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Syntheses of 2-Deoxy-2-[(2R,3S)-2-fluoro-3-hydroxytetradecanamido]-3-O-[(3R)-3-hydroxytetradecanoyl]-4-O-phosphono-D-glucopyranose and Its (2S,3R)-Isomer

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Syntheses of 2-Deoxy-2-[(2*R*,3*S*)-2-fluoro-3-hydroxytetradecanamido]-3-*O*-[(3*R*)-3-hydroxytetradecanoyl]-4-*O*-phosphono-D-glucopyranose and Its (2*S*,3*R*)-Isomer

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2-Deoxy-2-[(2*R*,3*S*)-2-fluoro-3-hydroxytetradecanamido]-3-*O*-[(3*R*)-3-hydroxytetradecanoyl]-4-*O*-phosphono-D-glucopyranose and its (2*S*,3*R*)-isomer were respectively synthesized from allyl 2-[(2*R*,3*S*)-3-(benzyloxycarbonyloxy)-2-fluorotetradecanamido]-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyranoside and its corresponding (2*S*,3*R*)-isomer. Both target compounds did not activate macrophage, but the (2*S*,3*R*)-analogue strongly inhibited the binding of LPS to macrophage.

Lipopolysaccharides (LPS),[1] and an example of which is shown in Fig. 1,[2] cover the outer surface membrane of such Gram-negative bacteria as *Salmonella minnesota*, *Salmonella typhirium*, and *Escherichia coli*, and are highly potent stimulators of the immune system. A variety of responses, both beneficial and harmful, can be elicited by LPS. One of these harmful responses is fatal endotoxic shock, and this fact has precluded the clinical use of LPS. Most of the biological activities of LPS reside in a relatively small portion of the molecule known as lipid A, which is composed of two β (1–6)-linked D-glucosamine units. Lipid A is a unique hydrophobic anchor substance holding an essentially linear polysaccharide chain to the cell wall. Furthermore, it has two (*R*)-3-hydroxytetradecanoyl groups at the 2- and 3-positions of glucosamine in the reducing terminus, and also has (*R*)-3-acyloxytetradecanoyl groups at the 2′- and 3′-positions of another non-reducing glucosamine moiety.[2,3]

Lipid A has been chemically synthesized by Imoto *et al.*[3] Lipid X corresponds to the reducing half of lipid A, and is one of the biosynthetic precursors of the latter.[4] Nishijima and Raetz[5] have found lipid X in certain mutants of *Escherichia coli* defective in phosphatidylglycerol synthesis.

In a series of investigations by Hasegawa and Kiso[6] on the relationship between the molecular structure and biological activity of non-reducing sugar subunit analogues of lipid A, it has been demonstrated that several kinds of biological activities of LPS can be expressed by certain 4-*O*-phosphono-D-glucosamine derivatives such as GLA-60.[6]

We have been investigating the biological activity of compounds related to GLA-60. In this paper, we describe the synthesis of 2-deoxy-2-[(2*R*,3*S*)-2-fluoro-3-hydroxytetradecanamido]-3-*O*-[(3*R*)-3-hydroxytetradecanoyl]-4-*O*-phosphono-D-glucopyranose (**1a**) and its respective (2*S*,3*R*)-isomer (**1b**) shown in Fig. 2 as compounds containing a fluorinated hydroxytetradecanoyl group.

The starting allyl 2-[(2*R*,3*S*)-3-(benzyloxycarbonyloxy)-2-fluorotetradecanamido]-2-deoxy-4,6-*O*-isopropylidene-β-D-glucopyranoside (**2a**)[7] or (2*S*,3*R*)-isomer (**2b**)[7] was converted to an ester (**3a** or **3b**), respectively, by treating with (*R*)-3-(benzyloxycarbonyloxy)tetradecanoic acid, 1,3-dicyclohexylcarbodiimide (DCC) and 4-dimethylaminopyridine (DMAP) in tetrahydrofuran (THF) at room temperature, or with (*R*)-3-(benzyloxy)tetradecanoyl chloride and triethylamine in THF at room temperature. Treatment of **3a** or **3b** with aqueous 80% or 90% acetic acid (AcOH) at 50°C for 30 min gave diol **4a** or **4b**, respectively. Protection of the primary alcohol of **4a** or **4b** with benzyl chloroformate and DMAP in methylene chloride afforded 6-*O*-benzyloxycarbonyl derivative **5a** or **5b**. Treatment of **5a** or **5b** with diphenyl chlorophosphate and DMAP in methylene chloride yielded **6a** or **6b**. Treatment of **6a** or **6b**, using

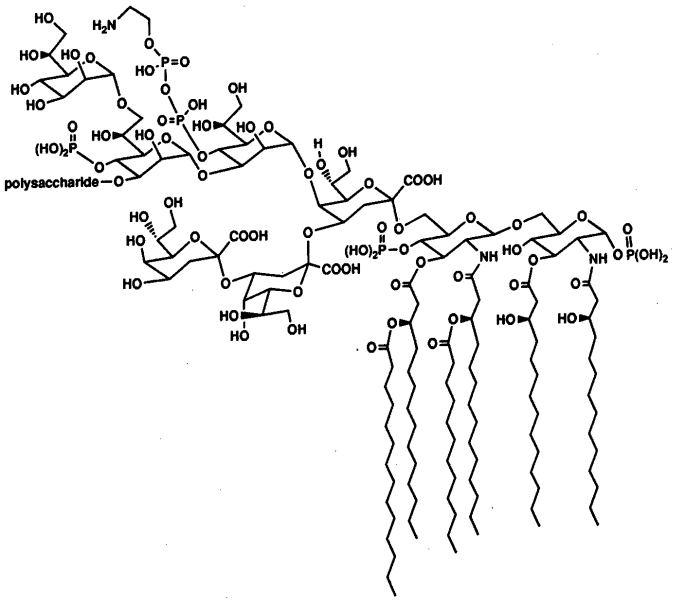

Fig. 1. Structure of Lipopolysaccharide (LPS).[2]

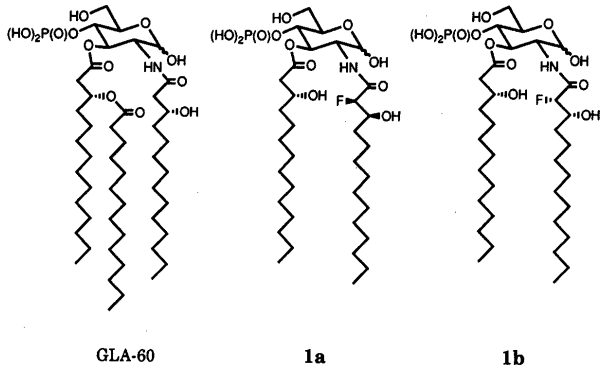

Fig. 2. Structures of GLA-60, **1a** and **1b**.

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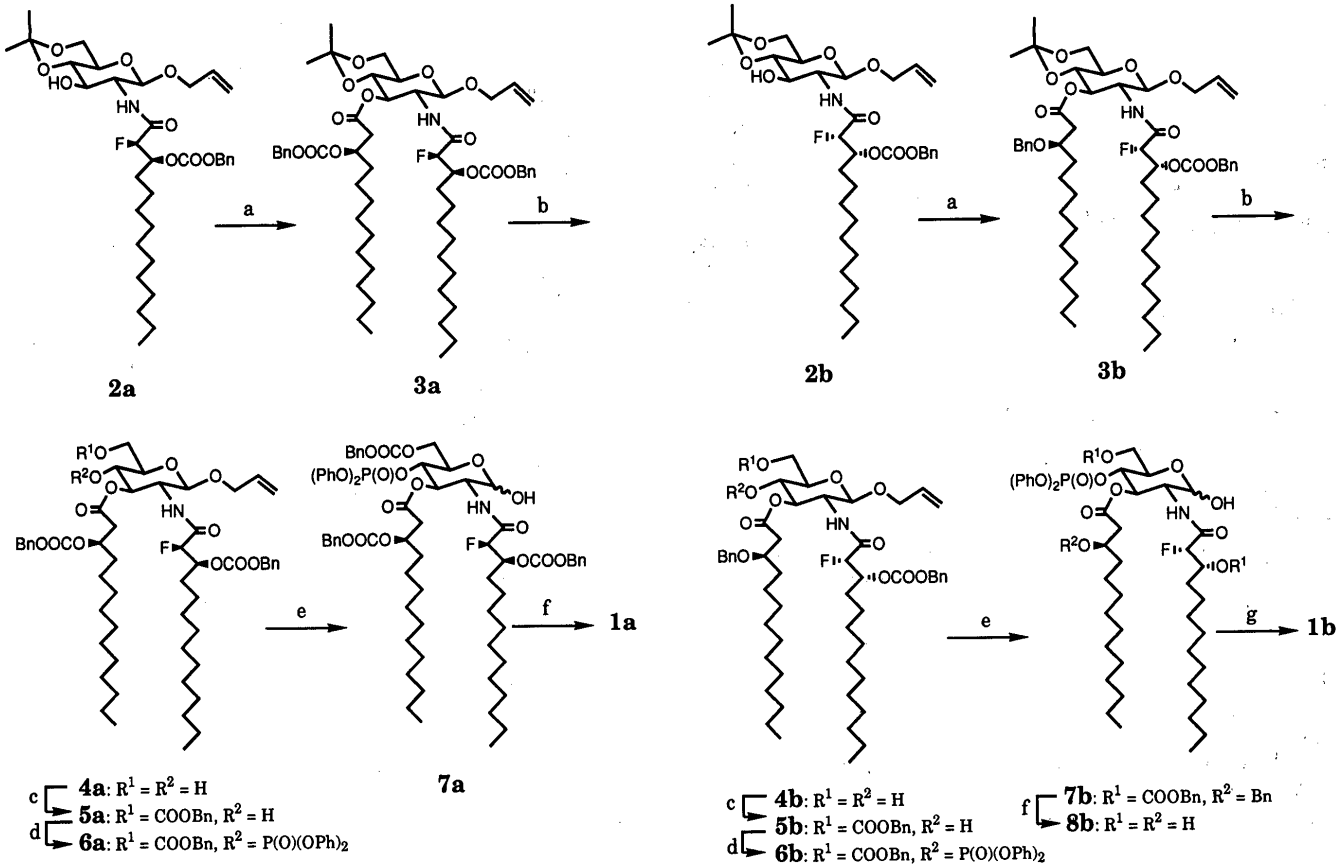

Scheme 1.

Scheme 2.

1,5-cyclooctadiene-bis(methyldiphenylphosphine)iridium hexafluorophosphate[8] ($[Ir(C_8H_{12})(PMePh_2)_2]PF_6$) as a catalyst in THF to isomerise the double bond of the 1-*O*-allyl group, and successive treatment of the resulting enol ether with iodine-pyridine-water[9] gave **7a** or **7b**. The three benzyloxycarbonyl groups of **7a** were removed by hydrogenolysis, using 10% Pd on carbon, and successive hydrogenolysis of the resulting triol, using PtO_2, afforded **1a**. Hydrogenolysis of one benzyl and two benzyloxycarbonyl groups of **7b**, using 10% Pd on carbon, gave **8b**. Final deprotection of **8b** with PtO_2 as a catalyst gave **1b**.

Compound **1a** and a defluorinated analogue of **1b** revealed neither activation toward macrophage nor inhibition of LPS binding to macrophage. Compound **1b** did not activate macrophage, but strongly inhibited the binding of LPS to macrophage. This suggests that **1b** may have bound specifically to the lipopolysaccharide-binding protein (LBP),[10] which carries LPS to the CD-14 receptor[11] of macrophage, thereby giving rise to macrophage activation.

Experimental

Melting point (mp) values are uncorrected. ^{1}H-NMR data were recorded at 60 MHz with a Varian T-60 or at 270 MHz with a JEOL JNN-270 spectrometer, using trimethylsilane as an internal standard. IR absorption spectra were determined with a Jasco IR A-2 spectrophotometer, and mass spectra were obtained with a JMS-O1SG mass spectrometer. Column chromatography was carried out on silica gel-60 (Merck, 230–400 mesh ASTM) at a slightly elevated pressure (1.2 atm) for easy elution.

*Allyl 2-[(2R,3S)-3-(benzyloxycarbonyloxy)-2-fluorotetradecanamido]-3-O-[(3R)-3-(benzyloxycarbonyloxy)tetradecanoyl]-2-deoxy-4,6-O-isopropylidene-β-*D*-glucopyranoside* (**3a**). To a solution of allyl 2-deoxy-2-[(2*R*,3*S*)-2-fluoro-3-hydroxytetradecanamido]-4,6-*O*-isopropylidene-β-D-glucopyranoside (**2a**[7]; 5.00 g, 7.84 mmol) in THF (100 ml) was added (*R*)-3-(benzyloxycarbonyloxy)tetradecanoic acid (3.56 g, 9.41 mmol, 1.20 equiv), DCC (1.62 g, 1.30 equiv) and DMAP (1.00 g, 1.05 equiv). The mixture was stirred for 1 h at 25°C. The reaction mixture was filtered, concentrated *in vacuo*, and diluted with ethyl acetate (EtOAc). This solution was washed with sat. $NaHCO_3$ and sat. NaCl, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to give an oily mixture, which was chromatographed in a silica gel column. Elution with cyclohexane–EtOAc (19 : 1) gave **3a** (6.10 g, 78% yield) as a gum. 60 MHz ^{1}H-NMR ($CDCl_3$) δ: 0.86–2.23 (52H, m), 2.45–2.84 (2H, m), 3.17–6.30 (19H, m, including 4H, s), 6.58 (1H, broad s), 7.33 (10H, s), IR ν_{max} (KBr): 1745, 1671 cm^{-1}. *Anal.* Found: C, 67.30; H, 8.57; N, 1.44; F, 2.12%. Calcd. for $C_{56}H_{84}NO_{13}F$ (998.3): C, 67.38; H, 8.48; N, 1.40; F, 1.90%.

*Allyl 2-[(2S,3R)-3-(benzyloxycarbonyloxy)-2-fluorotetradecanamido]-3-O-[(3R)-3-(benzyloxy)tetradecanoyl]-2-deoxy-4,6-O-isopropylidene-β-*D*-glucopyranoside* (**3b**). Allyl 2-deoxy-2-[(2*S*,3*R*)-2-fluoro-3-hydroxytetradecanamido]-4,6-*O*-isopropylidene-β-D-glucopyranoside (**2b**)[7] was treated with (*R*)-3-(benzyloxy)tetradecanoyl chloride (1.1 equiv) and Et_3N (1.2 equiv) in THF to give **3b** (76% yield) as a gum after cheomatographic purification in a silica gel column. 60 MHz ^{1}H-NMR ($CDCl_3$) δ: 0.65–2.08 (52H, m, including 3H, s, at δ 1.43), 2.43–2.72 (2H, m), 3.05–6.21 (19H, m, including two 2H, s, at δ 4.48 and 5.12), 6.31–6.67 (1H, m), 7.28 (5H, s), 7.30 (5H, s). IR ν_{max} (KBr): 1745, 1670 cm^{-1}. *Anal.* Found: C, 69.20; H, 8.97; N, 1.44; F, 1.85%. Calcd. for $C_{55}H_{84}NO_{11}F$ (954.3): C, 69.23;

H, 8.87; N, 1.47; F, 1.99%.

Allyl 2-[(2R,3S)-3-(benzyloxycarbonyloxy)-2-fluorotetradecanamido]-3-O-[(3R)-3-(benzyloxycarbonyloxy)tetradecanoyl]-2-deoxy-β-D-glucopyranoside (**4a**). A solution of **3a** (5.00 g, 5.24 mmol) in aqueous 80% AcOH was stirred for 30 min at 50°C. The reaction mixture was concentrated *in vacuo* to give **4a** (4.55 g, 95% yield). 270 MHz ^{1}H-NMR ($CDCl_3$) δ: 0.88 (6H, t, J=6.9 Hz), 1.08–1.84 (40H, m), 2.47 (1H, dd, J=8.1, 15.0 Hz), 2.58 (1H, dd, J=3.7, 15.0 Hz), 3.26 (1H, bs), 3.40–3.45 (1H, m), 3.61 (1H, t, J=9.2 Hz), 3.75–3.94 (3H, m), 4.00–4.31 (2H, m), 4.63 (1H, d, J=8.4 Hz), 4.82–5.28 (11H, m), 5.75–5.88 (1H, m), 6.00 (1H, dd, J=4.4, 8.4 Hz), 7.33–7.38 (10H, m). IR ν_{max} ($CHCl_3$): 1745, 1695 cm^{-1}. *Anal.* Found: C, 66.48; H, 8.72; N, 1.60; F, 1.96%. Calcd. for $C_{53}H_{80}NO_{13}F$ (958.2): C, 66.43; H, 8.42; N, 1.46; F, 1.98%.

Allyl 2-[(2S,3R)-3-(benzyloxycarbonyloxy)-2-fluorotetradecanamido]-3-O-[(3R)-3-(benzyloxy)tetradecanoyl]-2-deoxy-β-D-glucopyranoside (**4b**). Compound **3b** in aqueous 90% AcOH was treated as already described to give **4b** (96% yield). 60 MHz ^{1}H-NMR ($CDCl_3$) δ: 0.62–2.18 (46H, m), 2.32–2.91 (4H, m), 3.20–4.25 (8H, m), 4.28–4.71 (3H, m, including 2H, s, at δ 4.48), 4.86–6.19 (8H, m), 6.45–6.85 (1H, m), 7.28 (5H, s), 7.31 (5H, s). IR ν_{max} (KBr): 1742, 1669 cm^{-1}. *Anal.* Found: C, 68.14; H, 8.96; N, 1.59; F, 2.02%. Calcd. for $C_{52}H_{80}NO_{11}F$ (914.2): C, 68.32; H, 8.82; N, 1.53; F, 2.08%.

Allyl 6-O-benzyloxycarbonyl-2-[(2R,3S)-3-(benzyloxycarbonyloxy)-2-fluorotetradecanamido]-3-O-[(3R)-3-(benzyloxycarbonyloxy)tetradecanoyl]-2-deoxy-β-D-glucopyranoside (**5a**). To a solution of **4a** (4.30 g, 4.50 mmol) in CH_2Cl_2 (100 ml) were added DMAP (822 mg, 6.74 mmol) and a solution of benzyl chloroformate (0.95 ml, 5.38 mmol) in CH_2Cl_2 (10 ml). The mixture was stirred for 1 h at 25°C, concentrated *in vacuo*, and dissolved in EtOAc. The solution was washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give an oily mixture, which was chromatographed in a silica gel column. Elution with cyclohexane–EtOAc (5:1) gave **5a** (2.45 g, 50% yield) as a gum and a 4,6-dibenzyloxycarbonylated product. 60 MHz ^{1}H-NMR ($CDCl_3$) δ: 0.64–1.89 (46H, m), 2.37–2.64 (2H, m), 3.09–6.20 (22H, m, including 4H, s, at δ 5.09, and 2H, s, at δ 5.13), 6.49 (1H, broad s), 7.32 (15H, s). IR ν_{max} ($CHCl_3$): 1745, 1695 cm^{-1}. *Anal.* Found: C, 67.15; H, 8.09; N, 1.23; F, 1.56%. Calcd. for $C_{61}H_{86}NO_{15}F$ (1092.3): C, 67.08; H, 7.94; N, 1.28; F, 1.74%.

Allyl 6-O-benzyloxycarbonyl-2-[(2S,3R)-3-(benzyloxycarbonyloxy)-2-fluorotetradecanamido]-3-O-[(3R)-3-(benzyloxy)tetradecanoyl]-2-deoxy-β-D-glucopyranoside (**5a**). Compound **4b** was treated as already described to give **5b** (65% yield) as a gum and a 4,6-dibenzyloxycarbonylated product. 60 MHz ^{1}H-NMR ($CDCl_3$) δ: 0.85–2.08 (46H, m), 2.41–2.64 (2H, m), 3.00 (1H, broad), 3.48–6.08 (21H, m, including 4H, s), 6.18–6.72 (1H, m), 7.26–7.56 (15H, m). IR ν_{max} (KBr): 1750, 1727, 1676 cm^{-1}. *Anal.* Found: C, 68.61; H, 8.31; N, 1.40; F, 1.82%. Calcd. for $C_{60}H_{86}NO_{13}F$ (1048.3): C, 68.74; H, 8.27; N, 1.34; F, 1.81%.

Allyl 6-O-benzyloxycarbonyl-2-[(2R,3S)-3-(benzyloxycarbonyloxy)-2-fluorotetradecanamido]-3-O-[(3R)-3-(benzyloxycarbonyloxy)tetradecanoyl]-2-deoxy-4-O-diphenoxyphosphinyl-β-D-glucopyranoside (**6a**). To a solution of **5a** (2.20 g, 2.01 mmol) in CH_2Cl_2 (30 ml) were added DMAP (1.47 g, 12.1 mmol) and a solution of diphenyl chlorophosphate (1.62 g, 6.03 mmol) in CH_2Cl_2 (5 ml). The mixture was stirred for 1 h at 25°C, concentrated *in vacuo*, and dissolved in EtOAc. The solution was washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give an oily mixture, which was chromatographed in a silica gel column. Elution with cyclohexane–EtOAc (3:1) gave **6a** (2.65 g, 99% yield) as a gum. 60 MHz ^{1}H-NMR ($CDCl_3$) δ: 0.64–2.05 (46H, m), 2.25–2.51 (2H, m), 3.00–6.15 (21H, m, including 6H, s, at δ 5.08), 6.63 (1H, broad s), 7.18–7.33 (25H, m). IR ν_{max} ($CHCl_3$): 1747, 1690, 1590 cm^{-1}. *Anal.* Found: C, 66.01; H, 7.35; N, 1.03; F, 1.37; P, 2.41%. Calcd. for $C_{73}H_{95}NO_{18}FP$ (1324.5): C, 66.20; H, 7.23; N, 1.06; F, 1.43; P, 2.34%.

Allyl 6-O-benzyloxycarbonyl-2-[(2S,3R)-3-(benzyloxycarbonyloxy)-2-fluorotetradecanamido]-3-O-[(3R)-3-(benzyloxy)tetradecanoyl]-2-deoxy-4-O-diphenoxyphosphinyl-β-D-glucopyranoside (**6b**). Compound **5b** was treated as already described to give **6b** (99% yield) as a gum. 60 MHz ^{1}H-NMR ($CDCl_3$) δ: 0.72–1.87 (46H, m), 2.26–2.49 (2H, m), 3.45–6.05 (21H, m, including 2H, s, at δ 4.30, and 4H, s, at δ 5.05), 6.18–6.50 (1H, m), 7.15–7.40 (25H, m). IR ν_{max} (KBr): 1743, 1679 cm^{-1}. *Anal.* Found: C, 67.59; H, 7.56; N, 1.10; F, 1.37; P, 2.60%. Calcd. for $C_{72}H_{95}NO_{10}FP$ (1280.5): C, 67.53; H, 7.48; N, 1.09; F, 1.48; P, 2.42%.

6-O-Benzyloxycarbonyl-2-[(2R,3S)-3-(benzyloxycarbonyloxy)-2-fluorotetradecanamido]-3-O-[(3R)-3-(benzyloxycarbonyloxy)tetradecanoyl]-2-deoxy-4-O-diphenoxyphosphinyl-β-D-glucopyranoside (**7a**). To a solution of **6a** (2.50 g, 1.95 mmol) in THF (30 ml) was added $[Ir(C_8H_{12})(PMePh_2)_2]$-$PF_6$ (80 mg). The air in the reaction flask was completely replaced with nitrogen and then further replaced with hydrogen to activate the iridium complex. Immediately after 1 or 2 min, when the red-colored solution of the iridium complex had become almost colorless, the hydrogen was completely replaced with nitrogen. This solution was stirred for 2 h at 25°C. After confirming a double bond shift to an enol ether from the 1-allyloxy group by TLC (as indicated by a slightly higher R_f value), H_2O (3 ml), pyridine (0.3 ml) and iodine (300 mg) were added to this solution. After 30 min of stirring at 25°C, the mixture was concentrated *in vacuo*, diluted with EtOAc, successively washed with aq. 5% Na_2SO_3, sat. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated to give a mixture that was separated in a silica gel column. Elution with cyclohexane–EtOAc (3:1) gave **7a** (1.68 g, 69% yield) as a gum. 270 MHz ^{1}H-NMR ($CDCl_3$) δ: 0.88 (6H, t, J=6.2 Hz), 1.13–1.71 (40H, m), 2.37 (1H, dd, J=7.3, 17.2 Hz), 2.55 (1H, dd, J=5.1, 17.2 Hz), 3.61 (1H, broad s), 3.83–3.90 (1H, m), 4.16–4.37 (3H, m), 4.64–4.81 (2H, m), 4.96–5.28 (9H, m), 5.56 (1H, dd, J=9.2, 11.0 Hz), 6.48 (1H, dd, J=3.3, 7.7 Hz), 7.09–7.37 (25H, m). IR ν_{max} ($CHCl_3$): 1743, 1685, 1590 cm^{-1}. *Anal.* Found: C, 65.37; H, 7.16; N, 1.18; F, 1.51; P, 2.50%. Calcd. for $C_{70}H_{91}NO_{18}FP$ (1284.5): C, 65.46; H, 7.14; N, 1.09; F, 1.48; P, 2.41%.

6-O-Benzyloxycarbonyl-2-[(2S,3R)-3-(benzyloxycarbonyloxy)-2-fluorotetradecanamido]-3-O-[(3R)-3-(benzyloxy)tetradecanoyl]-2-deoxy-4-O-diphenoxyphosphinyl-β-D-glucopyranoside (**7b**). Compound **6b** was treated as already described to give **7b** (66% yield) as a gum. 60 MHz ^{1}H-NMR ($CDCl_3$) δ: 0.66–2.01 (46H, m), 2.16–2.56 (2H, m), 2.89 (1H, d, J=5 Hz), 3.38–5.71 (16H, m, including 2H, s, at δ 4.32 and 4H, s, at δ 5.10), 6.45–6.81 (1H, m), 7.08–7.45 (25H, m). IR ν_{max} (KBr): 1747, 1685, 1590 cm^{-1}. *Anal.* Found: C, 66.42; H, 7.41; N, 1.01; F, 1.42; P, 2.66%. Calcd. for $C_{69}H_{91}NO_{16}FP$ (1240.5): C, 66.81; H, 7.39; N, 1.13; F, 1.53; P, 2.50%.

2-Deoxy-4-O-diphenoxyphosphinyl-2-[(2S,3R)-2-fluoro-3-hydroxytetradecanamido]-3-O-[(3R)-3-hydroxytetradecanoyl]-β-D-glucopyranose (**8b**). Compound **7b** was hydrogenolized, using 10% Pd on carbon in THF, at 25°C for 3 h, before the product was purified in a silica gel column. Elution with EtOAc gave **8b** (56% yield) as a powder. 270 MHz ^{1}H-NMR ($CDCl_3$) δ: 0.82–0.97 (6H, m), 0.98–1.73 (40H, m), 2.08–2.30 (2H, m), 2.60–4.15 (8H, m), 4.20–4.41 (2H, m), 4.67 (1H, d, J=48.0 Hz), 4.79–4.99 (1H, m), 5.33–5.64 (2H, m), 6.83–6.93 (1H, m), 7.10–7.39 (10H, m). *Anal.* Found: C, 62.89; H, 8.24; N, 1.47; F, 2.15; P, 3.41%. Calcd. for $C_{46}H_{73}NO_{12}FP$ (882.1): C, 62.64; H, 8.34; N, 1.59; F, 2.15; P, 3.51%.

2-Deoxy-2-[(2R,3S)-2-fluoro-3-hydroxytetradecanamido]-3-O-[(3R)-3-hydroxytetradecanoyl]-4-O-phosphono-D-glucopyranose (**1a**). Hydrogenolysis of **7a** (1.30 g, 1.01 mmol) in THF (30 ml), using 10% Pd on carbon (1.0 g), at 25°C for 3 h gave a mixture which was filtered. To this filtrate was added PtO_2 (200 mg), and the mixture was hydrogenolized for 2 h at 25°C, filtered, and concentrated *in vacuo* to give a residue, which was then chromatographed in a silica gel column. Elution with $CHCl_3$–MeOH (9:1 and then 5:1) gave a powder (490 mg) containing **1a**, which was contaminated by a considerable amount of silica gel. This powder was suspended in 80 ml of 0.1 M HCl, and 300 ml of $CHCl_3$–MeOH (1:2) was added to this suspension. The mixture was sonicated to dissolve the powder. To this solution were added $CHCl_3$ (100 ml) and 0.1 M HCl (100 ml) to separate into two phases. The chloroform layer was collected and concentrated *in vacuo* to give **1a** (402 mg, 54% yield). 270 MHz ^{1}H-NMR ($CDCl_3$) δ: 0.85–1.00 (6H, m), 1.24–1.98 (40H, m), 2.68–2.95 (2H, m), 4.13–4.50 (5H, m), 4.56–4.70 (1H, m), 4.72–4.92 (1H, m), 5.10 (1H, d, J=46.9 Hz), 5.52 (1H, d, J=3.4 Hz), 5.74 (1H, t, J=9.3–9.8 Hz). IR ν_{max} (KBr): 1710, 1660 cm^{-1}. *Anal.* Found: C, 55.51; H, 8.79; N, 2.17; F, 2.44; P, 4.01%. Calcd. for $C_{34}H_{65}NO_{12}FP$ (729.9): C, 55.95; H, 8.98; N, 1.92; F, 2.60; P, 4.24%.

2-Deoxy-2-[(2S,3R)-2-fluoro-3-hydroxytetradecanamido]-3-O-[(3R)-3-hydroxytetradeconoyl]-4-O-phosphono-D-glucopyranose (**1b**). Compound **8b** (490 mg) was hydrogenolized, using PtO_2 (80 mg) as a catalyst, in THF (30 ml) at room temperature for 3 h. The reaction mixture was filtered to give **1b** (380 mg) in a 96% yield. 270 MHz ^{1}H-NMR (CF_3COOD) δ: 0.91

(6H, t, J=6.4–6.8 Hz), 1.20–1.98 (40H, m), 2.74–2.96 (2H, m), 4.07–4.51 (5H, m), 4.55–4.67 (1H, m), 4.82 (1H, q, J=9.3–9.8 Hz), 5.09 (1H, d, J=47.5 Hz), 5.53 (1H, d, J=3.9 Hz), 5.74 (1H, dd, J=9.3, 10.7 Hz). *Anal.* Found: C, 55.84; H, 9.22; N, 1.94; F, 2.51; P, 4.09%. Calcd. for $C_{34}H_{65}NO_{12}FP$ (729.9): C, 55.95; H, 8.98; N, 1.92; F, 2.60; P, 4.24%.

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