Synthesis of Amphiphilic Chitopentaose and Chitoheptaose Derivatives Using a Common Disaccharidic Synthon as the Chain Elongation Unit[1]

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With interest in clustering bioactive chitooligosaccharides, a pair of amphiphilic derivatives of around DP (degree of polymerization) 6, which has been considered to be the minimum molecular length for some kinds of bioactivity, was synthesized. Homologous derivatives of chitopentaose and chitoheptaose carrying tetradecanoyl and tetradecyloxy groups at the NH and C-1 of the reducing ends, respectively, were actually obtained using a 1,6-anhydro-2-azido-2-deoxy-β-D-glucopyranose derivative as the terminal precursor and a chitobiose derivative as the elongation unit. Micelle formation of both derivatives was assumed from the results obtained by dye solubilization tests.

In recent years, chitooligosaccharides and their derivatives have attracted much interest due to their diverse biological activities. For example, glycolipids derived from chitooligosaccharides of DP 2—4 showed certain immunostimulatory and antitumor activities in mice,[2] while one of the nodulation factors involved in *Rhizobium*-legume symbiosis was identified with a specifically modified chitotetraose derivative.[3] Simple chitooligosaccharides of more than DP 6 and their per-*N*-acetyl derivatives were also reported to show inhibitory effects on the growth of solid tumors implanted in mice[4] and to induce phytoalexin formation in rice cells,[5] respectively. These findings stimulated us to prepare homologous amphiphilic chitooligosaccharide derivatives that were composed of penta- and hepta-saccharides. We expected that those molecules would aggregate in water and form a micelle, which might improve the known biological activities, depending on the simple chitooligosaccharide skeletons, and/or exhibit new unknown functions. Referring to the physicochemical data on glycolipids,[6] we designed a chitooligosaccharide derivative carrying binary hydrophobic chains in the D-glucosamine moiety of the reducing end; i.e., one as an aglycone of *O*-glycoside and the other as an *N*-acyl group. Actually, tetradecyl 4-*O*-β-chitotetraosyl-2-deoxy-2-tetradecanamido-β-D-glucopyranoside (**2**) and its heptasaccharidic homolog **3** were prepared as well as the model preparation of the trisaccharidic homolog **1**, although **1** itself was unable to be finally characterized because of its extremely poor solubility (Fig. 1).

For the preparations of **1**, **2**, and **3**, we employed the following common synthetic scheme: First, the known 1,6-anhydro-2-azido-2-deoxy-3-*O*-benzyl-β-D-glucopyranose (**4**)[7] was utilized as a precursor for the D-glucosamine moiety of the reducing end of the target oligosaccharide skeletons (Fig. 2); second, 4-pentenyl *O*-(4-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (**5**) prepared from chitobiose peracetate was used as the common unit for chain elongation; and third, after completion of sugar-chain skeletons, tetradecanoyl and tetradecyl groups were introduced into the reducing D-glucosamine moiety derived from **4**.

Synthesis of Synthon 5 as the Chain Elongation Unit. We previously reported a large-scale preparation of chitobiose peracetate by enzymatic degradation of chitin and subsequent peracetylation of the product.[8] This disaccharide peracetate was converted into 4-pentenyl β-glycoside **6** according to the literature.[9] Compound **6** was benzylidenated with α,α-dimethoxytoluene and (+)-10-camphorsulfonic acid (CSA) in the usual way, and the resulting 4′,6′-*O*-benzylidene derivative, having very poor solubility in most solvents, was subjected to deacylation by a treatment with aqueous sodium hydroxide to afford a free diamino compound, which was then treated with phthalic anhydride and triethylamine, giving 4-pentenyl *O*-(4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-2-deoxy-2-phthalimido-β-D-glucopyranoside (**7**) as crystals (Scheme 1). After all of the hydroxy groups at the 3, 3′, and 6 positions had been benzylated, product **8** was subjected to a regioselective cleavage of the 4′,6′-*O*-benzylidene group under reductive conditions for deprotection at the 4′ position. The initial attempt using trimethylamine–borane (1/1) in the presence of anhydrous aluminum chloride[10] as the reagent system failed because the terminal double bond of the pentenyl group underwent partial hydroboration. However, the use of sodium cyanotrihydroborate in the presence of dry hydrogen chloride[11] was successful, giving the 6′-*O*-benzyl-

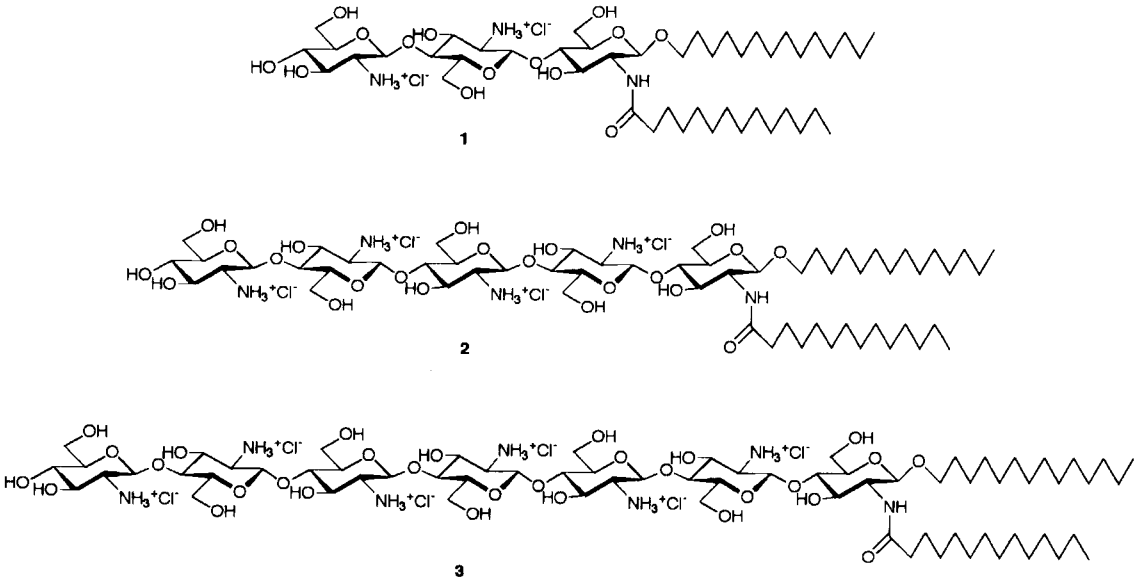


Fig. 1.

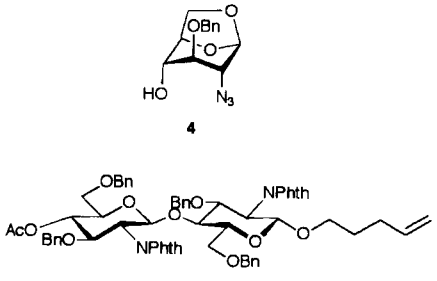
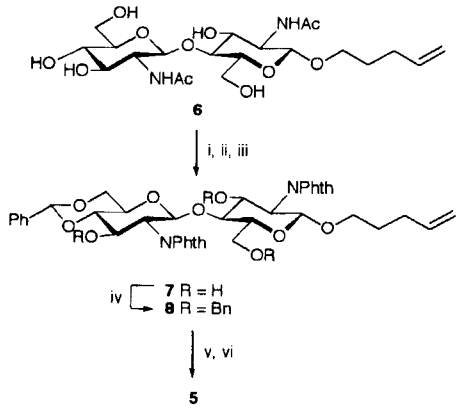


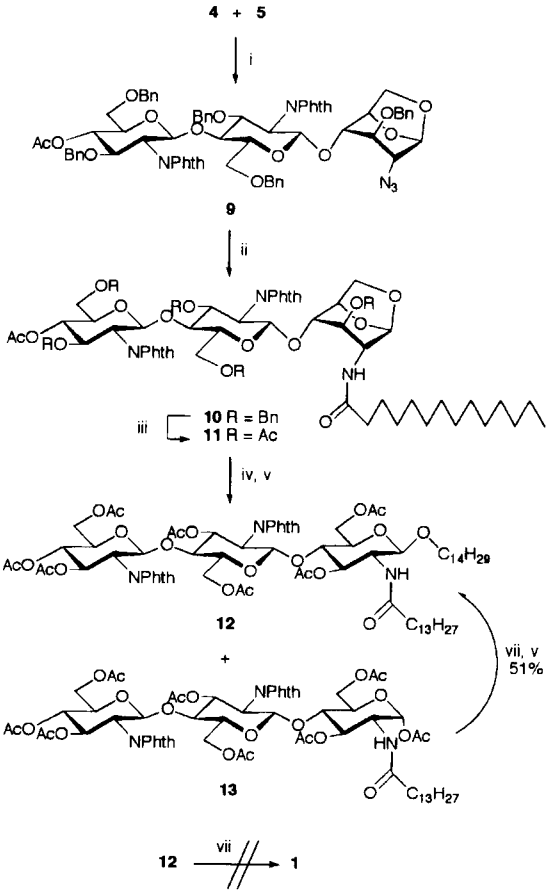
Fig. 2.



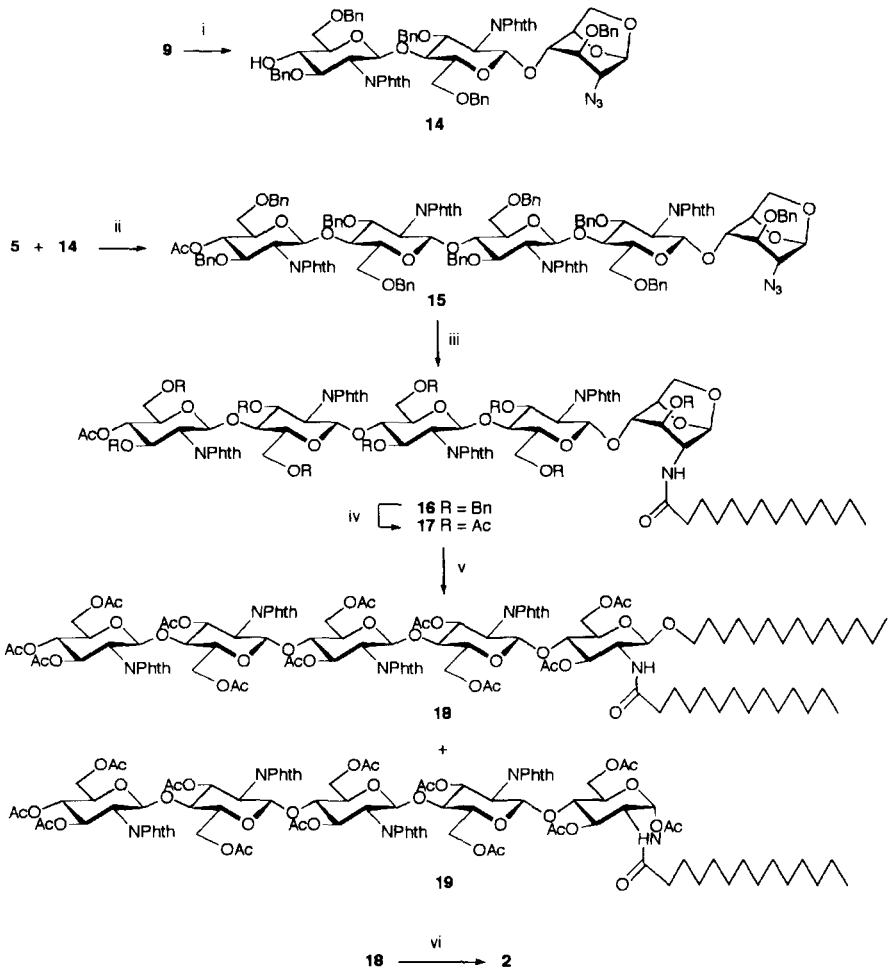
Scheme 1. Reagents and conditions: i, α,α-dimethoxytoluene, CSA, DMF, 50 °C; ii, EtOH–5M aq NaOH (4 : 1), 100 °C; iii, phthalic anhydride, Et_3N, MeOH, r.t.; then DMF, 120 °C, 69%; iv, BnBr, Bu_4NI, NaH, DMF ; v, sodium cyanotrihydroborate, HCl, molecular sieves 4A, THF, 0 °C, 92%; vi, Ac_2O, pyridine, r.t., 98%.

4′-hydroxy compound in very good yield. Finally, the resulting 4′-hydroxy group was acetylated to give the chain-elongation synthon **5**, which carries both potential functions as a glycosyl donor (4-pentenyl group) and as an acceptor (acylated hydroxy group).

Synthesis of Chitotriose Derivative 1 Attempted as a

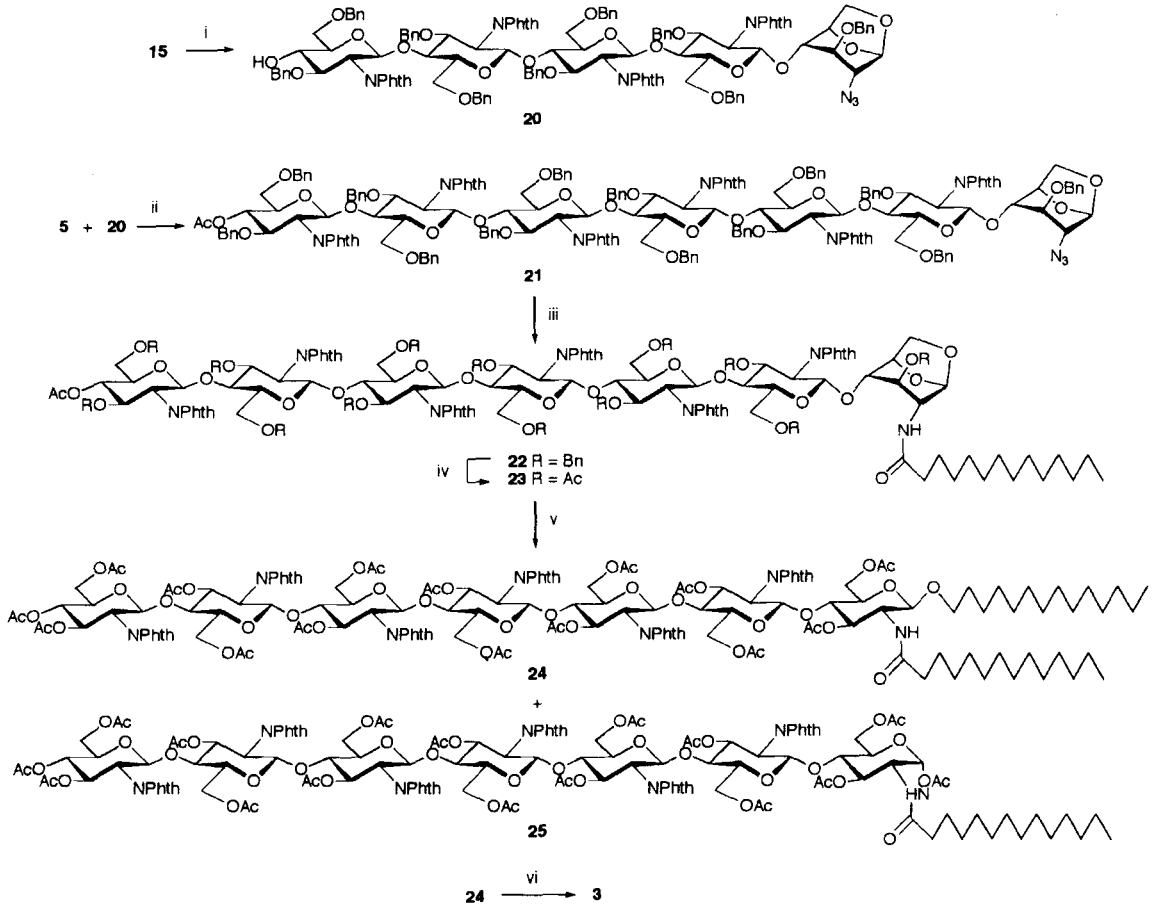


Scheme 2. Reagents and conditions: i, NIS, TESOTf, CH_2Cl_2, 0 °C, 83%; ii, H_2S, pyridine–Et_3N (7 : 3), r.t.; then myristoyl chloride, $CHCl_3$–MeOH (9 : 1), 0 °C, 95%; iii, $Pd(OH)_2/C$, H_2, AcOH, r.t.; then Ac_2O, pyridine, r.t., 83%; iv, TESOTf, Ac_2O, r.t.; v, 1-tetradecanol, CSA, 1,2-dichloroethane, 90 °C, 49% for **12**, 36% for **13**; vi, TMSOTf, 1,2-dichloroethane, 50 °C; vii, NaOMe, THF–MeOH (2 : 1), r.t.; then *n*-BuOH–ethylenediamine (5 : 1), 90 °C; then 0.01 M aq HCl, 72% (crude).



Scheme 3. Reagents and conditions: i, NaOMe, THF–NaOH (3 : 1), r.t., 95%; ii, NIS, TESOTf, CH_2Cl_2, −5 °C, 69% (r.t., 24%); iii, H_2S, pyridine–Et_3N (7 : 3), r.t.; then myristoyl chloride, Et_3N, $CHCl_3$–MeOH (9 : 1), 0 °C, 92%; iv, $Pd(OH)_2$/C, H_2, DMF, r.t.; then Ac_2O, pyridine, r.t., 81%; v, TESOTf, Ac_2O, r.t.; then 1-tetradecanol, CSA, 1,2-dichloroethane, 90 °C, 46% for **18**, 42% for **19**; vi, NaOMe, $CHCl_3$–MeOH (3 : 2), r.t.; then MeOH–EtOH–ethylenediamine (2 : 7 : 1), reflux; then 0.1 M aq HCl, 89%.

Model Reaction. The D-glucosamine precursor **4** was glycosylated with the elongation synthon **5** using *N*-iodosuccinimide (NIS) and triethylsilyl triflate (TESOTf)[12] as the activator for the glycosyl donor, giving trisaccharide **9** in 83% yield on the basis of **5** (Scheme 2). After reduction of the azido group by a treatment with hydrogen sulfide in pyridine–triethylamine, the resulting amine was acylated with tetradecanoyl chloride in methanol in the presence of triethylamine to give **10** bearing one hydrophobic chain. The benzyl groups attached to the primary hydroxy groups often undergo cleavage under strongly acidic conditions, such as those employed for the 1,6-anhydro ring opening. Therefore, the replacement of the benzyl groups in **10** with the acetyl groups was conducted prior to the manipulation of its 1,6-anhydro ring. Thus, **10** underwent catalytic hydrogenolysis with palladium(II) hydroxide on carbon in acetic acid and then acetylated, giving **11** in good overall yield. We already reported as a model reaction using a chitobiose derivative that acetolysis of 1,6-anhydro-2-deoxy-2-tetradecanamido-β-D-glucopyranosyl moiety with TESOTf as the acidic catalyst gave an oxazoline intermediate as the major product accompanied by α-glycosyl acetate as a by-product, and immediate treatment of this mixture with 1-tetradecanol and protic acid followed by a separation work-up efficiently led to the tetradecyl β-glycoside derivative.[13] In a similar way to the reaction with this disaccharidic model compound, **11** was treated with acetic anhydride-TESOTf at 15 °C and then with 1-tetradecanol in the presence of CSA at 90 °C. Chromatographic separation of the resulting mixture gave the desired tetradecyl β-glycoside **12** and α-glycosyl acetate **13**, in 49 and 36% yields, respectively. Compound **13** was also convertible into **12** in 51% yield by the same treatment as the reaction with **11**. An attempt to remove all protecting groups from **12** encountered serious difficulties because extremely poor solubility of partially deprotected products prevented completion of the reaction. Thus, successive treatments of **12** with methanolic sodium methoxide at room temperature (deacetylation), with ethylenediamine in 1-butanol at 90 °C (dephthaloylation),[14] and with dilute hydrochloric acid in methanol (hydrochloride formation) gave **1** contaminated with incompletely deprotected compounds, which was confirmed by the FAB mass spectrum. The obtained crude **1**



Scheme 4. Reagents and conditions: i, NaOMe, THF–MeOH (3 : 1), r.t., 91%; ii, NIS, TESOTf, −40 °C, 57% (0 °C, 18%); iii, H_2S, pyridine–Et_3N (7 : 3), r.t.; then myristoyl chloride, Et_3N, $CHCl_3$–MeOH, 0 °C, 93%; iv, $Pd(OH)_2$/C, H_2, DMF–AcOH (9 : 1), r.t.; then Ac_2O, pyridine, r.t., 99%; v, TESOTf, Ac_2O–$CHCl_3$ (1 : 2), 30 °C; then 1-tetradecanol, CSA, 1,2-dichloroethane, 90 °C, 53% for **24**, 19% for **25**, 26% recovered **23**; vi, NaOMe, $CHCl_3$–MeOH (3 : 2), r.t.; then MeOH–EtOH–ethylenediamine (4 : 5 : 1), reflux; then 0.1 M aq HCl, 66%.

never dissolved in aqueous, protic organic, or even dipolar aprotic solvents.

Synthesis of Chitopentaose Derivative 2. Deacetylation of the trisaccharide intermediate **9** with a base led to the generation of a new glycosyl acceptor **14**, which was glycosylated with the common donor **5** using a combination of NIS and TESOTf as the activator of **5**, similar to the preparation of **9**. The yields of the resulting pentasaccharide **15** seemed to depend on the temperature employed for activation of the glycosyl donor (Scheme 3). Thus, the yield was only 24% on the basis of **14** when the activation was carried out at room temperature, while **15** was obtainable in 69% yield by activation at −5 °C. Similar to the conversion of **9** →**10** →**11**, the compound **15** was subjected to reduction of the azido group and the subsequent *N*-tetradecanoylation to afford **16**, of which protecting groups were replaced from the *O*-benzyl to the *O*-acetyl group giving **17**. The one-pot conversion of the 1,6-anhydro-D-glucosamine moiety of **17** into the tetradecyl β-glycoside form via an oxazoline intermediate was performed just similarly to the model reaction[13] by acetolysis with TESOTf, followed by treatment of 1-tetradecanol in the presence of protic acid. After separation work-up using column chromatography, the desired **18** and the accompanied **19** were obtained in 46 and 42% yields, respectively. In a similar way to the case of **12**, **18** was subjected to successive treatments with sodium methoxide and ethylenediamine, giving the pentasaccharide derivative carrying 4 free amino groups, which was hardly soluble in basic media. In contrast to the trisaccharide homolog, this pentasaccharide derivative could be dissolved in acidic media such as aqueous acetic acid. Therefore, gel-filtration using Sephadex G-15 was used to purify this compound. Finally, lyophilization from dilute aqueous hydrochloric acid gave tetrahydrochloride salt **2** in a good overall yield from **18**.

Synthesis of Chitoheptaose Derivative 3. The success in obtaining a homogeneous pentasaccharide derivative **2** facilitated the preparation of its heptasaccharidic homolog **3**. Similar to the preparation of **2**, a sequence of reactions was repeated with a few modifications, starting from the pentasaccharide intermediate **15**. The new glycosyl acceptor **20**, obtained by the deacetylation of **15**, was glycosylated with the donor **5** by the action of NIS and TESOTf to give the heptasaccharide **21** (Scheme 4). Again, this glycosidation was temperature-dependent, requiring a lower temperature for the activation of **5**. Namely, the yields of **21** on the basis of **20** were 18 and 57% when **5** was activated at 0 and −40 °C,

respectively. After reduction of the azido group followed by *N*-tetradecanoylation, the resulting heptasaccharide **22** underwent *O*-debenzylation and subsequent *O*-acetylation to give **23**. Since **23** was hardly soluble in acetic anhydride, its acetolysis catalyzed with TESOTf for the oxazoline formation was accomplished in a mixture of acetic anhydride and chloroform at 30 °C. As shown in the following, it became apparent that this modification of the reaction conditions for acetolysis decreased the production of the undesirable α-glycosyl acetate. Treatment of the mixture produced by the acetolysis with 1-tetradecanol and protic acid and the subsequent separation work-up gave **24**, the desired heptasaccharide derivative carrying binary long carbon chains, and **25**, the α-glycosyl acetate remaining unaffected, in 53 and 19% overall yields, respectively. At the same time, 26% of the starting compound **23** was recovered from the reaction mixture. Two steps of the deprotection procedure were then applied to **24** by treatments with sodium methoxide and then with ethylenediamine. After purification of the resulting hexaamino compound by gel filtration with Sephadex G-15, it was converted to hexahydrochloride salt **3**, which gave satisfactory FAB mass spectrum data.

Physicochemical Properties of Compounds 2 and 3. Compounds **2** and **3** are soluble in water contrasting to **1**, since their proportion of the hydrophilic part (oligosaccharide moiety) to the lipophilic part is much larger than that of **1**. Thus, one of the physicochemical properties of **2** and **3** was examined through dye-solubilization checks. When methyl yellow crystals were added to water, the undissolved, floating crystals did not give any color to the water. On the other hand, a 3% aqueous solution of **2** or **3** completely dissolved methyl yellow crystals, giving a yellow solution. This suggested the potent detergent-like activity of **2** and **3**, which was probably due to micelle formation.

Conclusion

Employing a 1,6-anhydro-2-azido-2-deoxy-D-glucopyranose derivative **4** and a chitobiose derivative **5**, which can act as a key building block, amphiphilic chitopentaose and chitoheptaose derivatives, **2** and **3**, holding binary hydrophobic chains were synthesized. The preparation of a trisaccharidic homolog **1** was also attempted, but its extremely poor solubility impeded its purification and characterization. Although **1**, itself, could not be finely characterized, the synthetic process towards **1** was of great help as a model for the preparation of **2** and **3**. Both **2** and **3** gave satisfactory results in the dye solubilization check.

Experimental

General. Unless otherwise stated, all commercially available solvents and reagents were used without further purification. DMF, dichloromethane, chloroform, 1,2-dichloroethane, pyridine, and THF were stored over molecular sieves (MS 4A), and MeOH was stored over MS 3A before use. Mps were determined with a Laboratory Devices MELTEMP II apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-1000 polarimeter, using a 10-cm micro cell. IR spectra were measured with a JASCO FT/IR-300E spectrophotometer. FAB MS was performed on a JOEL JMS-HX 110 using a matrix of glycerol. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-200, AC-300, or AM-400 spectrometer for solutions in $CDCl_3$, unless otherwise specified. Chemical shifts are given in ppm and referenced to internal TMS (δ_H = 0.00) or acetone (δ_H = 2.04) or $CHCl_3$ (δ_H = 7.26 or δ_C = 77.00). *J* values are given in Hz. Proton assignments in NMR were made by a first-order analysis of the spectra, and were supported by homonuclear decoupling experiments. Elemental analyses were performed with Fisons EA1108 on samples extensively dried at 50—60 °C over phosphorus pentaoxide for 4—5 h in vacuo. TLC was performed on Merck precoated plates (20×20 cm; layer thickness, 0.25 mm; Silica Gel 60F_{254}); spots were detected by spraying with a solution of 85 : 10 : 5 (v/v/v) MeOH–*p*-anisaldehyde–concentrated sulfuric acid and heated at 180 °C for a half minute, and by short-wave UV light, when applicable. Column chromatography was performed on Silica Gel 60 (70—230 mesh; E. Merck) or Sephadex G-15 with the solvent systems specified, and the ratio of solvent systems was given in v/v. Organic extracts were dried over anhydrous Na_2SO_4, and solutions were concentrated under diminished pressure below 50 °C.

4-Pentenyl *O*-(4,6-*O*-Benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-2-deoxy-2-phthalimido-β-D-glucopyranoside (7). To a solution of compound **6**[8] (3.36 g, 6.8 mmol) in DMF (200 cm^3) were added α,α-dimethoxytoluene (2.05 cm^3, 13.7 mmol) and CSA (158 mg, 0.7 mmol). The mixture was stirred under diminished pressure (ca. 2.5 kPa) at 50 °C for 28 h and cooled to r.t. After the addition of MeOH (0.10 cm^3, 2.4 mmol), followed by stirring at r.t. for 2 h, the mixture was neutralized with Amberlite IR-93 ZU (OH^-; 3 cm^3), filtered, and concentrated. A suspension of the resulting residue in EtOH–5 M aq NaOH [150 cm^3 (4 : 1), (1 M = 1 mol dm^{-3})] was stirred at 100 °C for 2 d under an argon atmosphere, cooled, neutralized with solid CO_2 (200 g), and concentrated. A suspension of the residue in MeOH (300 cm^3) was stirred for 1 h with ultrasonication and filtered. The filtrate was concentrated to a residue, which was dissolved in MeOH (50 cm^3). Phthalic anhydride (6.0 g, 40 mmol) and Et_3N (5.8 cm^3, 42 mmol) were added at 0 °C to the solution and the mixture was stirred at r.t. for 36 h. After replacement of the solvent with DMF (50 cm^3), the stirring was continued at 120 °C for 3.5 h. The mixture was concentrated and the residue was chromatographed on silica gel with $CHCl_3$–MeOH (20 : 1) to give **7** (3.55 g, 68.8%) as a colorless syrup, which was recrystallized from toluene to give a white powder; mp 165—168 °C; $[\alpha]_D^{22}$ −35.8 (*c* 1.3, $CHCl_3$); ^{1}H NMR (200 MHz) δ_H = 1.5 (m, 2 H, OCH_2CH_2), 1.8 (m, 2 H, CH_2CH=), 3.16 (dd, 1 H, *J* = 3.7, 12.3 Hz), 3.3—3.5 (m, 3 H), 3.60 (t, 1 H, H-4′), 3.67—3.80 (m, 4 H), 4.09 (dd, 1 H, $J_{2,3}$ = 10.6 Hz, H-2), 4.28 (dd, 1 H, $J_{2',3'}$ = 10.4 Hz, H-2′), 4.34 (dd, 1 H), 4.38 (dd, 1 H, $J_{3,4}$ = 8.4 Hz, H-3), 4.63 (dd, 1 H, $J_{3',4'}$ = 8.6 Hz, H-3′), 4.7 (m, 2 H, CH=CH_2), 5.14 (d, 1 H, $J_{1,2}$ = 8.4 Hz, H-1), 5.43 (d, 1 H, $J_{1',2'}$ = 8.2 Hz, H-1′), 5.53 (s, 1 H, C*H*Ph), 5.55 (m, 1 H, C*H*=CH_2), 7.3—7.6 (m, 5 H, Ph), and 7.8—7.9 (m, 8 H, 2 Phth). Found: C, 63.31; H, 5.30; N, 3.65%. Calcd for $C_{40}H_{40}N_2O_{13}$: C, 63.49; H, 5.33; N, 3.70%.

4-Pentenyl *O*-(3-*O*-Benzyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (8). A solution of compound **7** (11.3 g, 15 mmol), *n*-Bu_4NI (66.5 g, 180 mmol), and benzyl bromide (21.7 cm^3, 180 mmol) in DMF (300 cm^3) was stirred for 2 h at r.t., being followed by the addition of sodium hydride (60% dispersion in mineral oil; 4.32 g) at 0 °C. After stirring the mixture for 5.5 h at r.t. and a subsequent addition of MeOH

(10.0 cm^3, 240 mmol) at 0 °C, the resulting mixture was poured into ice water and extracted with ether three times. The combined extracts were successively washed with cold 1 M aq HCl, saturated aq $NaHCO_3$, and water, and then dried, and evaporated. The residual syrup was chromatographed on silica gel with toluene–EtOAc (13 : 1) to give **8** (11.1 g, 72.1%) as a colorless amorphous material; $[\alpha]_D^{24}$ +21.3 (*c* 1.1, $CHCl_3$); ^{1}H NMR (200 MHz) δ_H = 1.4 (m, 2 H, OCH_2CH_2), 1.8 (m, 2 H, CH_2CH=), 3.11 (d, 1 H, *J* = 2.2 Hz), 4.94 (d, 1 H, $J_{1,2}$ = 7.8 Hz, H-1), 5.38 (d, 1 H, $J_{1',2'}$ = 8.2 Hz, H-1′), 5.51 (s, 1 H, CHPh), 5.51 (m, 1 H, CH=CH_2), 6.8—7.6 (m, 20 H, 4 Ph), and 7.6—7.9 (m, 8 H, 2 Phth). Found: C, 71.08; H, 5.65; N, 2.65%. Calcd for $C_{61}H_{58}N_2O_{13}$: C, 71.33; H, 5.69; N, 2.73%.

4-Pentenyl *O*-(4-*O*-Acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranoside (5). A mixture of **8** (2.56 g, 2.5 mmol), powdered molecular sieves 4A (3 g), and sodium cyanotrihydroborate (2.35 g, 37.4 mmol) in THF (40 cm^3) was stirred at r.t. for 1 h. Diethyl ether saturated with hydrogen chloride was added dropwise to the mixture at 0 °C until the evolution of gas ceased. Fifteen minutes later, Et_3N (2.0 cm^3) was added to the mixture, which was filtered through Celite and the filtrate was diluted with $CHCl_3$. The solution was washed successively with cold 1 M aq HCl, saturated aq $NaHCO_3$, and water, and then dried, and evaporated. The residual syrup was chromatographed on silica gel with toluene–EtOAc (5 : 1) to give a compound holding only a free OH group at C-4′ (2.32 g, 92.2%) as a colorless amorphous material; ^{1}H NMR (200 MHz) δ_H = 1.4 (m, 2 H, OCH_2CH_2), 1.8 (m, 2 H, CH_2CH=), 3.11 (d, 1 H), 4.93 (d, 1 H, $J_{1,2}$ = 7.2 Hz, H-1), 5.31 (d, 1 H, $J_{1',2'}$ = 7.8 Hz, H-1′), 5.52 (m, 1 H, CH=CH_2), 6.8—7.4 (m, 20 H, 4 Ph), and 7.6—7.9 (m, 8 H, 2 Phth). Acetylation of the 4′-hydroxy derivative (3.73 g, 3.62 mmol) with Ac_2O (3.4 cm^3) and pyridine (20 cm^3), followed by silica-gel chromatography with toluene–EtOAc (5 : 1) gave **5** (3.80 g, 97.9%) as a colorless amorphous material; $[\alpha]_D^{26}$ +35.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (200 MHz) δ_H = 1.4 (m, 2 H, OCH_2CH_2), 1.8 (m, 2 H, CH_2CH=), 1.92 (s, 3 H, Ac), 4.83 (d, 1 H, *J* = 12.1 Hz, PhCH_2), 4.93 (d, 1 H, $J_{1,2}$ = 7.4 Hz, H-1), 5.16 (t, 1 H, $J_{4',5'}$ = 8.8 Hz, H-4′), 5.31 (d, 1 H, $J_{1',2'}$ = 7.8 Hz, H-1′), 5.52 (m, 1 H, CH=CH_2), 6.8—7.4 (m, 20 H, 4 Ph), and 7.6—7.9 (m, 8 H, 2 Phth). Found: C, 70.82; H, 5.85; N, 2.56%. Calcd for $C_{63}H_{62}N_2O_{14}$: C, 70.64; H, 5.83; N, 2.62%.

***O*-(4-*O*-Acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-1,6-anhydro-2-azido-3-*O*-benzyl-2-deoxy-β-D-glucopyranose (9).** Triethylsilyl triflate (0.350 cm^3, 1.55 mmol) was added dropwise at 0 °C to a mixture of **5** (1.26 g, 1.18 mmol), **4**[6] (491 mg, 1.77 mmol), and NIS (319 mg, 1.42 mmol) in CH_2Cl_2 (20 cm^3). The mixture was stirred for 10 min at r.t., quenched with Et_3N, diluted with $CHCl_3$, and washed successively with 10% aq $Na_2S_2O_3$, saturated aq $NaHCO_3$, and water, and then dried, and concentrated. The residual syrup was chromatographed on silica gel with hexane–EtOAc (2 : 1, then 3 : 2) to give **9** [1.23 g, 83.1% (on the basis of **5**)] as a colorless amorphous material; $[\alpha]_D^{21}$ +43 (*c* 0.5, $CHCl_3$); ^{1}H NMR (200 MHz) δ_H = 1.92 (s, 3 H, Ac), 2.99 (brs, 1 H, H-2), 3.26 (dt, 1 H), 3.37 (brd, 1 H, $J_{3,4}$ = 2.64 Hz, H-3), 3.62 (brs, 1 H, H-4), 3.84 (brd, 1 H, H-6b), 4.07 (dd, 1 H, *J* = 8.5, 10.7 Hz), 4.16 (t, 1 H, *J* = 8.8 Hz), 4.18 (dd, 1 H, *J* = 8.6, 10.5 Hz), 4.60 (d, 1 H, *J* = 12.1 Hz, PhCH_2), 4.82 (d, 1 H, *J* = 12.4 Hz, PhCH_2), 5.18 (t, 1 H, $J_{4',5'}$ = 9.2 Hz, H-4″), 5.19 (brs, 1 H, H-1), 5.25 (d, 1 H, $J_{1',2'}$ = 8.4 Hz, H-1′), 5.31 (d, 1 H, $J_{1'',2''}$ = 8.4 Hz, H-1″), 6.82—7.38 (m, 25 H, 5 Ph), and 7.52—7.86 (m, 8 H, 2 Phth). Found: C, 67.38; H, 5.34; N, 5.49%. Calcd for $C_{71}H_{57}N_5O_{17}$: C, 67.56; H, 5.35; N, 5.55%.

***O*-(4-*O*-Acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-1,6-anhydro-3-*O*-benzyl-2-deoxy-2-tetradecanamido-β-D-glucopyranose (10).** Hydrogen sulfide was bubbled through a solution of compound **9** (825 mg, 0.654 mmol) in pyridine–Et_3N [40 cm^3 (7 : 3)] at r.t. for 30 min; the solution was allowed to stand for 1 d at r.t. The mixture was concentrated and co-evaporated 3 times with toluene. The residual syrup was chromatographed on silica-gel with $CHCl_3$–MeOH (30 : 1) to give a syrupy amine, which was dissolved in $CHCl_3$–MeOH [10 cm^3 (9 : 1)]; the solution was treated with myristoyl chloride (tetradecanoyl chloride) (0.21 cm^3, 0.77 mmol) and Et_3N (0.11 cm^3, 0.79 mmol) for 3 h at 0 °C. After the addition of MeOH (1 cm^3), the mixture was concentrated and chromatographed on silica gel with $CHCl_3$–MeOH (4 : 1) to give **10** (895 mg, 94.7%) as a colorless amorphous powder; $[\alpha]_D^{25}$ − 13.2 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz) δ_H = 0.88 (t, 3 H, CH_3), 1.26 (m, 22 H, CH_2), 1.56 (m, 2 H, $COCH_2CH_2$), 1.92 (s, 3 H, Ac), 3.16 (dd, 1 H, *J* = 9.7 Hz), 3.31 (dd, 1 H, *J* = 3.7, 11.1 Hz), 3.35 (brd, 1 H, *J* = 10.1 Hz), 4.28 (dd, 1 H, $J_{2'',3''}$ = 10.7 Hz, H-2″), 4.16 (t, 2 H, *J* = 12.3 Hz, PhCH_2), 4.39 (d, 1 H, *J* = 12.0 Hz, PhCH_2), 4.45 (d, 1 H, *J* = 12.6 Hz, PhCH_2), 4.45 (dd, 1 H, $J_{3'',4''}$ = 9.3 Hz, H-3″), 4.51 (d, 1 H, *J* = 12.6 Hz, PhCH_2), 4.51 (d, 1 H, *J* = 11.9 Hz, PhCH_2), 4.52 (d, 1 H, *J* = 12.0 Hz, PhCH_2), 4.62 (t, 2 H, *J* = 12.5 Hz, PhCH_2), 4.85 (d, 1 H, *J* = 12.5 Hz, PhCH_2), 4.92 (brs, 1 H, H-1), 4.95 (d, 1 H, $J_{1',2'}$ = 8.4 Hz, H-1′), 5.16 (t, 1 H, $J_{4'',5''}$ = 9.1 Hz, H-4″), 5.31 (d, 1 H, $J_{1'',2''}$ = 8.3 Hz, H-1″), 5.73 (d, 1 H, $J_{NH,2}$ = 9.9 Hz, N*H*), 6.84—7.38 (m, 25 H, 5 Ph), and 7.67—7.87 (m, 8 H, 2 Phth). Found: C, 70.34; H, 6.60; N, 2.88%. Calcd for $C_{85}H_{95}N_3O_{18}$: C, 70.57; H, 6.62; N, 2.91%.

***O*-(3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-*O*-(3,6-di-O-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-3-*O*-acetyl-1,6-anhydro-2-deoxy-2-tetradecanamido-β-D-glucopyranose (11).** A mixture of **10** (773 mg, 0.534 mmol) and 10% $Pd(OH)_2$/C in AcOH (50 cm^3) was shaken under a hydrogen atmosphere for 2 d at r.t. The catalyst was then filtered off and washed with aq AcOH, and the combined filtrate and washings were concentrated. A solution of the resulting residue in pyridine (5 cm^3) was treated with Ac_2O (1 cm^3) for 19 h at r.t., concentrated, co-evaporated with toluene, and chromatographed on silica gel with toluene–EtOAc (2 : 3) to give **11** (533 mg, 82.8%) as a colorless amorphous powder; ^{1}H NMR (400 MHz) δ_H = 0.86 (t, 3 H, CH_3), 1.25 (m, 22 H, CH_2), 1.58 (m, 2 H, $COCH_2CH_2$), 1.81, 1.92, 1.94, 1.98, 2.01, 2.09 (each s, 18 H, 6 Ac), 2.16 (m, 2 H, $COCH_2$), 3.52 (brs, 1 H, H-2), 3.57 (dd, 1 H, *J* = 5.9, 7.4 Hz), 4.10 (dd, 1 H, *J* = 2.2, 12.1 Hz), 4.16 (brd, 1 H, *J* = 5.2 Hz), 4.42 (dd, 1 H, *J* = 4.0, 12.5 Hz), 4.79 (brs, 1 H, H-3), 4.98 (brs, 1 H, H-1), 4.95 (d, 1 H, $J_{1',2'}$ = 8.4 Hz, H-1′), 5.15 (t, 1 H, $J_{4'',5''}$ = 9.6 Hz, H-4″), 5.43, 5.45 (each d, 2 H, *J* = 8.5, 8.5 Hz, H-1′, H-1″), 5.70 (dd, 1 H, *J* = 9.2, 10.3 Hz), 5.73 (d, 1 H, $J_{NH,2}$ = 10.7 Hz, N*H*), 5.80 (dd, 1 H, *J* = 8.8, 10.7 Hz), and 7.67—7.87 (m, 8 H, 2 Phth).

Tetradecyl *O*-(3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-*O*-(3,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-3,6-di-*O*-acetyl-2-deoxy-2-tetradecanamido-β-D-glucopyranoside (12) and *O*-(3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-*O*-(3,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-1,3,6-tri-*O*-acetyl-2-deoxy-2-tetradecanamido-α-D-glucopyranose (13). Triethylsilyl trifrate (0.094 cm^3, 0.42 mmol) was added dropwise at 0 °C to a solution of compound **11** (456 mg, 0.378 mmol) in Ac_2O (10 cm^3), and the mixture was kept at ambient temperature for 1 h. After the addition of Et_3N (0.50 cm^3),

the mixture was concentrated and co-evaporated with toluene. A solution of the residue, 1-tetradecanol (405 mg, 1.89 mmol) and CSA (9.0 mg, 0.039 mmol) in 1,2-dichloroethane (10 cm^3) was stirred at 90 °C for 1 h. After the addition of Et_3N (0.5 cm^3), the solution was concentrated and chromatographed on silica gel with hexane–EtOAc (2 : 3) to give **12** (268 mg, 48.5%) as a colorless amorphous material and glycosyl acetate **13** (179 mg, 36.1%) as a colorless amorphous powder.

Compound 12: $[\alpha]_D^{25}$ −6.79 (*c* 0.7, $CHCl_3$); ^1H NMR (400 MHz) δ_H = 0.87, 0.88 (each t, 6 H, $2CH_3$), 1.24 (m, 44 H, CH_2), 1.48 (m, 2 H, $COCH_2CH_2$), 1.69 (m, 2 H, OCH_2CH_2), 1.82, 1.87, 1.89, 1.94, 1.99, 2.00, 2.10 (each s, 21 H, 7 Ac), 2.09 (m, 2 H, $COCH_2$), 3.28 (td, 1 H, *J* = 6.3, 9.6 Hz), 3.40 (m, 1 H), 3.60 (dd, 1 H, *J* = 4.1, 12.5 Hz), 4.43 (dd, 1 H, *J* = 4.1, 12.5 Hz), 5.04 (t, 1 H, $J_{3,4}$ = 8.8 Hz, H-3), 5.14 (t, 1 H, $J_{4'',5''}$ = 9.5 Hz, H-4″), 5.33 (brd, 2 H, *J* = 8.4 Hz, H-1, H-1′), 5.42 (d, 1 H, $J_{1'',2''}$ = 8.4 Hz, H-1″), 5.71 (brt, 2 H, *J* = 9.2 Hz, H-3′, H-3″), 5.72 (d, 1 H, $J_{NH,2}$ = 10.5 Hz, N*H*), and 7.72—7.87 (m, 8 H, 2 Phth). Found: C, 62.26; H, 7.44; N, 2.76%. Calcd for $C_{76}H_{107}N_3O_{25}$: C, 62.41; H, 7.37; N, 2.87%.

Compound 13: $[\alpha]_D^{21}$ +32.5 (*c* 0.4, $CHCl_3$); ^1H NMR (400 MHz) δ_H = 0.88 (t, 3 H, CH_3), 1.25 (m, 22 H, CH_2), 1.49 (m, 2 H, $COCH_2CH_2$), 1.82, 1.86, 1.88, 1.97, 1.98, 2.00, 2.08, 2.09 (each s, 24 H, 8 Ac), 2.08 (m, 2 H, $COCH_2$), 3.56 (dd, 1 H, *J* = 2.6, 12.1 Hz), 3.95 (t, 1 H, *J* = 9.6 Hz), 4.43 (dd, 1 H, *J* = 3.7, 12.5 Hz), 5.15 (t, 1 H, $J_{3,4}$ = 9.6 Hz, H-3), 5.18 (t, 1 H, $J_{4'',5''}$ = 10.3 Hz, H-4″), 5.38 (d, 1 H, $J_{1',2'}$ = 8.1, H-1′), 5.45 (d, 1 H, $J_{1'',2''}$ = 8.5 Hz, H-1″), 5.59 (d, 1 H, $J_{NH,2}$ = 9.2 Hz, N*H*), 5.72 (brt, 2 H, *J* = 9.2 Hz, H-3′, H-3″), 5.97 (d, 1 H, $J_{1,2}$ = 3.7 Hz, H-1), and 7.66—7.81 (m, 8 H, 2 Phth). Found: C, 58.70; H, 6.25; N, 3.13%. Calcd for $C_{64}H_{81}N_3O_{26}$: C, 58.75; H, 6.24; N, 3.21%.

***O*-(3,6-Di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-1,6-anhydro-2-azido-3-*O*-benzyl-2-deoxy-β-D-glucopyranose (14).** 0.5 M Methanolic NaOMe (1.0 cm^3) was added to a solution of compound **9** (3.00 g, 2.38 mmol) in THF–MeOH [40 cm^3 (3 : 1)]; the mixture was stirred for 6 h at r.t., neutralized with Amberlite IR-120B (H^+; 1 cm^3), and filtered. The filtrate was concentrated to give a syrup, which was chromatographed on silica gel with toluene–EtOAc (5 : 1), giving **14** (2.74 g, 94.5%); $[\alpha]_D^{21}$ +21.5 (*c* 3.5, $CHCl_3$) as a colorless amorphous powder. Found: C, 68.02; H, 5.41; N, 5.49%. Calcd for $C_{69}H_{65}N_5O_{16}$: C, 67.91; H, 5.37; N, 5.74%.

***O*-(4-*O*-Acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-tris[*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)]-1,6-anhydro-2-azido-3-*O*-benzyl-2-deoxy-β-D-glucopyranose (15).** Triethylsilyl triflate (0.180 cm^3, 0.796 mmol) was added dropwise at −5 °C to a mixture of **14** (623 mg, 0.511 mmol), 5 (657 mg, 0.613 mmol), and NIS (166 mg, 0.738 mmol) in CH_2Cl_2 (12 cm^3). The mixture was stirred for 25 min at r.t. and quenched with Et_3N. After dilution with $CHCl_3$, the solution was washed successively with 10% aq $Na_2S_2O_3$, saturated aq $NaHCO_3$, and water, and then dried, and concentrated. Crystallization of the residue from EtOAc–EtOH afforded a colorless plate **15**, and the mother liquor was concentrated and chromatographed on silica gel with hexane–EtOAc (3 : 2) to give another **15** [total 776 mg, 68.9% (on the basis of **14**); (When TESOTf was added at r.t., the yield of **15** diminished to 24%)] as a colorless amorphous powder; $[\alpha]_D^{21}$ +35.6 (*c* 2.8, $CHCl_3$); mp 177—178 °C; ^1H NMR (400 MHz) δ_H = 1.88 (s, 3 H, Ac), 2.95 (brs, 1 H, H-2), 3.80 (brd, 1 H, H-6b), 3.94 (dd, 1 H, *J* = 8.7, 10.3 Hz), 4.58 (d, 1 H, *J* = 12.1 Hz, PhCH_2), 4.69 (d, 1 H, *J* = 12.8 Hz, PhCH_2), 4.76 (d, 1 H, *J* = 12.9 Hz, PhCH_2), 4.87 (d, 1 H, *J* = 12.5 Hz, PhCH_2), 5.03—5.18 (m, 5 H, H-$1^{1''-4''}$, and H-4^5), 5.28 (d, 1 H, *J* = 8.4 Hz, H-1^5), 6.65—7.33 (m, 45 H, 9 Ph), and 7.57—7.86 (m, 16 H, 4 Phth); ^{13}C NMR (100 MHz) δ_C = 96.55, 96.60, 96.71, 96.99, 100.50 (C-$1^{1''-5}$). Found: C, 69.31; H, 5.34; N, 4.42%. Calcd for $C_{127}H_{117}N_7O_{29}$: C, 69.17; H, 5.35; N, 4.45%.

***O*-(4-*O*-Acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-tris[*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)]-1,6-anhydro-3-*O*-benzyl-2-deoxy-2-tetradecanamido-β-D-glucopyranose (16).** Hydrogen sulfide was bubbled through a solution of compound **15** (1.33 g, 0.603 mmol) in pyridine–Et_3N [50 cm_3 (7 : 3)] at r.t. for 30 min. The solution was allowed to stand for 1 d at r.t., concentrated, and co-evaporated 3 times with toluene. The residual syrup was chromatographed on silica gel with $CHCl_3$–MeOH (50 : 1) to give a amino derivative, which was dissolved in $CHCl_3$–MeOH [10 cm^3 (9 : 1)] and treated with myristoyl chloride (0.20 cm^3, 0.73 mmol) and Et_3N (0.10 cm^3, 0.73 mmol) at 0 °C for 3 h. After addition of MeOH (1 cm^3), the mixture was concentrated and chromatographed on silica gel with $CHCl_3$–MeOH (4 : 1) to give **16** (1.33 g, 92.4%) as a colorless amorphous powder; $[\alpha]_D^{19}$ +3.65 (*c* 2.1, $CHCl_3$); ^1H NMR (400 MHz) δ_H = 0.89 (t, 3 H, CH_3), 1.25 (m, 22 H, CH_2), 1.58 (m, 2 H, $COCH_2CH_2$), 1.70, 1.78, 1.81, 1.86, 1.90, 1.94, 1.96, 1.98, 2.08, (each s, 33 H, 11 Ac), 3.27 (td, 1 H, *J* = 8.4, 9.6 Hz), 3.36 (brd, 1 H, *J* = 8.8 Hz), 4.38 (dd, 1 H, *J* = 3.3, 12.1 Hz), 4.99 (t, 1 H, *J* = 9.2 Hz), 5.13 (t, 1 H, *J* = 9.6 Hz), 5.25—5.34 (m, 4 H, H-$1^{1''-4''}$), 5.41 (d, 1 H, *J* = 8.5 Hz, H-1^5), 5.58—5.73 (m, 5 H, H-$3^{2''-5''}$, N*H*), and 7.69—7.86 (m, 16 H, 4 Phth). Found: C, 70.75; H, 6.10; N, 2.86%. Calcd for $C_{141}H_{145}N_5O_{30}$: C, 70.57; H, 6.62; N, 2.91%.

***O*-(3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-tris[*O*-(3,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)]-3-*O*-acetyl-1,6-anhydro-2-deoxy-2-tetradecanamido-β-D-glucopyranose (17).** A mixture of **16** (1.28 g, 0.536 mmol) and 10% $Pd(OH)_2$/C in DMF (50 cm^3) was shaken under a hydrogen atmosphere for 4 d at r.t. The catalyst was filtered off and washed with aq DMF, and the combined filtrate and washings were concentrated. A solution of the residue in pyridine (10 cm^3) was treated with Ac_2O (2 cm^3) for 19 h at r.t., concentrated, co-evaporated with toluene, and chromatographed on silica gel with toluene–EtOAc (1 : 3) to give **17** (851 mg, 81.0%) as a colorless amorphous powder; $[\alpha]_D^{27}$ −19.3 (*c* 1.53, $CHCl_3$); ^1H NMR (400 MHz) δ_H = 0.88 (t, 3 H, CH_3), 1.26 (m, 22 H, CH_2), 1.57 (m, 2 H, $COCH_2CH_2$), 1.74, 1.78, 1.81, 1.87, 1.93, 1.95, 1.97, 1.99, 2.01, 2.08 (each s, 30 H, 10 Ac), 2.12 (m, 2 H, $COCH_2$), 3.52 (brs, 1 H), 4.43 (dd, 1 H, *J* = 3.7, 12.1 Hz), 4.76 (brs, 1 H, H-3^1), 4.97 (brs, 1 H, H-1^1), 5.13 (t, 1 H, *J* = 9.6 Hz, H-4^5), 5.32, 5.33, 5.38, 5.41 (each d, 4 H, *J* = 8.1, 8.1, 8.5, and 8.1 Hz, H-$1^{2''-5''}$), 5.58—5.78 (m, 5 H, H-$3^{2''-5''}$, N*H*), and 7.7—7.9 (m, 16 H, 4 Phth). Found: C, 59.00; H, 6.25; N, 3.13%. Calcd for $C_{64}H_{81}N_3O_{26}$: C, 58.75; H, 6.24; N, 3.21%.

Tetradecyl *O*-(3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-tris[*O*-(3,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)]-3,6-di-*O*-acetyl-2-deoxy-2-tetradecanamido-β-D-glucopyranoside (18) and *O*-(3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-tris[*O*-(3,6-di-O-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-1,3,6-tri-*O*-acetyl-2-deoxy-2-tetradecanamido-α-D-glucopyranose (19). Triethylsilyl triflate (0.090 cm^3, 0.40 mmol) was added dropwise at 0 °C to a solution of compound **17** (739 mg, 0.378 mmol) in Ac_2O (10 cm^3), and the mixture was kept at ambient temperature for 80 min. After the addition of Et_3N

(0.3 cm^3), the mixture was concentrated and co-evaporated with toluene. A solution of the residue, 1-tetradecanol (405 mg, 1.89 mmol) and CSA (9.0 mg, 0.04 mmol) in 1,2-dichloroethane (10 cm^3) was stirred at 90 °C for 1 h. After the addition of Et_3N (0.5 cm^3), the solution was concentrated, and chromatographed on silica gel with hexane–EtOAc (2 : 3) to give a colorless amorphous powder **18** (380 mg, 45.5%) and glycosyl acetate **19** (328 mg, 42.2%) as a colorless amorphous powder.

Compound 18: $[\alpha]_D^{24}$ −4.94 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz) δ_H = 0.87, 0.88 (each t, 6 H, 2 CH_3), 1.23 (m, 44 H, CH_2), 1.43 (m, 2 H, $COCH_2CH_2$), 1.51 (m, 2 H, OCH_2CH_2), 1.70, 1.72, 1.81, 1.86, 1.90, 1.94, 1.96, 1.98, 2.08 (each s, 33 H, 11 Ac), 2.04 (m, 2 H, $COCH_2$), 3.52 (brs, 1 H), 4.43 (dd, 1 H, *J* = 3.7, 12.1 Hz), 4.99 (t, 1 H), 5.13 (t, 1 H, *J* = 9.6 Hz), 5.26, 5.28, 5.30, 5.32, 5.41 (each d, 5 H, *J* = 8.1, 8.9, 8.5, 8.6, and 8.5 Hz, H-$1^{1—5}$), 5.58—5.78 (m, 5 H, H-3^2, H-3^3, H-3^4, H-3^5, N*H*), and 7.7—7.9 (m, 16 H, 4 Phth). Found: C, 60.88; H, 6.53; N, 3.10%. Calcd for $C_{112}H_{141}N_5O_{41}$: C, 60.78; H, 6.42; N, 3.16%.

Compound 19: $[\alpha]_D^{20}$ −22.9 (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz) δ_H = 0.88 (t, 3 H, CH_3), 1.22 (m, 22 H, CH_2), 1.48 (m, 2 H, $COCH_2CH_2$), 1.71, 1.73, 1.81, 1.82, 1.86, 1.94, 1.96, 1.98, 2.07 (each s, 36 H, 12 Ac), 2.04 (m, 2 H, $COCH_2$), 5.13 (brt, 2 H), 5.25—5.35 (m, 3 H), 5.42 (brt, 2 H), 5.5—5.7 (m, 4 H), 5.96 (d, H-1, *J* = 3.3 Hz, H-1^1) and 7.71—7.80 (m, 16 H, 4 Phth). Found: C, 58.07; H, 5.58; N, 3.30%. Calcd for $C_{100}H_{115}N_5O_{42}$: C, 58.33; H, 5.63; N, 3.40%.

Tetradecyl *O*-(*β*-Chitotetraosyl)-(1→4)-2-deoxy-2-tetradecanamido-*β*-D-glucopyranoside Tetrahydrochloride (2). After 0.2 M methanolic NaOMe (10 cm^3) was added to a solution of compound **18** (235 mg, 0.106 mmol) in $CHCl_3$ (15 cm^3), the solution was stirred for 20 h at r.t., neutralized with 0.5 M aq HCl (ca. 4 cm^3), and concentrated. A suspension of the residue in MeOH–EtOH–ethylenediamine mixture [100 cm^3 (2 : 7 : 1)] was refluxed at 90 °C for 3 d and allowed to stand for 1 d at r.t. The resulting amorphous solid was collected by filtration, washed with MeOH, and chromatographed on Sephadex G-15 with AcOH–H_2O–EtOH (5 : 55 : 40) to give acetic acid salt. The acetic acid salt was freeze-dried from 0.1 M aq HCl (5 cm^3) to give hydrochloride salt **2** (130 mg, 89.0%) as a white power; $[\alpha]_D^{28}$ − 14 (*c* 0.8, H_2O); ^{1}H NMR (400 MHz, D_2O, 55 °C) δ_H = 0.81, 0.83 (each t, 6 H, 2 CH_3), 1.25 (m, 44 H, CH_2), 1.5—1.6 (m, 4 H, $COCH_2CH_2$, OCH_2CH_2), 2.25 (m, 2 H, $COCH_2$), 3.15 (t, 1 H, *J* = 9.1 Hz), 3.2—3.3 (m, 4 H), 3.4—3.7 (m, 5 H), 4.48 (d, 1 H, *J* = 7.8 Hz), and 4.8—5.0 (m, 4 H); FAB-MS Calcd for $[M+H^+]$: 1230.78. Found: *m/z* 1230.74.

***O*-(3,6-Di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→4)-tris[*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→4)]-1,6-anhydro-2-azido-3-*O*-benzyl-2-deoxy-*β*-D-glucopyranose (20).** After 0.5 M methanolic NaOMe (0.40 cm^3) was added to a solution of compound **15** (2.00 g, 0.907 mmol) in THF–MeOH [28 cm^3 (3 : 1)], the solution was stirred for 6 h at r.t., neutralized with Amberlite IR-120B (H^+; 1 cm^3), filtered, and the filtrate was concentrated. The residue was chromatographed on silica gel with toluene–EtOAc (5 : 1) to give **20** (1.79 g, 91.3%) as a colorless amorphous powder; $[\alpha]_D^{19}$ +20.0 (*c* 1.7, $CHCl_3$). Found: C, 69.39; H, 5.33; N, 4.49%. $C_{125}H_{115}N_7O_{28}$: C, 69.40; H, 5.36; N, 4.53%.

***O*-(4-*O*-Acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→4)-pentakis[*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→4)]-1,6-anhydro-2-azido-3-*O*-benzyl-2-deoxy-*β*-D-glucopyranose (21).** Triethylsilyl triflate was added dropwise at −40 °C to a mixture of **20** (404 mg, 0.187 mmol), **5** (300 mg, 0.280 mmol), and NIS (76 mg, 0.34 mmol) in CH_2Cl_2 (9 cm^3). The mixture was stirred for 50 min and quenched with Et_3N. The solution was diluted with $CHCl_3$, washed successively with 10% aq $Na_2S_2O_3$, saturated aq $NaHCO_3$, and water, and then dried, and concentrated. Crystallization of the residue from EtOAc–EtOH afforded **21** [333 mg, 56.6% (on the basis of **20**)] as a plate; $[\alpha]_D^{21}$ +32.5 (*c* 1.1, $CHCl_3$); mp 200—202 °C; ^{1}H NMR (400 MHz) δ_H = 1.87 (s, 3 H, Ac), 2.94 (brs, 1 H, H-2^1), 3.79 (brd, 1 H, H-6^1b), 3.91 (t, 1 H, *J* = 10.2 Hz), 4.57 (d, 1 H, *J* = 12.0 Hz, PhCH_2), 4.66 (d, 1 H, *J* = 12.8 Hz, PhCH_2), 4.72 (d, 1 H, *J* = 12.5 Hz, PhCH_2), 4.74 (d, 1 H, *J* = 12.8 Hz, PhCH_2), 4.75 (d, 1 H, *J* = 12.9 Hz, PhCH_2), 4.85 (d, 1 H, *J* = 12.5 Hz, PhCH_2), 4.98—5.16 (m, 7 H, H-$1^{1—6}$, and H-4^7), 5.27 (d, 1 H, *J* = 8.5 Hz, H-1^7), 6.63—7.25 (m, 65 H, 13 Ph), and 7.59—7.83 (m, 24 H, 6 Phth); ^{13}C NMR (100 MHz) δ_C = 96.40×2, 96.45, 96.50, 96.59, 96.87, 100.38 (C-$1^{1—7}$). Found: C, 69.69; H, 5.27; N, 3.96%. Calcd for $C_{183}H_{167}N_9O_{41}$: C, 69.81; H, 5.35; N, 4.00%.

***O*-(4-*O*-Acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→4)-pentakis[*O*-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→4)]-1,6-anhydro-3-*O*-benzyl-2-deoxy-2-tetradecanamido-*β*-D-glucopyranose (22).** Hydrogen sulfide was bubbled through a solution of compound **21** (597 mg, 0.190 mmol) in pyridine–Et_3N [20 cm^3 (7 : 3)] for 30 min at r.t. The solution was allowed to stand for 1 d at r.t., concentrated, and co-evaporated 3 times with toluene. The residual syrup was chromatographed on silica gel with $CHCl_3$–MeOH (50 : 1) to give an amino derivative, which was dissolved in $CHCl_3$–MeOH [10 cm^3 (9 : 1)] and treated with myristoyl chloride (0.062 cm^3, 0.23 mmol) and Et_3N (0.032 cm^3, 0.23 mmol) at 0 °C for 15 min. After the addition of MeOH (1 cm^3), the mixture was concentrated and chromatographed on silica gel with $CHCl_3$–MeOH (50 : 1) to give **22** (585 mg, 92.6%) as a colorless amorphous powder; $[\alpha]_D^{25}$ +5.1 (*c* 1.3, $CHCl_3$); ^{1}H NMR (400 MHz) δ_H = 0.88 (t, 3 H, CH_3), 1.22 (m, 22 H, CH_2), 1.48 (m, 2 H, $COCH_2CH_2$), 1.69, 1.81 (each s, 30 H, 10 Ac), 2.12 (m, 2 H, $COCH_2$), 4.58 (d, 1 H, *J* = 12.1 Hz, PhCH_2), 4.60 (d, 1 H, *J* = 11.8 Hz, PhCH_2), 4.69 (d, 1 H, *J* = 12.5 Hz, PhCH_2), 4.74 (d, 1 H, *J* = 12.5 Hz, PhCH_2), 4.75 (d, 1 H, *J* = 12.9 Hz, PhCH_2), 4.76 (d, 1 H, *J* = 12.5 Hz, PhCH_2), 5.13 (t, 1 H, *J* = 9.2 Hz, H-4^7), 5.28 (d, 1 H, *J* = 8.5 Hz, H-1^7), 5.70 (d, 1 H, $J_{NH,2}$ = 9.9 Hz, N*H*), 6.7—7.4 (m, 65 H, 13 Ph), and 7.6—7.9 (m, 24 H, 6 Phth). Found: C, 70.97; H, 5.90; N, 2.90%. Calcd for $C_{197}H_{195}N_7O_{42}$: C, 71.00; H, 5.90; N, 2.94%.

***O*-(3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→4)-pentakis[*O*-(3,6-di-*O*-acetyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→4)]-3-*O*-acetyl-1,6-anhydro-2-deoxy-2-tetradecanamido-*β*-D-glucopyranose (23).** A mixture of **22** (499 mg, 0.150 mmol) and 10% $Pd(OH)_2$/C in DMF–AcOH [50 cm^3 (9 : 1)] was shaken under hydrogen atmosphere for 5 d at r.t. The catalyst was filtered off and washed with aq DMF, and the filtrate and washings were concentrated. A solution of the resulting residue in pyridine (20 cm^3) was treated with Ac_2O (2 cm^3) for 3 d at r.t., concentrated, co-evaporated with toluene, and chromatographed on silica gel with toluene–EtOAc (1 : 3) to give **23** (402 mg, 99.3%) as a colorless amorphous powder; $[\alpha]_D^{28}$ − 13 (*c* 0.6, $CHCl_3$); ^{1}H NMR (400 MHz) δ_H = 0.88 (t, 3 H, CH_3), 1.26 (m, 22 H, CH_2), 1.58 (m, 2 H, $COCH_2CH_2$), 1.71, 1.73, 1.77, 1.81, 1.87, 1.92, 1.93, 1.95, 1.99, 2.00, 2.08 (each s, 42 H, 14 Ac), 2.10 (m, 2 H, $COCH_2$), 4.77 (brs, 1 H, H-3^1), 4.98 (brs, 1 H, H-1^1), 5.13 (t, 1 H, *J* = 9.3 Hz, H-4^7), 5.26—5.43 (m, 7 H, H-$1^{2—7}$, H-3^1), 5.54—5.75 (m, 7 H, H-$3^{2—7}$, N*H*), and 7.7—7.9 (m, 24 H, 4 Phth). Found: C, 58.65; H, 5.34; N, 3.48%. Calcd for $C_{132}H_{143}N_7O_{55}$: C, 58.56; H, 5.32; N, 3.62%.

Tetradecyl *O*-(3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-

β-D-glucopyranosyl)-(1→4)-pentakis[*O*-(3,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)]-3,6-di-*O*-acetyl-2-deoxy-2-tetradecanamido-β-D-glucopyranoside (24) and *O*-(3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)-pentakis[*O*-(3,6-di-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→4)]-1,3,6-tri-*O*-acetyl-2-deoxy-2-tetradecanamido-α-D-glucopyranose (25). Triethylsilyl triflate (0.013 cm^3, 0.057 mmol) was added dropwise at 0 °C to a solution of compound **23** (149 mg, 0.055 mmol) in Ac_2O (1.0 cm^3) and $CHCl_3$ (2.0 cm^3), and the mixture was kept at 30 °C for 4 h. After the addition of Et_3N (0.04 cm^3), the mixture was concentrated, and co-evaporated with toluene. A solution of the residue, 1-tetradecanol (59 mg, 0.28 mmol) and CSA (1.3 mg, 0.006 mmol) in 1,2-dichloroethane (3 cm^3) was stirred at 90 °C for 1 h. After the addition of Et_3N (0.05 cm^3), the solution was concentrated and chromatographed on silica gel with $CHCl_3$–MeOH (100 : 1) to give a colorless amorphous powder **24** (86 mg, 53%) and glycosyl acetate **25** (29 mg, 19%) as a colorless amorphous powder and recovered **23** (43 mg, 26%).

Compound 24: $[\alpha]_D^{25}$ −4.2 (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz) δ_H = 0.87, 0.88 (each t, 6 H, 2 CH_3), 1.23 (m, 44 H, CH_2), 1.43 (m, 2 H, $COCH_2CH_2$), 1.51 (m, 2 H, OCH_2CH_2), 1.69, 1.69, 1.72, 1.81, 1.86, 1.89, 1.91, 1.93, 1.95, 1.98, 2.07 (each s, 45 H, 15 Ac), 2.04 (m, 2 H, $COCH_2$), 4.99 (t, 1 H, *J* = 9.7 Hz, H-3^1), 5.12 (t, 1 H, *J* = 9.6 Hz, H-4^7), 5.24—5.30 (m, 6 H), 5.40 (d, 1 H, *J* = 8.4 Hz), 5.54—5.71 (m, 7 H, H-3$^{2—7}$, N*H*), and 7.7—7.9 (m, 24 H, 4 Phth). Found: C, 59.91; H, 5.93; N, 3.21%. Calcd for $C_{148}H_{175}N_7O_{57}$: C, 59.97; H, 5.95; N, 3.31%.

Compound 25: $[\alpha]_D^{24}$ +5.2 (*c* 0.03, $CHCl_3$); ^{1}H NMR (300 MHz) δ_H = 0.88 (t, 3 H, CH_3), 1.23 (m, 22 H, CH_2), 1.48 (m, 2 H, $COCH_2CH_2$), 1.69, 1.72, 1.80, 1.86, 1.91, 1.93, 1.95, 1.98, 2.04, 2.07 (each s, 48 H, 16 $COCH_3$), 2.07 (m, 2 H, $COCH_2$), 5.13 (t, 1 H, *J* = 9.9 Hz, H-4^7), 5.23—5.31 (m, 7 H), 5.40 (d, 1 H, *J* = 8.1 Hz), 5.53—5.72 (m, 7 H, H-3$^{2—7}$, N*H*), 5.95 (d, 1 H, *J* = 3.7 Hz, H-1^1) and 7.7—7.9 (m, 24 H, 6 Phth). Found: C, 58.46; H, 5.58; N, 3.24%. Calcd for $C_{136}H_{149}N_7O_{58}$: C, 58.14; H, 5.35; N, 3.49%.

Tetradecyl *O*-(β-Chitohexaosyl)-(1→4)-2-deoxy-2-tetradecanamido-β-D-glucopyranoside Hexahydrochloride (3). After 0.2 M methanolic NaOMe (10 cm^3) was added to a solution of compound **24** (223 mg, 0.075 mmol) in $CHCl_3$ (15 cm^3), the solution was stirred for 1 d at r.t. The resulting mixture was neutralized with 0.5 M aq HCl (ca. 4 cm^3), concentrated, and suspended in MeOH–EtOH–ethylenediamine mixture [100 cm^3 (4 : 5 : 1)]. The suspension was refluxed for 4 d, allowed to stand for 1 d at r.t., and filtered. The amorphous solid was washed with MeOH and chromatographed on Sephadex G-15 with AcOH–H_2O–EtOH (5 : 55 : 40) to give acetic acid salt. The acetic acid salt was freeze-dried from 0.1 M aq HCl (5 cm^3) to give hydrochloride salt **3** (77 mg, 65.8%) as a white powder; $[\alpha]_D^{31}$ −13 (*c* 0.7, H_2O); ^{1}H NMR (400 MHz, D_2O, 55 °C) δ_H = 0.82 (m, 6 H, 2 CH_3), 1.23 (m, 44 H, CH_2), 1.4—1.6 (m, 4 H, $COCH_2CH_2$, OCH_2CH_2), 2.21 (m, 2 H, $COCH_2$), 3.0—3.2 (m, 6 H), 4.45 (d, 1 H, *J* = 7.9 Hz), and 4.8—4.9 (m, 6 H). FAB MS Calcd for [M+H$^+$]: 1552.9. Found: *m/z* 1552.8.

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