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Note

Synthesis of 3-*O*-[(3*R*)-3-acyloxytetradecanoyl]-2-deoxy-2-[(3*R*)-3-hydroxytetradecanamido]-4-*O*-phosphono-D-glucose derivatives related to bacterial lipid A

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Lipid A is known[1] as the active center of bacterial lipopolysaccharide (LPS)[2], which exhibits a variety of biological activities. We have been continuing efforts[3] to clarify the relationship between the chemical structure of lipid A subunit analogs and the biological activities by preparing a variety of 4-*O*-phosphono-D-glucosamine derivatives carrying different acyl groups.

The critical importance of fatty acid substituents for the expression of immunopharmacological activities has been demonstrated[4]. In a series of 3-*O*-(acyloxytetradecanoyl) derivatives[3a,b], GLA-60 and GLA-63, which respectively bear a 3-*O*-linked (3*R*)-3-(tetradecanoyloxytetradecanoyl) and (3*R*)-3-(dodecanoyloxytetradecanoyl) group, were found the most beneficial compounds, possessing strong immunomodulating activities. However, GLA-64, carrying a (3*R*)-3-(hexadecanoyloxytetradecanoyl) group at O-3 in the sugar moiety, did not show any significant immunopharmacological activities.

To obtain further information on the fine-structural requirement for manifestation of the activity, we synthesized a variety of 3-*O*-[(3*R*)-3-(acyloxytetradecanoyl)]-2-deoxy-2-[(3*R*)-3-(hydroxytetradecanamido)]-4-*O*-phosphono-D-glucose derivatives (**19–24**) which carry acyl groups of different length of carbon chain, including odd-numbered acids, at C-3 of the 3-*O*-linked (3*R*)-3-hydroxytetradecanoyl moiety.

2-(Trimethylsilyl)ethyl 2-deoxy-4,6-*O*-isopropylidene-2-{(3*R*)-3-[(2-trimethylsilylethoxy)methoxy]tetradecanamido}-β-D-glucopyranoside[5] (**1**) was treated with (3*R*)-3-(benzyloxymethoxy)tetradecanoic acid in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodi-imide hydrochloride (WSC) and 4-(dimethylamino)-pyridine (DMAP), to give **2** in 90% yield. The isopropylidene group of **2** was removed with aqueous acetic acid, giving **3**, and a *tert*-butyldimethylsilyl group was introduced at O-6 of **3**, giving **4**. Compound **4** was phosphorylated at O-4 to give **5**, which was hydrogenolyzed over 10% palladium-on-carbon to remove the

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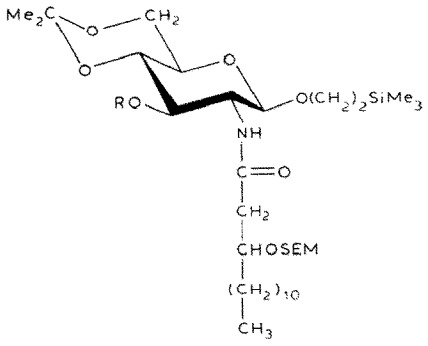
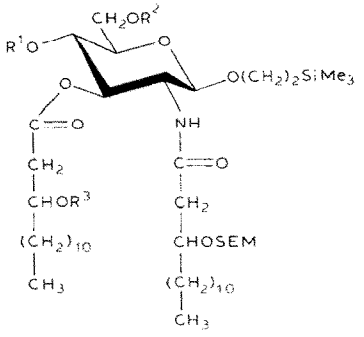


SEM = $Me_3Si(CH_2)_2OCH_2$

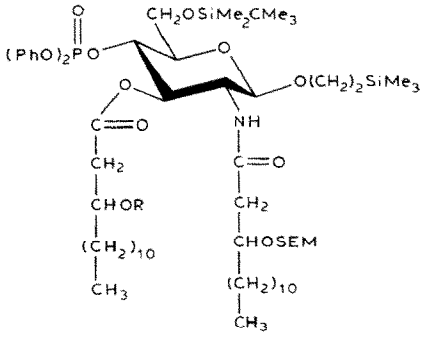
	R
1	H
2	$CH_3(CH_2)_{10}CHCH_2C(O)$ OCH_2OCH_2Ph



	R^1	R^2	R^3
3	H	H	$PhCH_2OCH_2$
4	H	Me_3CMe_2Si	$PhCH_2OCH_2$
5	$(PhO)_2P(O)$	Me_3CMe_2Si	$PhCH_2OCH_2$

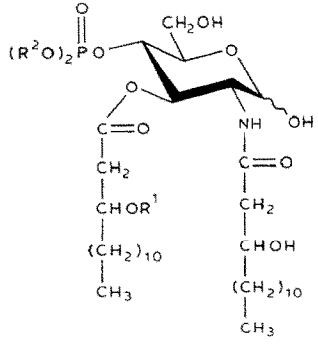
benzyloxymethyl group. The resulting **6** was esterified to afford compounds **7–12** in high yields.

The 2-(trimethylsilyl)ethyl, (2-trimethylsilylethoxy)methyl, and *tert*-butyldimethylsilyl groups of **7–12** were simultaneously removed by treatment with boron trifluoride etherate[6], to give **13–18**. Finally, the phenyl groups were cleaved by hydrogenolysis, to yield the desired analogs **19–24** (GLA 87–92) as colorless powders.



	R
6	H
7	Ac
8	C_8
9	C_{10}
10	C_{11}
11	C_{13}
12	C_{15}

C_n = $CH_3(CH_2)_{n-2}C(O)$



	R^1	R^2
13	Ac	Ph
14	C_8	Ph
15	C_{10}	Ph
16	C_{11}	Ph
17	C_{13}	Ph
18	C_{15}	Ph
19	Ac	H
20	C_8	H
21	C_{10}	H
22	C_{11}	H
23	C_{13}	H
24	C_{15}	H

EXPERIMENTAL

General methods. — Melting points were determined with a Yanagimoto micro melting-point apparatus and are uncorrected. Concentrations and evaporations were conducted *in vacuo*. Preparative chromatography on Silica Gel (Wako Co.; 200 mesh) was accomplished with the solvent systems specified. Specific rotations were determined with a Union PM-201 polarimeter, and i.r. spectra were recorded with a Jasco A-100 spectrophotometer. ^{1}H-N.m.r. spectra were recorded at 270 MHz with a JEOL JNM-GX 270 spectrometer.

2-(Trimethylsilyl)ethyl 3-O-[(3R)-3-(benzyloxymethoxy)tetradecanoyl]-2-deoxy-4,6-O-isopropylidene-2-[(3R)-3-[(2-trimethylsilylethoxy)methoxy]tetradecanamido]-β-D-glucopyranoside (**2**). — To a solution of 2-(trimethylsilyl)ethyl 2-deoxy-4,6-*O*-isopropylidene-2-{(3*R*)-3-[(2-trimethylsilylethoxy)methoxy]tetradecanamido}-β-D-glucopyranoside[5] (**1**; 3.2 g) in dichloromethane (50 mL) were added (3*R*)-3-(benzyloxymethoxy)tetradecanoic acid[3a] (2.5 g), 1-ethyl-3-(3-dimethylaminopropyl)carbodi-imide hydrochloride (WSC; 2.03 g), and 4-(dimethylamino)pyridine (DMAP; 0.2 g), and the mixture was stirred overnight at room temperature. The mixture was evaporated and the residue was chromatographed on a column of silica gel with 6:1 hexane–ethyl acetate, to give **2** (4.4 g; 90%) as a syrup; $[\alpha]_D$ −3.6° (*c* 0.94, dichloromethane); ν_{max} 3300 (NH), 2930, 2850 (CH), 1730 (ester), 1650, 1550 (amide), 860, 830 (Si-C, Me_2C), and 730–680 cm^{-1} (Ph); ^{1}H-n.m.r. data ($CDCl_3$): δ 0.0 (s, 18 H, 2 Me_3Si), 0.75–1.0 (m, 10 H, Me_3SiCH_2 and CH_3), 1.1–1.7 (m, 40 H, CH_2), 1.30, 1.41 (2 s, 6 H, Me_2C), 2.25–2.70 (m, 4 H, 2 $COCH_2$), 3.33 (m, 1 H, H-5), 3.45–4.10 (m, 10 H, $Me_3SiCH_2CH_2$, H-3 of C_{14}-OSEM, H-3 of C_{14}-OBOM*, H-2,4,6), 4.5–4.85 (m, 7 H, $PhCH_2$, OCH_2O, and H-1), 5.16 (t, 1 H, $J_{2,3} = J_{3,4}$ = 10 Hz, H-3), 6.28 (d, 1 H, $J_{2,NH}$ 8.8 Hz, NH), and 7.2–7.4 (m, 5 H, Ph-H).

Anal. Calc. for $C_{56}H_{103}NO_{11}Si_2$ (1022.61): C, 65.77; H, 10.15; N, 1.37. Found: C, 65.65; H, 9.91; N, 1.44.

2-(Trimethylsilyl)ethyl 3-O-[(3R)-3-(benzyloxymethoxy)tetradecanoyl]-2-deoxy-2-{(3R)-3-[(2-trimethylsilylethoxy)methoxy]tetradecanamido}-β-D-glucopyranoside (**3**). — A mixture of **2** (3.6 g) and 80% aqueous acetic acid (240 mL) was heated, with stirring, for 1.5 h at 45°, and evaporated. The residue was chromatographed on a column of silica gel with 200:1 dichloromethane–methanol, to afford **3** (3 g; 87%) as a syrup; $[\alpha]_D$ −17.6° (*c* 0.89, dichloromethane); ν_{max} 3300 (OH, NH), 2930, 2850 (CH), 1730 (ester), 1650, 1540 (amide), 860, 830 (Si-C), and 720–680 cm^{-1} (Ph); ^{1}H-n.m.r. data ($CDCl_3$): δ 0.0 (s, 18 H, Me_3Si), 0.75–1.0 (m, 10 H, Me_3SiCH_2 and CH_3), 1.1–1.7 (m, 40 H, CH_2), 2.25–2.70 (m, 4 H, $COCH_2$), 3.35 (m, 1 H, H-5), 3.4–4.1 (m, 10 H, $Me_3SiCH_2CH_2$, H-3 of C_{14}-OSEM, H-3 of C_{14}-OBOM, H-2,4,6), 4.45–4.8 (m, 7 H, $PhCH_2$, OCH_2O, and H-1), 5.05 (t, 1 H, $J_{2,3} = J_{3,4}$ = 10 Hz, H-3), 6.41 (d, 1 H, $J_{2,NH}$ 8.8 Hz, NH), and 7.2–7.4 (m, 5 H, Ph-H).

*BOM = Ph CH_2OCH_2.

Anal. Calc. for $C_{53}H_{99}NO_{11}Si_2$ (982.54): C, 64.79; H, 10.16; N, 1.43. Found: C, 65.01; H, 10.44; N, 1.69.

2-(Trimethylsilyl)ethyl 3-O-[(3R)-3-(benzyloxymethoxy)tetradecanoyl]-6-O-tert-butyldimethylsilyl-2-deoxy-2-[(3R)-3-[(2-trimethylsilylethoxy)methoxy]tetradecanamido]-β-D-glucopyranoside (**4**). — To a solution of **3** (3 g) in pyridine (30 mL) was added *tert*-butyldimethylsilyl chloride (0.93 g); stirring was continued overnight at room temperature. Methanol was added and then solvents were evaporated. The residue was chromatographed on a column of silica gel with 350:1 dichloromethane–methanol, to afford **4** (4 g; 97%); $[\alpha]_D$ −12.9° (*c* 0.9, dichloromethane); ν_{max} 3400 (OH, NH), 2930, 2850 (CH), 1730 (ester), 1650, 1550 (amide), 850, 830 (Si-C), and 720–680 cm^{-1} (Ph); ^{1}H-n.m.r. data ($CDCl_3$): δ 0.0 (s, 24 H, CH_3Si), 0.8–1.0 [m, 19 H, $(CH_3)_3C$, Me_3SiCH_2, and CH_3], 1.1–1.8 (m, 40 H, CH_2), 2.25–2.70 (m, 4 H, $COCH_2$), 3.3–4.15 (m, 12 H, $Me_3SiCH_2CH_2$, H-3 of C_{14}-OSEM*, H-3 of C_{14}-OBOM, OH, H-2,4,6), 4.4–4.85 (m, 7 H, $PhCH_2$, OCH_2O, and H-1), 5.03 (t, 1 H, $J_{2,3} = J_{3,4}$ = 8.2 Hz, H-3), 6.09 (d, 1 H, $J_{2,NH}$ 8.8 Hz, NH), and 7.2–7.4 (m, 5 H, Ph-H).

Anal. Calc. for $C_{59}H_{113}NO_{11}Si_3$ (1096.81): C, 64.61; H, 10.39; N, 1.28. Found: C, 64.73; H, 10.59; N, 1.28.

2-(Trimethylsilyl)ethyl 3-O-[(3R)-3-(benzyloxymethoxy)tetradecanoyl]-6-O-tert-butyldimethylsilyl-2-deoxy-4-O-diphenoxyphosphinyl-2-[(3R)-3-[(2-trimethylsilylethoxy)methoxy]tetradecanamido]-β-D-glucopyranoside (**5**). — A solution of **4** (4 g), DMAP (0.9 g), and diphenyl phosphorochloridate (1.98 g) in 2:1 pyridine–dichloromethane (60 mL) was stirred overnight at room temperature. Methanol was added, and the mixture was evaporated. The residue was extracted with dichloromethane, and the extract was successively washed with 2M hydrochloric acid and water, dried (sodium sulfate), and evaporated. The residual syrup was chromatographed on a column of silica gel with 400:1 dichloromethane–methanol to give **5** (4.3 g; 88%); $[\alpha]_D$ +11.2° (*c* 0.86, dichloromethane); ν_{max} 3300 (NH), 2930, 2850 (CH), 1740 (ester), 1660, 1540 (amide), 950 (P-O-Ph), 860, 840 (Si-C), and 780–680 cm^{-1} (Ph); ^{1}H-n.m.r. data ($CDCl_3$): δ 0.0 (s, 24 H, CH_3Si), 0.8–1.0 [m, 19 H, $(CH_3)_3C$, Me_3SiCH_2, and CH_3], 1.1–1.7 (m, 40 H, CH_2), 2.25–2.45 (m, 4 H, $COCH_2$), 3.45–4.0 (m, 10 H, $Me_3SiCH_2CH_2$, H-3 of C_{14}-OSEM, H-3 of C_{14}-OBOM, H-2,5, and 6), 4.4–4.75 (m, 7 H, $PhCH_2$, OCH_2O, and H-4), 4.79 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 5.52 (t, 1 H, $J_{2,3} = J_{3,4}$ = 8.8 Hz, H-3), 6.23 (d, 1 H, $J_{2,NH}$ 8 Hz, NH), and 7.1–7.4 (m, 15 H, Ph-H).

Anal. Calc. for $C_{71}H_{122}NO_{14}PSi_3$ (1328.98): C, 64.17; H, 9.25; N, 1.05. Found: C, 64.31; H, 9.34; N, 0.91.

2-(Trimethylsilyl)ethyl 6-O-tert-butyldimethylsilyl-2-deoxy-4-O-diphenoxyphospinyl-3-O-[(3R)-3-hydroxytetradecanoyl]-2-[(3R)-3-[(2-trimethylsilylethoxy)methoxy]tetradecanamido]-β-D-glucopyranoside (**6**). — To a solution of **5** (3 g) in methanol (100 mL) was added 10% palladium-on-carbon (1 g), and the mixture

*SEM = $Me_3Si(CH_2)_2OCH_2$.

was stirred overnight in a hydrogen atmosphere. The catalyst was filtered off, and washed with methanol. The filtrate and washings were combined, and evaporated. The residue was chromatographed on a column of silica gel with 250:1 dichloromethane–methanol to afford **6** (2.4 g; 86.6%); $[\alpha]_D$ +3.5° (*c* 0.4, dichloromethane); ν_{max} 3500 (OH), 3300 (NH), 2930, 2850 (CH), 1740 (ester), 1660, 1550 (amide), 960 (P-O-Ph), 860, 840 (Si-C), and 780–680 cm^{-1} (Ph); ^{1}H-n.m.r. data ($CDCl_3$): δ 0.0 (s, 24 H, CH_3Si), 0.8–1.0 [m, 19 H, $(CH_3)_3C$, Me_3SiCH_2, and CH_3], 1.1–1.7 (m, 40 H, CH_2), 2.15–2.45 (m, 4 H, $COCH_2$), 3.40 (broad s, 1 H, O*H*), 3.5–4.0 (m, 10 H, $Me_3SiCH_2CH_2$, H-3 of C_{14}-OH, H-3 of C_{14}-OSEM, H-2,5,6), 4.6–4.75 (m, 3 H, OCH_2O and H-4), 4.76 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 5.51 (t, 1 H, $J_{2,3} = J_{3,4}$ = 9.5 Hz, H-3), 6.41 (d, 1 H, $J_{2,NH}$ 8.4 Hz, N*H*), and 7.1–7.4 (m, 10 H, Ph-*H*).

Anal. Calc. for $C_{63}H_{114}NO_{13}PSi_3$ (1208.83): C, 62.60; H, 9.51; N, 1.16. Found: C, 62.58; H, 9.46; N, 1.30.

*2-(Trimethylsilyl)ethyl 3-*O*-[(3*R*)-3-acetoxytetradecanoyl]-6-*O*-tert-butyldimethylsilyl-2-deoxy-4-*O*-diphenoxyphosphinyl-2-[(3*R*)-3-[(2-trimethylsilylethoxy)methoxy]tetradecanamido]-β-*D*-glucopyranoside* (**7**). — To a cooled solution of **6** (0.3 g) in pyridine (6 mL) was added acetic anhydride (3 mL). The mixture was stirred overnight at room temperature. Methanol was added, and the mixture was evaporated. The residue was extracted with dichloromethane, and the extract was washed successively with 2M hydrochloric acid and water, dried (sodium sulfate), and evaporated. The residual syrup was chromatographed on a column of silica gel with 300:1 dichloromethane–methanol to give **7** (0.28 g; 90%); $[\alpha]_D$ +7.3° (*c* 0.71, dichloromethane); ν_{max} 3300 (NH), 2930, 2850 (CH), 1740 (ester), 1660, 1550 (amide), 960 (P-O-Ph), 860, 840 (Si-C), and 780–680 cm^{-1} (Ph); ^{1}H-n.m.r. data ($CDCl_3$): δ 0.0 (s, 24 H, CH_3Si), 0.8–1.0 [m, 19 H, $(CH_3)_3C$, Me_3SiCH_2, and CH_3], 1.93 (s, 3 H, CH_3COO), 2.25–2.45 (m, 4 H, $COCH_2$), 3.5–4.0 (m, 9 H, $Me_3SiCH_2CH_2$, H-3 of C_{14}-OSEM, H-2,5,6), 4.60 (q, 1 H, $J_{3,4} = J_{4,5} = J_{4,P}$ = 9.5 Hz, H-4), 4.70 (m, 2 H, OCH_2O), 4.86 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1), 5.14 (m, 1 H, H-3 of C_{14}-OAc), 5.53 (t, 1 H, $J_{2,3} = J_{3,4}$ = 9 Hz, H-3), 6.26 (d, 1 H, $J_{2,NH}$ 8.1 Hz, N*H*), and 7.1–7.4 (m, 10 H, Ph-*H*).

Anal. Calc. for $C_{65}H_{116}NO_{14}PSi_3$ (1250.87): C, 62.41; H, 9.35; N, 1.12. Found: C, 62.63; H, 9.11; N, 1.03.

*2-(Trimethylsilyl)ethyl 6-*O*-tert-butyldimethylsilyl-2-deoxy-4-*O*-diphenoxyphosphinyl-3-*O*-[(3*R*)-3-octanoyloxytetradecanoyl]-2-[(3*R*)-3-[(2-trimethylsilylethoxy)methoxy]tetradecanamido]-β-*D*-glucopyranoside* (**8**). — A solution of **6** (0.3 g), octanoic acid (71 mg), DMAP (50 mg), and WSC (0.14 g) in dichloromethane (10 mL) was stirred overnight at room temperature. The mixture was chromatographed on a column of silica gel with 300:1 dichloromethane–methanol, to afford **8** (0.33 g; quant.); $[\alpha]_D$ +6.7° (*c* 0.83, dichloromethane); i.r. data were similar to those of **7**; ^{1}H-n.m.r. data ($CDCl_3$): δ 0.0 (s, 24 H, CH_3Si), 0.8–1.0 [m, 22 H, $(CH_3)_3C$, Me_3SiCH_2, and CH_3], 1.1–1.7 (m, 50 H, CH_2), 2.1–2.5 (m, 6 H, $COCH_2$), 3.5–4.0 (m, 9 H, $Me_3SiCH_2CH_2$, H-3 of C_{14}-OSEM, H-2,5,6), 4.60 (q, 1 H, $J_{3,4} = J_{4,5} = J_{4,P}$ = 9.5 Hz, H-4), 4.70 (m, 2 H, OCH_2O), 4.86 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1),

5.14 (m, 1 H, H-3 of C_{14}-O-C_8), 5.54 (t, 1 H, $J_{2,3} = J_{3,4} = 9$ Hz, H-3), 6.27 (d, 1 H, $J_{2,NH}$ 8.2 Hz, N*H*), and 7.1–7.4 (m, 10 H, Ph-*H*).

Anal. Calc. for $C_{71}H_{128}NO_{14}PSi_3$ (1335.03): C, 63.88; H, 9.66; N, 1.05. Found: C, 64.13; H, 9.76; N, 1.12.

*Other 2-(trimethylsilyl)ethyl 3-*O*-[(3R)-3-acyloxytetradecanoyl]-6-O-tert-butyldimethylsilyl-2-deoxy-4-O-diphenoxyphosphinyl-2-[(3R)-3-[(2-trimethylsilylethoxy)methoxy]tetradecanamido]-β-*D*-glucopyranosides* (**9–12**). — Compounds **9–12** were obtained by esterification of **6** with the corresponding fatty acids in 85–95% yields, respectively, as described for **8**. I.r. and ^{1}H-n.m.r. data were consistent with the structures assigned.

Compound **9** had $[\alpha]_D$ +7.4° (*c* 1.05, dichloromethane).

Anal. Calc. for $C_{73}H_{132}NO_{14}PSi_3$ (1363.08): C, 64.33; H, 9.76; N, 1.03. Found: C, 64.09; H, 9.53; N, 1.03.

Compound **10** had $[\alpha]_D$ +7.5° (*c* 0.77, dichloromethane).

Anal. Calc. for $C_{74}H_{134}NO_{14}PSi_3$ (1377.11): C, 64.52; H, 9.81; N, 1.02. Found: C, 64.77; H, 9.76; N, 1.30.

Compound **11** had $[\alpha]_D$ +7.7° (*c* 0.6, dichloromethane).

Anal. Calc. for $C_{76}H_{138}NO_{14}PSi_3$ (1405.16): C, 64.96; H, 9.90; N, 1.00. Found: C, 64.80; H, 9.61; N, 0.70.

Compound **12** had $[\alpha]_D$ +7.0° (*c* 0.74, dichloromethane).

Anal. Calc. for $C_{78}H_{142}NO_{14}PSi_3$ (1433.22): C, 65.37; H, 9.99; N, 0.98. Found: C, 65.15; H, 9.95; N, 1.04.

3-O-[(3R)-3-Acetoxytetradecanoyl]-2-deoxy-4-O-diphenoxyphosphinyl-2-[(3R)-3-hydroxytetradecanamido]-D-glucopyranose (**13**). — To a solution of **7** (0.24 g) in dichloromethane (10 mL) was added boron trifluoride etherate (0.5 mL) at 0°, and the mixture was stirred for 1 h at the same temperature, successively washed with M sodium hydrogencarbonate and water, dried (sodium sulfate), and evaporated. The residue was chromatographed on a column of silica gel with 50:1 dichloromethane–methanol, to afford **13** (0.13 g; 75%) which was lyophilized from 1,4-dioxane solution; m.p. 127–128°, $[\alpha]_D$ +5.0° (*c* 0.7, dichloromethane); ν_{max} 3400 (OH, NH), 2930, 2850 (CH), 1740 (ester), 1640, 1540 (amide), 960 (P-O-Ph), and 780–680 cm^{-1} (Ph); ^{1}H-n.m.r. data ($CDCl_3$): δ 0.88 (t, 6 H, CH_3), 1.0–1.6 (m, 40 H, CH_2), 1.94 (s, 3 H, CH_3COO), 2.1–2.5 (m, 4 H, $COCH_2$), 3.4–4.1 (m, 6 H, H-3 of C_{14}-OH, H-5,6, and O*H*), 4.22 (m, 1 H, H-2), 4.71 (q, 1 H, $J_{3,4} = J_{4,5} = J_{4,P} = 9.5$ Hz, H-4), 5.10 (m, 1 H, H-3 of C_{14}-OAc), 5.26 (d, 1 H, $J_{1,2}$ 3.3 Hz, H-1), 5.49 (t, 1 H, $J_{2,3} = J_{3,4} = 9.5$ Hz, H-3), 5.65 (broad s, 1 H, O*H*), 6.56 (d, 1 H, N*H*), and 7.1–7.4 (m, 10 H, 2 Ph-*H*).

Anal. Calc. for $C_{48}H_{76}NO_{13}P$ (906.10): C, 63.63; H, 8.45; N, 1.55. Found: C, 63.37; H, 8.23; N, 1.37.

Other desilylated derivatives (**14–18**). — Crystalline compounds **14–18** were prepared by desilylation of **8–12** in 80–95% yields, respectively, according to the method described for **13**. I.r. and ^{1}H-n.m.r. data were consistent with the structures assigned.

Compound **14** had m.p. 123–124°, $[\alpha]_D$ +7.9° (*c* 0.6, dichloromethane).

Anal. Calc. for $C_{54}H_{88}NO_{13}P$ (990.27): C, 65.50; H, 8.96; N, 1.41. Found: C, 65.21; H, 8.70; N, 1.60.

Compound **15** had m.p. 118–120°, $[\alpha]_D$ +9.3° (*c* 0.6, dichloromethane).

Anal. Calc. for $C_{56}H_{92}NO_{13}P$ (1018.32): C, 66.05; H, 9.11; N, 1.38. Found: C, 66.32; H, 8.96; N, 1.32.

Compound **16** had m.p. 89–90°, $[\alpha]_D$ +10.9° (*c* 0.74, dichloromethane).

Anal. Calc. for $C_{57}H_{94}NO_{13}P$ (1032.35): C, 66.32; H, 9.18; N, 1.36. Found: C, 66.53; H, 9.26; N, 1.63.

Compound **17** had m.p. 105–107°, $[\alpha]_D$ +12.2° (*c* 0.63, dichloromethane).

Anal. Calc. for $C_{59}H_{98}NO_{13}P$ (1060.40): C, 66.82; H, 9.32; N, 1.32. Found: C, 66.94; H, 9.14; N, 1.27.

Compound **18** had m.p. 111–112°, $[\alpha]_D$ +5.5° (*c* 0.8, dichloromethane).

Anal. Calc. for $C_{61}H_{102}NO_{13}P$ (1088.45): C, 67.31; H, 9.45; N, 1.29. Found: C, 67.27; H, 9.41; N, 1.47.

*3-O-[(3R)-3-Acetoxytetradecanoyl]-2-deoxy-2-[(3R)-3-hydroxytetradecanamido]-4-O-phosphono-*D*-glucopyranose* (**19**; GLA-87). — To a solution of **13** (70 mg) in ethanol (80 mL) was added pre-reduced Adams' platinum catalyst (70 mg), and the mixture was stirred overnight in a hydrogen atmosphere. The catalyst was filtered off, and washed with ethanol. The filtrate and washings were combined, and evaporated, to yield compound **19** (53 mg; 91%) which was lyophilized from a 1,4-dioxane suspension. It gave a positive test for phosphate group on using the phosphomolybdate spray reagent[7]; m.p. 157–159°, $[\alpha]_D$ +12.7° (*c* 0.1, 3:1 chloroform–methanol); ν_{max} 3400 (OH, NH), 2930, 2850 (CH), 1720 (ester), and 1640 and 1540 cm^{-1} (amide).

Anal. Calc. for $C_{36}H_{68}NO_{13}P$ (753.91): C, 57.35; H, 9.09; N, 1.86. Found: C, 57.09; H, 8.97; N, 1.60.

*Other 3-O-[(3R)-3-acyloxytetradecanoyl]-2-deoxy-2-[(3R)-3-hydroxytetradecanamido]-4-O-phosphono-*D*-glucopyranoses* (**20–24**; GLA 88–92). — Compounds **14–18** were hydrogenolyzed to afford compounds **20–24** in 90–95% yields, as described for **19**, and their i.r. data were similar to those for **19**.

Compound **20** had m.p. 157–159°, $[\alpha]_D$ +14.6° (*c* 0.1, 3:1 chloroform–methanol).

Anal. Calc. for $C_{42}H_{80}NO_{13}P$ (838.07): C, 60.19; H, 9.62; N, 1.67. Found: C, 60.23; H, 9.49; N, 1.48.

Compound **21** had m.p. 157–159°, $[\alpha]_D$ +12.3° (*c* 0.15, 3:1 chloroform–methanol).

Anal. Calc. for $C_{44}H_{84}NO_{13}P$ (866.12): C, 61.02; H, 9.98; N, 1.62. Found: C, 61.27; H, 9.99; N, 1.40.

Compound **22** had m.p. 157–159°, $[\alpha]_D$ +10.8° (*c* 0.13, 3:1 chloroform–methanol).

Anal. Calc. for $C_{45}H_{86}NO_{13}P$ (880.15): C, 61.41; H, 9.85; N, 1.59. Found: C, 61.15; H, 10.14; N, 1.83.

Compound **23** had m.p. 157–159°, $[\alpha]_D$ +11.4° (*c* 0.14, 3:1 chloroform–methanol).

Anal. Calc. for $C_{47}H_{90}NO_{13}P$ (908.21): C, 62.16; H, 9.99; N, 1.54. Found: C, 61.88; H, 10.08; N, 1.51.

Compound **24** had m.p. 157–159°, $[\alpha]_D$ +11.0° (*c* 0.22, 3:1 chloroform–methanol).

Anal. Calc. for $C_{49}H_{94}NO_{13}P$ (936.26): C, 62.86; H, 10.12; N, 1.50. Found: C, 63.02; H, 10.02; N, 1.66.

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