underline{H}_2Ph$), 7.25—7.34 (10H, m, Ph). *Anal.* Calcd for $C_{52}H_{68}Cl_6N_2O_{12}\cdot 3H_2O$: C, 52.93; H, 6.32; N, 2.37. Found: C, 52.77; H, 5.78; N, 2.48.

***N*-Tetradecanoyl-*O*-[4,6-di-*O*-benzyl-2-deoxy-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine Benzyl Ester (18a)** Activated zinc powder (65 mg, 1.0 mmol) was added to a solution of **16** (827 mg, 0.87 mmol) in AcOH (5 ml), and the mixture was vigorously stirred at 40—50 °C for 16 h. After removal of the insoluble materials by filtration, the solvent was evaporated *in vacuo*. The residue was dissolved in CH_2Cl_2, washed with saturated aqueous $NaHCO_3$ and brine, and dried ($MgSO_4$). Evaporation of the solvent gave **17** as a syrup. DCC (450 mg, 2.18 mmol) was added to a solution of (*R*)-3-tetradecanoyloxytetradecanoic acid (991 mg, 2.18 mmol), this syrup and 4-dimethylaminopyridine (DMAP, 106 mg, 0.87 mmol) in CH_2Cl_2 (20 ml) at 0 °C under argon. The mixture was stirred for 15 h at room temperature. The precipitated dicyclohexylurea was filtered off, and the filtrate was concentrated by evaporation. The residue was dissolved with AcOEt, and then washed successively with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated *in vacuo*. The residue was purified by silica gel column chromatography using CH_2Cl_2–CH_3COCH_3 (50 : 1) to give **18a** (682 mg, 48%) as a syrup, $[\alpha]_D$ −1.5° (c = 1.31, $CHCl_3$). IR (KBr): 3295, 1742, 1645, 1555 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (15H, t, J = 6.7 Hz, –CH_3), 1.25 (96H, br s, –CH_2–), 1.51—1.64 (10H, m, –CH_2–), 2.19—2.45 (10H, m, –CH_2–), 3.42—3.46 (2H, m, $OC\underline{H}_2CHN$), 3.68—3.87 (2H, m, H-6), 4.27 (1H, dd, J = 11.0, 3.7 Hz, $OCH_2C\underline{H}NH$), 4.46—4.65 (4H, m, $OC\underline{H}_2Ph\times 2$), 4.77 (1H, d, J = 8.5 Hz, H-1), 5.14, 5.17 (each 1H, d, J = 12.5 Hz, $COOC\underline{H}_2Ph$), 7.22—7.33 (15H, m, Ph). *Anal.* Calcd for $C_{100}H_{166}N_2O_{14}\cdot H_2O$: C, 73.40; H, 10.22; N, 1.71. Found: C, 73.29; H, 9.85; N, 1.81.

***N*-Tetradecanoyl-*O*-[4,6-di-*O*-benzyl-2-deoxy-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine Benzyl Ester (19)** As described for **18a**, compound **17** (70 mg, 0.094 mmol) was treated with (*R*)-3-tetradecanoyloxytetradecanoic acid (64 mg, 0.14 mmol) and DCC (35 mg, 0.14 mmol) to give **19** (65 mg, 59%) as a white powder, mp 72—74 °C, $[\alpha]_D$ −9.5° (c = 1.30, $CHCl_3$). IR (KBr): 3300, 1728, 1645, 1545 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (9H, t, J = 6.9 Hz, –CH_3), 1.25 (58H, br s, –CH_2–), 1.59—1.78 (6H, m, –CH_2–), 1.90—2.46 (6H, m, –CH_2–), 4.03—4.09 (2H, m, H-6), 4.46—4.62 (4H, m, $OC\underline{H}_2Ph\times 2$), 5.17 (2H, br s, $COOC\underline{H}_2Ph$), 7.22—7.36 (15H, m, Ph). *Anal.* Calcd for $C_{72}H_{114}N_2O_{11}\cdot H_2O$: C, 71.96; H, 9.56; N, 2.33. Found: C, 71.54; H, 9.53; N, 2.78.

***N*-Tetradecanoyl-*O*-[4,6-di-*O*-benzyl-2-deoxy-3-*O*-tetradecanoyl-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine Benzyl Ester (18b)** Tetradecanoyl chloride (16 mg, 0.064 mmol) was added to a solution of **19** (63 mg, 0.053 mmol), pyridine (6 mg, 0.08 mmol) and DMAP (3 mg, 0.027 mmol) in CH_2Cl_2 (2 ml) at 0 °C under argon, and the mixture was stirred at room temperature for 20 h. The mixture was diluted in CH_2Cl_2, washed with saturated aqueous $NaHCO_3$ and brine, and dried ($MgSO_4$). After evaporation of the solvent, the residue was purified by silica gel column chromatography using CH_2Cl_2–CH_3COCH_3 (10 : 1) to give **18b** (42 mg, 57%) as a white powder, mp 66—68 °C, $[\alpha]_D$ −10.0° (c = 0.78, $CHCl_3$). IR (KBr): 3322, 1719, 1639, 1557 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (12H, t, J = 6.7 Hz, –CH_3), 1.25 (78H, br s, –CH_2–), 1.59—1.72 (8H, m, –CH_2–), 1.90—2.46 (8H, m, –CH_2–), 4.46—4.62 (4H, m, $OC\underline{H}_2Ph\times 2$), 5.17 (2H, br s, $COOC\underline{H}_2Ph$), 6.79 (1H, d, J = 8.1 Hz, NH), 7.26—7.32 (15H, m, Ph). *Anal.* Calcd for $C_{86}H_{140}N_2O_{12}\cdot 2H_2O$: C, 72.23; H, 9.87; N, 1.96. Found: C, 72.02; H, 9.86; N, 2.31.

***N*-Tetradecanoyl-*O*-[2-deoxy-3-*O*-[(*R*)-tetradecanoyloxytetradecanoyl]-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine (4)** Palladium-black (40 mg) was added to a solution of **18a** (39 mg, 0.024 mmol) in MeOH–THF (2 : 1) (3 ml), and the mixture was stirred under a hydrogen atmosphere for 24 h at room temperature. The catalyst was filtered off and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography using CH_2Cl_2–MeOH (10 : 1) to give **4** (23 mg, 66%) as a white powder, after lyophilization from dioxane, $[\alpha]_D$ −9.3° (c = 0.28, $CHCl_3$). IR (KBr): 1743, 1696, 1658 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (15H, t, J = 6.7 Hz, –CH_3), 1.25 (96H, br s, –CH_2–), 1.44—1.59 (10H, m, –CH_2–), 2.23—2.42 (10H, m, –CH_2–). *Anal.* Calcd for $C_{80}H_{150}N_2O_{14}\cdot 6H_2O$: C, 66.80; H, 10.69; N, 1.81. Found: C, 66.33; H, 10.27; N, 1.89.

***N*-Tetradecanoyl-*O*-[2-deoxy-3-*O*-tetradecanoyl-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine (5)** As described for **4**, compound **18b** (22 mg, 0.016 mmol) was subjected to hydrogenolysis over palladium-black (22 mg) to give **5** (12 mg, 68%) as a white powder, after lyophilization from dioxane, $[\alpha]_D$ −8.2° (c = 0.22, $CHCl_3$: MeOH = 1 : 1). IR (KBr): 1745, 1695, 1658 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (12H, t, J = 6.7 Hz, –CH_3), 1.25 (78H, br s, –CH_2–), 1.56—1.75 (8H, m, –CH_2–), 2.21—2.59 (8H, m, –CH_2–). *Anal.* Calcd for $C_{65}H_{122}N_2O_{12}\cdot 10H_2O$: C, 59.88; H, 9.43; N, 2.15. Found: C, 59.13; H, 9.57; N, 2.33.

Allyl 6-*O*-Benzyloxymethyl-2-deoxy-3-*O*-(2,2,2-trichloro-*tert*-butoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (20) Benzyl chloromethyl ester (6.26 g, 40 mmol) was added to a solution of **12** (12 g, 20 mmol) and 1,1,3,3-tetramethylurea (6.97 g, 60 mmol) in CH_2Cl_2 (150 ml) at 0 °C under argon, and the mixture was stirred at room temperature for 20 h. The mixture was washed with saturated aqueous $NaHCO_3$ and brine, and dried ($MgSO_4$). After evaporation of the solvent, the residue was purified by silica gel column chromatography using CH_2Cl_2–CH_3COCH_3 (50 : 1) to give **20** (9.45 g, 66%), $[\alpha]_D$ +51.3° (c = 1.99, $CHCl_3$). IR (KBr): 3418, 1746, 1725, 722, 692 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.91, 1.95 (each 3H, s, TCBOC), 3.78—3.83 (2H, m, H-4, H-6), 3.85 (1H, ddd, J = 9.5, 4.0 Hz, H-5), 3.92 (1H, dd, J = 11.0, 3.5 Hz, H-6), 4.00 (1H, dd, J = 6.5, 11.0 Hz, $OC\underline{H}_2CH=CH_2$), 4.04 (1H, m, H-2), 4.11 (1H, dd, J = 12.5, 5.5 Hz, $OC\underline{H}_2CH=CH_2$), 4.63 (2H, s, $OC\underline{H}_2OCH_2Ph$), 4.65, 4.76 (each 1H, d, J = 12.0 Hz, $OCH_2OC\underline{H}_2Ph$), 4.80, 4.83 (each 1H, d, J = 11.0 Hz, CH_2CCl_3), 4.93 (1H, d, J = 3.5 Hz, H-1), 4.97 (1H, dd, J = 10.3 Hz, H-3), 5.22—5.32 (2H, m, $OCH_2CH=C\underline{H}_2$), 5.38 (1H, d, J = 10.0 Hz, NH), 5.83—5.92 (1H, m, $OCH_2C\underline{H}=CH_2$), 7.26—7.37 (5H, m, Ph).

Allyl 6-*O*-Benzyloxymethyl-2-deoxy-4-*O*-diphenylphosphono-3-*O*-(2,2,2-trichloro-*tert*-butoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranoside (21) Diphenylphosphoryl chloride (15.7 g, 58.5 mmol) was added to a solution of **20** (8.4 g, 11.7 mmol), pyridine (4.63 g, 58.5 mmol) and DMAP (1.43 g, 11.7 mmol) in CH_2Cl_2 (100 ml) at 0 °C under argon, and the mixture was stirred at room temperature for 20 h. The mixture was washed with saturated aqueous $NaHCO_3$ and brine, and dried ($MgSO_4$). After evaporation of the solvent, the residue was purified by silica gel column chromatography using CH_2Cl_2–CH_3COCH_3 (100 : 1) to give **21** (9.88 g, 89%) as a white powder, mp 146—147 °C, $[\alpha]_D$ +42.6° (c = 0.61, $CHCl_3$). IR (KBr): 3434, 1733, 1275, 947, 687 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.66, 1.84 (each 3H, s, TCBOC), 3.65 (1H, dd, J = 11.0, 4.0 Hz, H-6), 3.76 (1H, dd, J = 11.0, 2.1 Hz, H-6), 3.97—4.01 (1H, m, H-5), 4.04 (1H, dd, J = 11.0, 4.0 Hz, $OC\underline{H}_2CH=CH_2$), 4.17 (1H, m, H-2), 4.23 (1H, dd, J = 5.5, 11.0 Hz, $OC\underline{H}_2CH=CH_2$), 4.53, 4.59 (each 1H, d, J = 12.0 Hz, $OCH_2OC\underline{H}_2Ph$), 4.67, 4.69 (each 1H, d, J = 12.5 Hz, CH_2CCl_3), 4.90 (1H, dd, J = 9.5 Hz, H-4), 4.97 (1H, d, J = 3.5 Hz, H-1), 5.24—5.30 (2H, m, $OCH_2CH=C\underline{H}_2$), 5.36 (1H, dd, J = 10.3 Hz, H-3), 5.86—5.99 (1H, m, $OCH_2C\underline{H}=CH_2$), 7.26—7.30 (15H, m, Ph). *Anal.* Calcd for $C_{37}H_{40}Cl_6NO_{13}P\cdot C_5H_5N$: C, 48.95; H, 4.40; N, 2.72. Found: C, 48.02; H, 4.10; N, 2.02.

6-*O*-Benzyloxymethyl-2-deoxy-4-*O*-diphenylphosphono-3-*O*-(2,2,2-trichloro-*tert*-butoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-α-D-glucopyranose (22) Compound **21** (827 mg, 0.8 mmol) was treated with 1,5-cyclooctadienebis(methyldiphenylphosphine)iridium hexafluorophosphate (37 mg, 0.044 mmol) in THF, and then with iodine (440 mg, 1.74 mmol), pyridine (2.8 g, 3.5 mmol) and H_2O (3.0 ml) as described for the preparation of **14**. Purification by column chromatography on silica gel using CH_2Cl_2–CH_3COCH_3 (100 : 1) afforded **22** (643 mg, 81%) as a white powder, mp 53—55 °C, $[\alpha]_D$ +20.0° (c = 0.99, $CHCl_3$). IR (KBr):

1754, 1733, 1263, 720, 695 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.65, 1.84 (each 3H, s, TCBOC), 3.64 (1H, dd, J=11.0, 5.0, H-6), 3.74 (1H, dd, J=11.0, 2.1 Hz, H-6), 4.13 (1H, m, H-2), 4.23—4.25 (1H, m, H-5), 4.51, 4.56 (each 1H, d, J=12.0 Hz, OCH_2OCH_2Ph), 4.62, 4.72 (each 1H, d, J=11.5 Hz, CH_2CCl_3), 5.28 (1H, d, J=3.5 Hz, H-1), 5.34 (1H, dd, J=10.0, 9.5 Hz, H-3), 5.51 (1H, d, J=9.5 Hz, NH), 7.13—7.32 (15H, m, Ph). *Anal.* Calcd for $C_{34}H_{36}Cl_6NO_{13}P$: C, 44.81; H, 3.98; N, 1.54. Found: C, 45.24; H, 3.79; N, 1.57.

***N*-Tetradecanoyl-*O*-[6-*O*-benzyloxymethyl-2-deoxy-4-*O*-diphenylphosphono-3-*O*-(2,2,2-trichloro-*tert*-butoxycarbonyl)-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranosyl]-L-serine Benzyl Ester (24)** As described for the preparation of **16**, compound **22** (270 mg, 0.3 mmol) was treated with thionyl bromide (1.0 M solution in CH_2Cl_2) (0.9 ml) in CH_2Cl_2–DMF and the resulting oil **23** was treated with **8**, $HgBr_2$ (108 mg, 0.3 mmol) and molecular sieves 4 Å (300 mg) in CH_2Cl_2 (10 ml). Purification by column chromatography on silica gel using CH_2Cl_2–CH_3COCH_3 (10 : 1) gave **24** (129 mg, 33%) as an amorphous powder, $[\alpha]_D$ + 3.1° (c=1.24, $CHCl_3$). IR (KBr): 1737, 1648, 1589 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, J=6.7 Hz, $-CH_3$), 1.25 (20H, br s, $-CH_2-$), 1.61—1.67 (2H, m, $CH_2CH_2C_{11}H_{23}$), 2.24 (2H, t, J=7.5 Hz, $CH_2C_{12}H_{25}$), 3.59—3.61 (1H, m, H-6), 3.76 (1H, dd, J=13.5, 5.0 Hz, H-6), 4.24—4.26 (1H, m, OCH_2CHNH), 4.49, 4.53 (each 1H, d, J=12.0 Hz, CH_2CCl_3), 4.58, 4.64 (each 1H, d, J=6.5 Hz, OCH_2OCH_2Ph), 4.90 (1H, d, J=8.1 Hz, H-1), 5.12, 5.20 (each 1H, d, J=12.0 Hz, $COOCH_2Ph$), 5.34 (1H, dd, J=10.0, 9.5 Hz, H-3), 7.12—7.18, 7.26—7.34 (20H, m, Ph). *Anal.* Calcd for $C_{58}H_{73}Cl_6N_2O_{16}P$: C, 53.63; H, 5.67; N, 2.16. Found: C, 54.06; H, 5.83; N, 1.88.

***N*-Tetradecanoyl-*O*-[6-*O*-benzyloxymethyl-2-deoxy-4-*O*-diphenylphosphono-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine Benzyl Ester (26)** As described for **18a**, compound **24** (49 mg, 0.038 mmol) was reacted with zinc powder in AcOH, and the resulting syrup **25** was treated with (*R*)-3-tetradecanoyloxytetradecanoic acid (52 mg, 0.11 mmol), DMAP (5 mg, 0.038 mmol) and DCC (23 mg, 0.11 mmol) to give **26** (38 mg, 56%) as a syrup, $[\alpha]_D$ −2.4° (c=0.34, $CHCl_3$). IR (KBr): 1731, 1676, 1559, 1225 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (15H, t, J=6.7 Hz, $-CH_3$), 1.25 (96H, br s, $-CH_2-$), 1.56—1.65 (10H, m, $-CH_2-$), 2.16—2.40 (10H, m, $-CH_2-$), 3.49—3.61 (2H, m, H-6), 4.47—4.66 (4H, m, $-CH_2OCH_2Ph$), 5.14 (2H, br s, CO_2CH_2Ph), 6.30 (1H, br d, J=6.5 Hz, NH), 6.95 (1H, br d, J=8.5 Hz, NH), 7.12—7.33 (20H, m, Ph). *Anal.* Calcd for $C_{106}H_{171}N_2O_{18}P \cdot 10H_2O$: C, 64.54; H, 8.74; N, 1.42. Found: C, 64.26; H, 8.63; N, 1.52.

***N*-Tetradecanoyl-*O*-[2-deoxy-4-*O*-phosphono-3-*O*-[(*R*)-3-tetradecanoyloxytetradecanoyl]-2-[(*R*)-3-tetradecanoyloxytetradecanoylamino]-β-D-glucopyranosyl]-L-serine (6)** Palladium-black (18 mg) was added to a solution of **26** (18 mg, 0.01 mmol) in MeOH (3 ml), and the mixture was stirred under a hydrogen atmosphere for 5 h at 40—45 °C. The catalyst was filtered off and the filtrate was concentrated under reduced pressure, then the resulting syrup was dissolved in MeOH (2 ml). Next, platinum dioxide (13 mg) was added to the solution and the mixture was stirred under a hydrogen atmosphere for 18 h at 40—45 °C. The catalyst was filtered off, the filtrate was concentrated under reduced pressure, and the resulting residue was purified by silica gel column chromatography using CH_2Cl_2–MeOH (4 : 1) to give **6** (7 mg, 44%) as a white powder, after lyophilization from dioxane, $[\alpha]_D$ −2.5° (c= 0.16, $CHCl_3$), IR (KBr): 1731, 1676, 1559, 1225 cm^{-1}. ^{1}H-NMR ($CDCl_3$–CD_3OD) δ: 0.88 (15H, t, J=6.7 Hz, $-CH_3$), 1.25 (96H, br s, $-CH_2-$), 1.56—1.65 (10H, m, $-CH_2-$), 2.16—2.40 (10H, m, $-CH_2-$). *Anal.* Calcd for $C_{79}H_{149}N_2O_{17}P \cdot 3H_2O$: C, 63.94; H, 10.12; N, 1.89. Found: C, 63.85; H, 9.86; N, 1.77.

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