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PAPER

Synthesis of serine-based glycolipids as potential TLR4 activators†

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A new series of monosaccharide-based glycolipids devoid of phosphate groups and with two lipid chains were rationally designed by varying the lipid chain lengths and saccharide structure of a α-GalCer-derived lead compound (**CCL-34**) that is a potent TLR4 agonist. The NF-κB activity of a 60-membered galactosyl serine-based synthetic library containing compounds with various lipid chain lengths was measured in a HEK293 cell line that stably expressed human TLR4, MD2, and CD14 (293-hTLR4/MD2-CD14). The results showed that the optimal carbon chain lengths for the lipid amine and fatty acid to activate TLR4 were 10–11 and 12, respectively. Evaluation of a 20-membered synthetic glycosyl serine-based lipid library containing compounds with various saccharide moieties and fixed lipid chain lengths revealed that the galactose moiety in **CCL-34** could be replaced by glucose without loss of activity (**CCL-34-S3** and **CCL-34-S16**). Changing the orientation of the anomeric glycosidic bond of **CCL-34** resulted in a complete loss of activity (**β-CCL34**). Surprisingly, a change in configuration of the anomeric glycosidic bond in a glucosyl glycolipid is tolerable (**CCL-34-S14**). Another noteworthy observation is that the activity of a L-fucosyl derived glycolipid (**CCL-34-S13**) was comparable to that of **CCL-34**. In sum, this study determines the structural features that are crucial for an optimal TLR4-stimulating activity. It also provides several molecules with immunostimulating potential.

Introduction

Glycolipids[1] are components of the ubiquitous membrane that is found in many species. In general, they are constituted by a hydrophobic lipid group and a hydrophilic carbohydrate moiety, which is linked to the terminal hydroxyl group of sphingosine or glycerol/inositol. Glycolipids are essential components of cell membranes in the body; they are primarily located in the outer layer of the plasma membranes, where they interact with the extracellular environment. Thus, glycolipids play important roles in the regulation of cell-growth and development. They also serve as important epitopes in cell recognition, *e.g.*, in cell-cell communication[2] and microbial infections.[3,4] In addition, recent studies have shown that glycolipids may serve as immunomodulators with therapeutic potential for Parkinson's disease, Alzheimer's disease, psoriasis, AIDS treatment, and antiviral infections.[5–7]

Lipopolysaccharide (LPS),[8] an amphiphilic glycolipid located in the outer membrane of Gram-negative bacteria, is associated with pathogen recognition by the host innate immune system. Cellular recognition for LPS is mediated by Toll-like receptor 4 (TLR4), a key member of pattern recognition receptors that are involved in the induction of innate and adaptive immune responses.[9] Structurally, LPS is composed of a polysaccharide and lipid A; the latter is involved in many LPS-mediated responses.[10] Indeed, lipid A is the main region of LPS that interacts with TLR4 and can trigger innate immune systems.[11] It is thought that TLR4 agonists are potent immunostimulators with multiple therapeutic applications, such as vaccine adjuvants and cancer immunotherapeutic agents. On the other hand, TLR4 antagonists may be therapeutically useful for inflammatory diseases.[12] Substantial efforts have been devoted to the synthesis of molecules that mimic lipid A and can serve as agonists or antagonists for TLR4 activation processes.[13,14] Most of the currently available bioactive lipid A analogs contain a phosphate saccharide scaffold with lipid substituents.[15–18] Such molecules (*e.g.*, monophosphoryl lipid A (MPL)[19] and aminoalkylglucosaminide 4-phosphates (AGPs)[20]) have yielded promising results in clinical trials in which they were used as therapeutic vaccines/adjuvants against cancer, infectious diseases, and allergies. Interestingly, it was recently found that some compounds with structures totally different to that of lipid A, *e.g.*, taxol,[21] flavolipin,[22] vitamin D,[23] and lipids linked to a phosphate-containing acyclic backbone,[24–26] exhibited activities towards TLR4 that were similar to that of LPS.

In our continuous efforts[27–29] to develop a α-GalCer analog as a vaccine adjuvant, we have found that serine-based α-GalCer analogs could activate the TLR4 signaling pathway.

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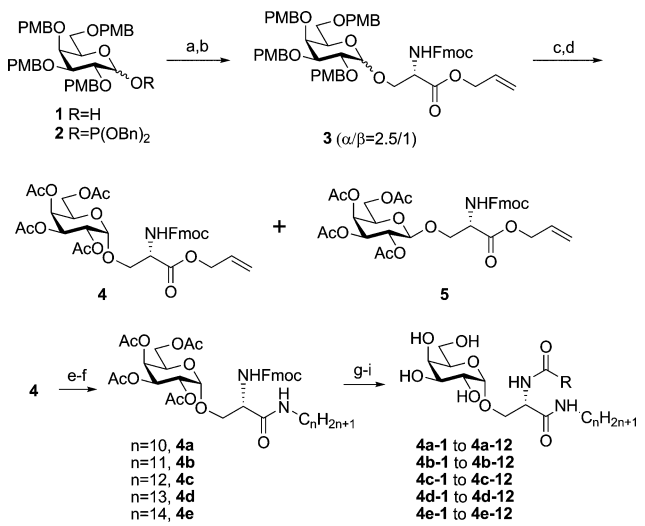
In our previous studies,[30] among the forty-seven serine-based glycolipids tested, two α-GalCer analogs (**CCL-34** and **CCL-25**) stimulated a TLR4-dependent NF-κB activity in a murine macrophage cell line RAW 264.7 and in a human HEK293 cell line that stably expressed TLR4, MD2, and CD14 (293-hTLR4/MD2-CD14). No activity was detected for α-GalCer. Furthermore, TNF-α production in **CCL-34**-treated primary bone marrow cells was also found to be TLR4-dependent. These results are interesting for the development of a new class of potent monosaccharide immunomodulators.[30] As the structure of **CCL-34** is relatively simple and the synthesis of serine-based glycolipids is straightforward, **CCL-34** can be easily derivatized to obtain a new generation of compounds. To study the structure–activity relationship of serine-based glycolipids, we have synthesized many serine-based derivatives of **CCL-34** by either changing the lipid or the carbohydrate moiety. The bioactivity results showed that the optimal chain length for the lipid moiety was eleven or twelve carbons and that the galactose in **CCL-34** could be replaced by glucose or fucose without losing any activity.

Results and discussion

Synthesis of serine-based galactosyl lipids

We had previously synthesized a library of 47 serine-based galactosyl lipids[30] and had found that the length of both the fatty acid and the lipid amine that is linked to serine had a profound effect on the activation of TLR4. To determine the structure–activity relationship of serine-based galactosyl lipids, a new synthetic library featuring lipids of different lengths and various sugar moieties was synthesized. As shown in Scheme 1, the synthesis of compound **4** started with the glycosylation of the donor **2** with the Fmoc-Ser-OAll acceptor to give a galactosyl serine mixture **3** (85% yield, α/β = 2.5/1). As the α/β anomers could not be separated, the *para*-methoxybenzyl protecting groups of **3** were replaced by acetyl groups to give the separable compounds **4** and **5**. Deprotection of the allyl group of **4** using $Pd(PPh_3)_4$ followed by amidation with five different lipid amines containing ten- to fourteen-carbon linear chains afforded compounds **4a–4e** in 71–84% yields. Removal of the Fmoc group with piperidine in CH_2Cl_2, coupling with different fatty acids, and deacetylation gave sixty serine-based galactosyl lipids with total yields of 54–65% over three steps. The NF-κB activation assays were performed in 293-hTLR4/MD2-CD14 cells. The results revealed that the most effective lengths of fatty acid chain and lipid amine for NF-κB activation were eleven and twelve carbons, respectively (**CCL-34**; named as **4b-3** in Scheme 1 and S1 in supporting information). Although the compound **4a-3** containing a ten-carbon lipid amine showed a NF-κB-stimulating activity comparable to that of **4b-3**, compounds with other chain lengths had significantly lower activities (see supporting information S3).



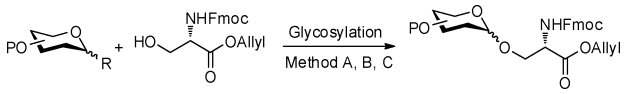
Scheme 1 Reagents and conditions: (a) DDP, 1-H-tetrazole, DCM, 4 Å MS, rt; (b) Fmoc-Ser-OAll, TMSOTf, DCM, 4 Å MS, 0 °C, 85% for two steps; (c) TFA, DCM; (d) Ac_2O, Pyr., DMAP, 70% for two steps; (e) $Pd(PPh_3)_4$, MeNHPh, THF; (f) lipid amine, EDC, HOBt, NMM, DCM, 71–84% for two steps; (g) piperidine, DCM; (h) fatty acid, EDC, HOBt, TEA, DCM, 65–73%; (i) NaOMe, MeOH, 85–90%. The structures of compounds **4a-1** to **4e-12** are shown in supporting information S1.

Development of α-selective galactosylation

Even though galactosyl lipids could be obtained following the synthetic procedures described in Scheme 1, the moderate α-selectivity of galactosylation and the difficulty in separating the α/β mixture hampered further investigations on the structure–activity relationship of the carbohydrate moiety on the glycolipid activity. We therefore developed a new glycosylation strategy that led to a higher α-selectivity. As previously reported, an exclusive α-selectivity (Table 1, entry 1) can be achieved by using a phosphite **6** as the glycosyl donor.[31] However, the preparation of the saccharide donor itself is tedious and time-consuming, as it requires nine steps (from galactose). The use of thiocresol as the leaving group in the donor **7** with PMB (*p*-methoxybenzyl) as hydroxyl protecting group did not lead to an acceptable α-selectivity with Fmoc-Ser-OAll as the glycosylation acceptor (Table 1, entries 2 and 3). However, when compound **8** was used as the donor, the desired α-glycoside was obtained in 55% yield at low temperature (–40 °C to RT) and in 63% yield at room temperature (Table 1, entries 4 and 5). To further improve the yield of the α-anomer, Gervay-Hague's method[22] was adopted because it has been shown to give a high yield and a high α-selectivity in galactosylation reactions. Reaction between the donor **9** and Fmoc-Ser-OAll as the acceptor led to the degradation of the starting material during the generation of iodide in the first step (Table 1, entry 6). This may be due to the undesired deprotection of the acid-sensitive *p*-methoxybenzyl group by iodotrimethylsilane (TMSI). The reaction between the iodide donor generated *in situ* from galactosyl acetate **10**[32] and TBAI and Fmoc-Ser-OAll (1.2 equiv) acceptor in the presence of DIPEA, 4 Å MS, and toluene gave the galactoside **10α** in 60% yield with an exclusive α-selectivity (Table 1, entry 7). When the same method was applied to glucose, 3- and 4-allylated galactose, and fucose (Table 1, entries 8–11), the α-anomers were obtained with high selectivity. The good α-selective galactosylation procedure allowed us to modify the carbohydrate moiety of galactosyl lipids for further SAR investigations.

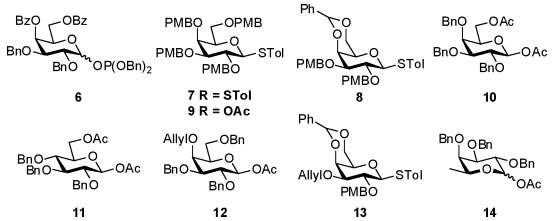
Initially, we focused on the modification of the galactose moiety of **CCL-34**. For example, we replaced the C6 hydroxyl group with an amino or carboxylic group. We also *O*-alkylated the C3 or C4 hydroxyl group and changed the sugar moiety to glucose. As shown in Scheme 2, deprotection of the allyl group of **10α**,

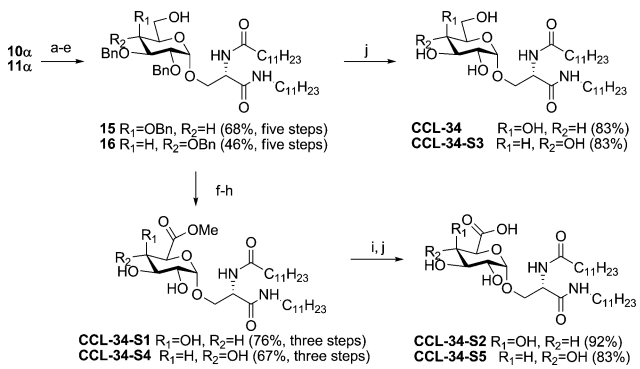
Table 1 Studies of α-selective galactosylation



entry	Condition	donor	% yield	Product (α/β)
1	A	**6**	95	**6α** (α only)
2	B_1	**7**	71	**3α/β** (2 : 1)
3	B_2	**7**	95	**7α/β** (1.5 : 1)
4	B_3	**8**	55	**8α** (α only)
5	B_4	**8**	63	**8α** (α only)
6	C	**8**	—[a]	—
7	C	**10**	60	**10α** (α only)
8	C	**11**	54	**11α** (α only)
9	C	**12**	66	**12α** (α only)
10	C	**13**	57	**13α** (α only)
11	C	**14**	56	**14α** (α only)

[a] Starting material was decomposed during reaction. Condition A: TfOH, CH_2Cl_2, 4 Å MS, 60 min, 0 °C–RT; B_1: NIS, TfOH, CH_2Cl_2, 4 Å MS, 10 min, RT; B_2: NIS, TfOH, CH_2Cl_2, 4 Å MS, 120 min, –40 °C; B_3: NIS, TfOH, CH_2Cl_2, 4 Å MS, 60 min, –40 °C–RT; B_4: NIS, TfOH, CH_2Cl_2, 4 Å MS, 120 min, RT; C: (i) TMSI, 4 Å MS, CH_2Cl_2, 10 min, 0 °C; (ii) TBAI, DIPEA, toluene, 4 Å MS, 180 min, 80 °C.

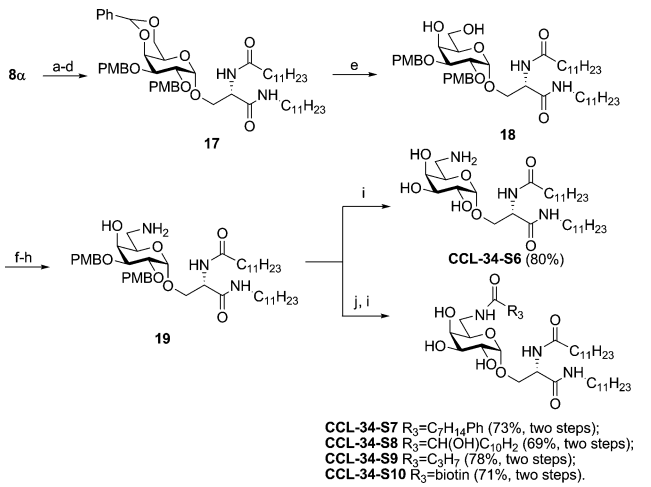




Scheme 2 Reagents and conditions: (a) $Pd(PPh_3)_4$, MeNHPh, THF; (b) n-undecylamine, EDC, HOBt, NMM, DCM; (c) piperidine, DCM; (d) lauric acid, EDC, HOBt, TEA, DCM; (e) NaOMe, MeOH, DCM; (f) TEMPO, BAIB, DCM-H_2O (2 : 1); (g) MeI, Cs_2CO_3, DMF; (h) H_2, Pd/C, MeOH, DCM; (i) LiOH, H_2O–THF–MeOH (1 : 2 : 1); (j) Pd/C, H_2, MeOH, DCM.

coupling with n-undecylamine, deprotection of the Fmoc group, coupling with lauric acid, and deacetylation gave compound **15** in an overall yield of 68%. A TEMPO-mediated oxidation of **15** generated the corresponding sugar acid that was esterified using MeI and Cs_2CO_3 in DMF and then full deprotected to give **CCL-34-S1** in 76% yield (over three steps). De-esterification of **CCL-34-S1** under mild reaction conditions in the presence of LiOH gave the sugar acid **CCL34-S2** in 83% yield. It is noteworthy that both methods tested to obtain **CCL34-S2**, *i.e.*, either selectively oxidizing the primary hydroxyl group in **CCL-34** or deprotecting the benzyl groups prior to the esterification of the acid, resulted in relatively low yields and purification difficulties. Glucosyl lipids **CCL-34-S3**, **CCL-34-S4**, and **CCL-34-S5** were obtained in good yields following a similar synthetic procedures described above.

In addition to the oxidation of the C6 hydroxyl group of **CCL-34**, amination of the C6 position of galactose was also performed (Scheme 3). The direct transformation of the C6 hydroxyl group of **15** into an amino group resulted in an incomplete reaction, which may be due to the steric hindrance of the C4 benzyl protection. In order to circumvent the above problem, compound **18** with a free C4 hydroxyl group was synthesized starting from **8α**. Selective deprotection of the 4,6-*O*-benzylidene group in **17**, which was synthesized in 53% yield (over four steps) from **8α**, was achieved by using $VO(OTf)_2$[33] and gave compound **18**. Tosylation of the C6 hydroxyl group of **18** followed by a S_N2 reaction with sodium azide and the reduction of the azido group gave the amine **19**.

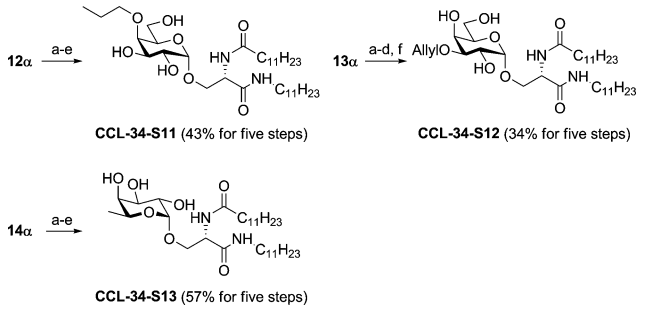


Scheme 3 Reagents and conditions: (a) $Pd(PPh_3)_4$, MeNHPh, THF; (b) n-undecylamine, EDC, HOBt, NMM, DCM; (c) piperidine, DCM; (d) lauric acid, EDC, HOBt, TEA, DCM, 53% for four steps; (e) $VO(OTf)_2$, MeOH–MeCN–DCM (2 : 6 : 1), 76%; (f) TsCl, Pyridine; (g) NaN_3, DMF, 71% for two steps; (h) Pd/C, H_2, DCM–MeOH, 86%; (i) TFA, DCM; (j) R_3-acid, EDC, HOBt, TEA, DCM.

Acylation of the amino group in the presence of EDCI, HOBt, and TEA in CH_2Cl_2 with different acids and deprotection of the PMB groups with TFA in CH_2Cl_2 afforded **CCL-34-S7**, **CCL-34-S8**, **CCL-34-S9**, and **CCL-34-S10** in good yields. Deprotection of the PMB groups in **19** with TFA provided **CCL-34-S6** in 80% yield.

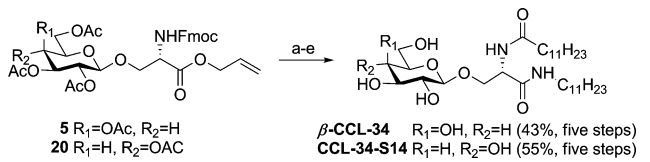
The alkylation of the C4 and C3 hydroxyl groups of the galactose moiety of **CCL-34** was then undertaken (Scheme 4). The desired lipid chains were introduced as described in Scheme 1. Reduction of the benzyl groups and unsaturation of the C4 allyl group using H_2 and Pd/C in MeOH followed by deprotection of the PMB and benzylidene groups gave **CCL-34-S11** and **CCL-34-S12** in 43% and 34% (over 5 steps), respectively. Similarly, the fucosyl lipid **CCL-34-S13** was obtained from **14α** in five steps with 57% overall yield.

The orientation of the glycosidic linkage might influence the interaction between the molecule and the protein receptor. To study the importance of the α-orientation of the glycosidic bond



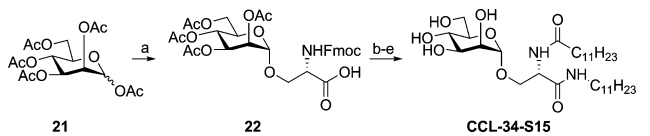
Scheme 4 Reagents and conditions: (a) piperidine, DCM; (b) lauric acid, EDC, HOBt, TEA, DCM; (c) $Pd(PPh_3)_4$, MeNHPh, THF; (d) n-undecylamine, EDC, HOBt, TEA, DCM; (e) H_2, Pd/C, MeOH, DCM; (f) TFA, DCM.

in serine-based glycolipids, the β-galactosyl lipid β-**CCL-34** and the β-glucosyl lipid **CCL-34-S14** were synthesized from **5** and **20** in 43% and 55% overall yields, respectively (Scheme 5).



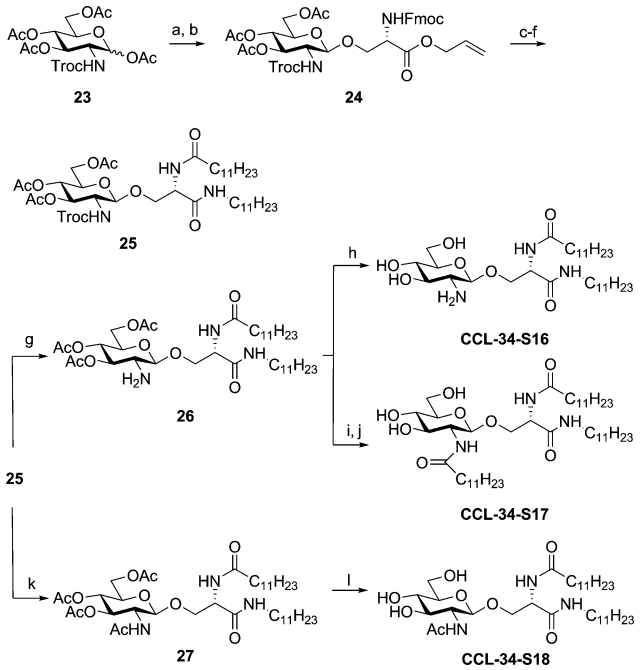
Scheme 5 Reagents and conditions: (a) $Pd(PPh_3)_4$, MeNHPh, THF; (b) n-undecylamine, EDC, HOBt, NMM, DCM; (c) piperidine, DCM; (d) lauric acid, EDC, HOBt, TEA, DCM; (e) NaOMe, MeOH.

To investigate whether the alteration of the sugar moiety affects the activity of **CCL-34**, the galactose of **CCL-34** was replaced with different monosaccharides, such as mannose and glucosamine. As shown in Scheme 6, glycosylation of the peracetylated mannoside **21** with Fmoc-Ser-OH using $BF_3{\cdot}OEt_2$ as the promoter gave the α-anomer **22** in 67% yield. Compound **22** was then transformed into **CCL-34-S15** by following the standard five-step sequence (34% overall yield).



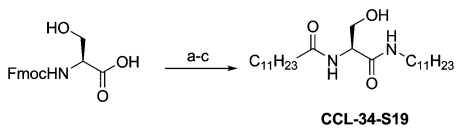
Scheme 6 Reagents and conditions: (a) Fmoc-Ser-OH, BF_3–OEt_2, DCM, 67%; (b) EDC, HOBt, n-undecylamine, NMM, DCM, 87%; (c) piperidine, DCM; (d) lauric acid, EDC, HOBt, TEA, DCM, 73%, two steps; (e) NaOMe, MeOH, 80%.

A literature survey of TLR-4 ligands, lipid A, and its mimics[14,34] reveals that the polar head group is mostly GlcNAc and that the lipid moiety is linked to the C2 or C3 position of GlcNAc This implies that a lipid extended from the C2 position of a glycolipid sugar may interact with a receptor and affect the immune response. Thus, GlcNAc serine-based glycolipids were also synthesized (Scheme 7). The anomeric acetate of the known compound **23**[35] was converted into bromide and then coupled with Fmoc-Ser-OAll to yield **24** (86% yield over two steps). The precursor **25** for the synthesis of compounds **CCL-34-S16**, **S17**, and **S18** was obtained in 57% yield by using the linear four-step sequence previously described. Selective deprotection of the Troc group at position C2 in compound **25** using Zn and HOAc in



Scheme 7 Reagents and conditions: (a) HBr, HOAc; (b) Fmoc-Ser-OAll, AgOTf, DCM, 4 Å MS, 86%; (c) $Pd(PPh_3)_4$, MeNHPh, THF; (d) undecylamine, EDC, HOBt, TEA, DCM, 80% for two steps; (e) piperidine, DCM, 90%; (f) lauric acid, EDC, HOBt, TEA, DCM, 80%; (g) Zn, HOAc, THF, 95%; (h) NaOMe, MeOH, DCM, 60%; (i) lauric acid, EDC, HOBt, TEA, DCM, 54%; (j) NaOMe, MeOH, DCM, 60%; (k) Zn, Ac_2O, HOAc, THF, 72%; (l) NaOMe, MeOH, DCM, 82%.

THF gave the free amine **26** (95% yield). This amine was then deacetylated in the presence of NaOMe and MeOH to give **CCL-34-S16** in 60% yield. Coupling of the free amino group in **26** with lauric acid followed by deacetylation afforded **CCL-34-S17** with three lipid chains in 32% yield. On the other hand, deprotection of the Troc group in the presence of acetic anhydride gave the *N*-acetyl protected product **27** in 72% yield. Removal of the *O*-acetyl groups in **27** afforded the *N*-acetylated glycolipid **CCL-34-S18** in 59% yield. Finally, in order to determine the importance of the carbohydrate part for the immunostimulating activity of **CCL-34**, a sugarless serine lipid **CCL-34-S19** (shown in Scheme 8) was also synthesized using the procedures described in Scheme 1.



Scheme 8 Reagents and conditions: (a) n-undecylamine, EDC, HOBt, DIPEA, DCM, 93%; (b) piperidine, DCM; (c) lauric acid, EDC, HOBt, DIPEA, DCM, 71% for two steps.

Bioactivities of glycosyl serine-based lipids: SAR analysis

The strategy to identify TLR4 activators has been described in detail in our previous study.[30] In short, 293-hTLR4/MD2-CD14 cells seeded in 24-well plates at a density of 2×10^5 cells per well were grown overnight and treated for 5 h with LPS (10 ng ml^{-1}; the positive control) or the synthesized glycosyl lipids (10 μM). The glycosyl lipids that were able to activate NF-κB, a downstream

signaling molecule of the TLR4 pathway, were identified using a NF-κB activity-based reporter assay as described previously.

Fig. 1 summarizes the NF-κB activity induced by **CCL-34** and the synthesized glycosyl lipid derivatives. The lack of activity of the serine lipid **CCL-34-S19** suggests that the sugar part is indispensable for TLR4 stimulation. Of all the synthesized glycosyl lipids tested, five derivatives (*i.e.*, **CCL-34-S2**, **CCL-34-S3**, **CCL-34-S13**, **CCL-34-S14**,and **CCL-34-S16**) displayed significant NF-κB activities. The glucosyl lipid derivative **CCL-34-S3** induced a NF-κB activation that was similar to that of **CCL-34**, suggesting that the configuration of the 4-hydroxyl group is not crucial for activity. Although the β-anomer of **CCL-34** did not show any activity, the glucosyl lipid derivative with a β-anomeric configuration (**CCL-34-S14**) still induced significant NF-κB activation. The glucosamine lipid derivative **CCL-34-S16** showed a good activity, but any further derivatization of the free amino group led to a complete loss of NF-κB activity, as clearly evidenced in the cases of **CCL-34-S17** and **CCL-34-S18**. On the other hand, the mannosyl lipid derivative **CCL-34-S15** with a change in configuration of the C2 hydroxyl group showed 60% of the NF-κB activity of **CCL-34**, indicating the importance of the equatorial configuration of the C2 functional group on the sugar moiety. It is noteworthy that the L-fucosyl lipid derivative **CCL-34-S13** has a NF-κB activity comparable to that of **CCL-34**. Nevertheless, the C3-*O*-alkylated derivatives of **CCL-34**, namely **CCL-34-S12**, did not give promising results.

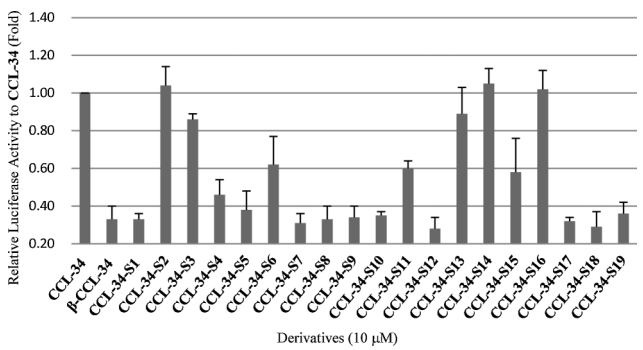


Fig. 1 The activities of glycolipids on NF-κB activation in 293-hTLR4/MD2-CD14 cells.

The biological results also indicate that the galacturonic acid glycolipid **CCL-34-S2** has an activity similar to that of **CCL-34**. However, its methyl ester derivative **CCL-34-S1** did not have any activity. Substitution of the C6 hydroxy group by an amino group (**CCL-34-S6**) and amidation (**CCL-34-S7–S10**) resulted in a significant decrease in activity, indicating that the modification of the C6 hydroxyl group of galactose was acceptable but that any elongation at this location was detrimental. In contrast, the glucuronic acid glycolipid **CCL-34-S5** and its methyl ester derivative **CCL-34-S4** did not have any activity, indicating that the C6 hydroxyl group cannot be modified on a glucose lipid derivative.

Based on the above-described structure–activity-relationship studies, it can be concluded that the C2, C3 and C6 positions of the saccharide moiety cannot be further modified to obtain new derivatives with improved activity. The observed loss of activity may be attributed to (1) crowding in the pocket in which the glycolipid is inserted and (2) the decrease of the strength of the hydrogen bonding or dipole–dipole interaction between the hydroxyl groups of the saccharide moiety and the receptor when the hydroxyl groups were transformed into an ethoxy or amino group. The modification of the C4-hydroxyl group resulted in promising results and further investigation is needed.

Conclusions

In conclusion, we have synthesized a library of serine-based lipids with high efficiency and demonstrated that an acid (R_x) with 12 carbons and an amine (R_y) with 11 carbons are the most effective components for TLR4 activation. In addition, the synthesis of 19 serine-based glycolipids with different saccharide moieties and orientations of glycosidic linkage was also achieved. The bioassay results revealed that out of the 19 compounds synthesized, five compounds possessed an activity that was comparable to that of **CCL-34**. It is noteworthy that the serine-based β-glucosyl lipid **CCL-34-S14** could be easily synthesized in six steps with an overall yield of 30%. This compounds displayed a TLR4-stimulating activity that was comparable to that of **CCL-34**, suggesting that this glycolipid is a potential immunostimulator, although further studies are required.

Experimental

Compounds **1**,[36] **2**, **3α**,[30] **3β**, **4**, **5**,[37] **6**,[31] **6α**,[31] **7**,[36] **8**,[38] **10**,[39] **11**,[40] **14**,[41] **20**,[37] **22**,[42] and **23**[35] were previously reported. Our prepared samples showed consistent ^{1}H and ^{13}C NMR spectral data. All reagents were purchased from commercial suppliers and used without further purification unless otherwise noted. Dichloromethane (DCM) and toluene were distilled from calcium hydride under N_2. Tetrahydrofuran (THF) was distilled under N_2 from sodium prior to use. Powdered molecular sieves (4 Å MS) were activated *in vacuo* at 150 °C for 8 h and cooled to room temperature *in vacuo* prior to use. Analytical thin layer chromatography was performed on E. Merck silica gel 60 F254 plates (0.25 mm). Liquid column chromatography was performed using a forced flow of the indicated solvent on silica gel 60 (E. Merck Co.). NMR spectra were recorded on Bruker 400 Hz instruments and are reported in parts per million (δ) units. Coupling constants (J) are reported in hertz (Hz). ^{1}H NMR spectra were recorded in $CDCl_3$ and referenced to residual $CHCl_3$ at 7.24 ppm. ^{13}C NMR spectra were referenced to the central peak of $CDCl_3$ at 77.0 ppm. Assignment of ^{1}H NMR signals was achieved using 2D methods (COSY). High-resolution mass spectra were obtained by means of a Micromass (Autospec) mass spectrometer. All reactions were carried out in oven-dried glassware (104 °C) under an atmosphere of nitrogen unless otherwise indicated.

N-(9-Fluorenylmethoxycarbonyl)-*O*-(2,3-di-*O*-*para*-methoxybenzyl-4,6-*O*-benzylidene-α-D-galactopyranosyl)-L-serine allyl ester (8α)

A mixture of the glycosyl donor 8 (2.15 g, 3.49 mmol), Fmoc-Ser-OAll (1.15 g, 3.13 mmol), and 4 Å MS (2 g) in dried CH_2Cl_2 (30 mL) was stirred for 10 min at room temperature under N_2. A solution of NIS (1.46 g, 6.49 mol) in dried CH_2Cl_2 (5 mL) and diluted with TfOH (85 μL, 0.97 mmol) was then added sequentially. The

reaction mixture was stirred at room temperature for 0.5 h and monitored by TLC. After the reaction was complete (based on TLC analysis), the molecular sieves were removed by filtration over Celite. The filtrate was diluted with EtOAc and the organic layer was washed with saturated aqueous $Na_2S_2O_3$, $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$, concentrated, and subjected to a flash silica gel column chromatography to give **8a** (exclusive α-anomer) as a white foam (1.69 g, 1.97 mmol, 63%). R_f 0.14 (1 : 2 EtOAc–hexane); ^{1}H (400 MHz, $CDCl_3$) δ 3.63 (1H, br s), 3.76 (3H, s), 3.77 (3H, s), 3.82 (1H, dd, J = 3.0, 11.3 Hz), 3.87 (1H, dd, J = 3.0, 10.1 Hz), 3.90 (1H, d, J = 13.4 Hz), 4.03 (1H, dd, J = 3.4, 10.1 Hz), 4.13 (1H, d, J = 3.0 Hz), 4.16–4.23 (3H, m), 4.34 (1H, dd, J = 7.2, 10.6 Hz), 4.41 (1H, dd, J = 7.2, 10.6 Hz), 4.48–4.52 (1H, m), 4.54 (1H, d, J = 10.2), 4.60 (1H, dd, J = 10.1, 3.0 Hz), 4.65 (1H, d, J = 11.3 Hz), 4.72 (1H, d, J = 10.2 Hz), 4.74 (1H, d, J = 11.3 Hz), 4.80 (1H, d, J = 3.4 Hz), 5.20 (1H, d, J = 10.5 Hz), 5.30 (1H, d, J = 17.2 Hz), 5.45 (1H, s), 5.81–5.91 (1H, m), 6.16 (1H, d, J = 8.4 Hz), 6.84 (4H, dd, J = 6.5, 8.5 Hz), 7.25–7.40 (11H, m), 7.50 (1H, d, J = 1.3 Hz), 7.52 (1H, d, J = 1.9 Hz), 7.58 (2H, d, J = 7.4 Hz), 7.75 (2H, d, J = 7.6 Hz); ^{13}C (100 MHz, $CDCl_3$) δ 46.90, 54.62, 55.04, 63.19, 66.05, 67.04, 69.08, 70.31, 71.51, 73.11, 74.32,74.82, 75.08, 100.18, 100.74, 113.56, 113.60, 118.55, 119.86, 124.87, 124.95, 126.14, 126.92, 126.96, 127.57, 127.93, 128.69, 129.10, 129.37, 130.49, 130.54, 131.36, 137.66, 141.09, 143.58, 155.92, 159.09, 169.76; HRMS (ESI) calc. for $C_{50}H_{50}NO_{12}$ $[M - H]^+$ 856.3333, found 856.3334.

N-(9-Fluorenylmethoxycarbonyl)-*O*-(3,4,5-tri-*O*-benzyl-6-acetoxy-α-D-galactopyranosyl)-L-serine allyl ester (10α)

TMSI (0.3 mL, 2.10 mmol) was added to a solution of the glycosyl acetate (1.01 g, 1.89 mmol) and 4 Å MS (1 g) in CH_2Cl_2 (20 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 20 min and then 3 mL of anhydrous toluene were added. The molecular sieves were removed by filtration over Celite. After concentrating the filtrate and azeotroping three times with toluene, the obtained yellow residue was dissolved in toluene (3 mL) and kept under N_2. In a separate flask, 4 Å MS, TBAI (1.42 g, 3.84 mmol), Fmoc-Ser-OAll (0.50 g, 1.37 mmol), and DIPEA (0.50 mL, 3.03 mmol) were mixed in toluene (20 mL). The mixture was stirred under N_2 at 80 °C for 20 min. Glycosyl iodide was then cannulated into the reaction mixture. After the reaction mixture was stirred at 80 °C for 3 h. The reaction was stopped by adding EtOAc (10 mL) and cooling to 0 °C. The white precipitate and the molecular sieves were removed by filtration over Celite. The filtrate was washed with saturated aqueous $Na_2S_2O_3$ and brine. The organic layer was dried over $MgSO_4$, concentrated, and subjected to a flash silica gel column chromatography to give **10a** (exclusive α-anomer) as a white foam (0.69 g, 0.82 mmol, 60%). R_f 0.38 (1 : 1 EtOAc–hexane); ^{1}H (400 MHz, $CDCl_3$) δ 1.94 (3H, s), 3.83 (1H, dd, J = 2.9, 11.2 Hz), 3.86–3.90 (3H, m), 4.05 (1H, dd, J = 3.5, 10.6), 4.09–4.18 (3H, m), 4.21 (1H, t, J = 7.0 Hz), 4.38 (2H, d, J = 7.0 Hz), 4.53–4.56 (1H, m), 4.58–4.64 (4H, m), 4.73–4.78 (3H, m), 4.85 (1H, d, J = 11.7 Hz), 4.97 (1H, d, J = 11.4 Hz), 5.18 (1H, dd, J = 1.1, 10.3 Hz), 5.28 (1H, dd, J = 1.1, 17.2 Hz), 5.85 (1H, ddd, J = 5.7, 10.3, 17.2 Hz), 6.14 (1H, d, J = 8.5 Hz), 7.25–7.40 (19H, m), 7.59 (2H, d, J = 7.5 Hz), 7.73 (2H, d, J = 7.6 Hz); ^{13}C (100 MHz, $CDCl_3$) δ 20.37, 46.76, 54.43, 63.31, 65.76, 66.70, 69.06, 70.04, 72.94, 74.24, 74.38, 76.01, 76.68, 77.00, 77.32, 78.18, 99.14, 118.30, 119.64, 124.76, 126.72, 127.15, 127.31, 127.36, 127.47, 128.04, 128.09, 131.22, 137.83, 138.08, 138.24, 140.93, 143.49, 155.63, 169.30, 170.23; HRMS (ESI) calc. for $C_{50}H_{52}NO_{11}$ $[M + H]^+$ 842.3540, found 842.3522.

General procedure for the deprotection of the allyl ester and the amidation

N-Methylaniline (3 mmol) was added to a solution of serine glycoside (1 mmol) and $Pd(PPh_3)_4$ (0.3 mmol) in THF (10 mL). The reaction mixture was stirred at room temperature for 2 h, and then the solvent was removed. The crude was diluted with EtOAc, washed by water, 10% aqueous HCl, brine, dried with $MgSO_4$, concentrated, and subjected to a short pad of silica gel to remove residual *N*-methylaniline. The crude product was dissolved in dry CH_2Cl_2 (10 mL) and EDCI (2 mmol), HOBt (2 mmol), lipid amine (1.5 mmol), and NMM (2 mmol) were successively added. The reaction mixture was stirred at room temperature for 2 h. The solvent was removed *in vacuo* and the residue was diluted with EtOAc and washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$, concentrated, and subjected to a flash silica gel column chromatography to give the desired product.

General procedure for the deprotection of the Fmoc group and the amidation

Piperidine (1 mL) was added to a solution of the Fmoc-protected glycoside (1 mmol) in CH_2Cl_2 (10 mL). The reaction mixture was stirred at room temperature for 20 min and then the solvent was removed. The crude was subjected to silica gel column chromatography to give the deprotected product that was dissolved in dry CH_2Cl_2 (10 mL). EDCI (2 mmol), HOBt (2 mmol), lipid acid (1.5 mmol), and DIPEA (2 mmol) were successively added and the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was then diluted with CH_2Cl_2 and washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$, concentrated, and subjected to a flash silica gel column chromatography to give the di-lipid product.

O-(2,3,4-Tri-*O*-benzyl-6-hydroxy-α-D-galactopyranosyl)-*N*-dodecanoyl-L-serine undecylamide (15)

Compound **15** was obtained in 68% from **10α** as a white foam. R_f 0.25 (1 : 1 EtOAc–hexane); ^{1}H (400 MHz, $CDCl_3$) δ 0.86 (6H, t, J = 6.6), 1.21–1.27 (34H, m), 1.50–1.66 (2H, m), 2.16 (2H, t, J = 7.9), 2.63–2.71 (1H, m), 3.04–3.12 (1H, m), 3.43 (1H, dd, J = 9.1, 11.5), 3.47 (1H, dd, J = 4.8, 11.1), 3.72 (1H, dd, J = 7.1, 11.1), 3.79–3.88 (3H, m), 3.93 (1H, dd, J = 4.4, 11.5), 4.11 (1H, dd, J = 3.7, 10.0), 4.39 (1H, ddd, J = 4.4, 6.6, 9.1), 4.61 (1H, d, J = 11.6), 4.69 (1H, d, J = 10.8), 4.75 (1H, d, J = 11.8), 4.85 (1H, d, J = 11.8), 4.85 (1H, d, J = 10.8), 4.93 (1H, d, J = 11.6), 5.12 (1H, d, J = 3.7), 6.66 (1H, d, J = 6.6), 6.94 (1H, t, J = 5.4), 7.26–7.40 (15H, m); ^{13}C (100 MHz, $CDCl_3$) δ 13.94, 22.50,25.37, 26.72, 29.16, 29.34, 29.44, 31.73, 36.25, 39.39, 51.48, 62.05, 68.48, 71.46, 72.81, 74.41, 76.41, 79.34, 98.37, 127.18, 127.55, 127.67, 127.96, 128.14, 128.21, 128.30, 128.35, 137.46, 138.08, 138.21, 169.42, 173.15; HRMS (ESI) calc. for $C_{53}H_{80}N_2O_8Na$ $[M + Na]^+$ 895.5812, found 895.5818.

_N_-(9-Fluorenylmethoxycarbonyl)-_O_-(2,3,4-tri-_O_-benzyl-6-_O_-acetoxy-α-D-glucopyranosyl)-L-serine allyl ester (11α)

Compound **11α** was obtained in 54% from **11** as white foam. R_f 0.32 (1 : 2 EtOAc–hexane);^{1}H NMR (400 MHz, $CDCl_3$) δ 3.47 (1H, dd, J = 9.4, 9.4), 3.53 (1H, dd, J = 3.5, 9.4), 3.82–3.86 (1H, m), 3.89 (1H, dd, J = 2.9, 10.7 Hz), 3.96 (1H, dd, J = 9.4, 9.4 Hz), 4.09 (1H, dd, J = 3.2, 10.7 Hz), 4.21–4.26 (2H, m), 4.32 (1H, dd, J = 1.4, 11.8 Hz), 4.39 (2H, d, J = 6.5 Hz), 4.56–4.65 (5H, m), 4.70 (1H, d, J = 12.2), 4.73 (1H, d, J = 3.5), 4.83 (1H, d, J = 10.8), 4.88 (1H, d, J = 10.8 Hz), 4.99 (1H, d, J = 10.8 Hz), 5.20 (1H, d, J = 10.5 Hz), 5.30 (1H, d, J = 17.2 Hz), 5.83–5.93 (1H, m), 5.99 (1H, d, J = 8.6 Hz), 7.27–7.39 (19H, m), 7.61 (2H, d, J = 7.4 Hz), 7.75 (1H, d, J = 7.6 Hz);^{13}C (100 MHz, $CDCl_3$) δ 20.33, 46.67, 54.22, 62.59, 65.81, 66.78, 69.04, 69.30, 72.46, 74.63, 75.20, 76.82, 79.54, 81.21, 97.75, 118.34, 119.58, 124.73, 126.69, 127.29, 127.38, 127.52, 127.73, 128.02, 128.05, 131.13, 137.43, 137.69, 138.22, 140.85, 143.42, 155.54, 169.20, 170.09; HRMS (ESI) calc. for $C_{50}H_{52}NO_{11}$ $[M + H]^+$ 842.3540, found 842.3544.

_O_-(2,3,4-Tri-_O_-benzyl-6-hydroxy-α-D-glucopyranosyl)-_N_-dodecanoyl-L-serine undecylamide (16)

Compound **16** was obtained in 46% from **11α** as white foam. R_f 0.32 (1 : 1 EtOAc-hexane); ^{1}H (400 MHz, $CDCl_3$) δ 0.83–0.87 (6H, m), 1.18–1.25 (34H, m), 1.56–1.66 (2H, m), 2.17 (2H, t, J = 7.9 Hz), 2.65–2.73 (1H, m), 3.11–3.18 (1H, m), 3.42 (1H, dd, J = 9.9, 11.1 Hz), 3.55 (1H, dd, J = 9.7, 9.7 Hz), 3.57 (1H, dd, J = 3.6, 9.7 Hz), 3.64–3.70 (2H, m, H-5), 3.77 (1H, d, J = 9.4 Hz), 3.90 (1H, dd, J = 9.7, 9.7 Hz), 3.90 (1H, dd, J = 4.2, 11.1 Hz), 4.33 (1H, ddd, J = 4.2, 6.2, 9.9 Hz), 4.64 (1H, d, J = 11.0 Hz), 4.68 (1H, d, J = 10.8 Hz), 4.79 (1H, d, J = 10.8 Hz), 4.84 (1H, d, J = 11.0 Hz), 4.85 (1H, d, J = 11.0 Hz), 4.90 (1H, d, J = 11.0 Hz), 5.12 (1H, d, J = 3.6 Hz), 6.57 (1H, d, J = 6.2 Hz), 6.94 (1H, t, J = 5.7 Hz), 7.25–7.34 (15H, m); ^{13}C (100 MHz, $CDCl_3$) δ 14.04, 22.60, 25.44, 26.83, 29.26, 29.41, 29.54, 31.82, 36.40, 39.56, 51.14, 61.50, 67.11, 71.58, 74.49, 74.99, 75.57, 77.50, 79.83, 82.07, 97.05, 127.51, 127.65, 127.78, 128.37, 128.39, 128.51, 128.59, 136.98, 137.96, 138.40, 169.21, 173.12; HRMS (ESI) calc. for $C_{53}H_{81}N_2O_8$ $[M + H]^+$ 873.5993, found 873.5991.

General procedure for the catalytic hydrogenation

To a solution of the target compound (0.1 mmol) in a co-solvent system of CH_2Cl_2 and methanol (1 : 1, 5 mL), Pd/C (20 mg) was added. The reaction was shaken under a high pressure of hydrogen (50 kg cm^{-2}) for 6 h. The reaction mixture was filtered over a short pad of Celite, and the solid residue was washed with CH_2Cl_2/MeOH (1 : 1). The filtrate was concentrated under reduced pressure, and the resulting residue was purified by silica gel chromatography to give the product.

Methyl 1-(_N_-dodecanoyl undecylcarbamoyl-L-serine)-α-D-galactopyranosiduronate (CCL-34-S1)

To a vigorously stirred solution of **15** (130 mg, 0.15 mmol) in CH_2Cl_2(2 mL), acetone (1 mL), and H_2O (1 mL), TEMPO (12 mg, 0.08 mmol) and BAIB (257 mg, 0.38 mmol) were added. After being stirred at room temperature for 3 h, the reaction mixture was quenched by addition of a saturated $Na_2S_2O_3$ solution. The mixture was then extracted twice with EtOAc and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated. The resulting residue was then dissolved in DMF and caesium carbonate (147 mg, 0.45 mmol) and iodomethane (20 μL, 0.30 mmol) were added. The reaction mixture was stirred at room temperature for another 2 h, after which TLC analysis showed completion of the reaction. The solvent was removed under reduced pressure and EtOAc was added. The organic layer was washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give the esterified product (117 mg, 0.13 mmol, 88% over two steps). The esterified product was subjected to a catalytic hydrogenation to give **CCL-34-S1** as a white foam (62 mg, 0.10 mmol, 76%). R_f 0.53 (1 : 9 MeOH–CH_2Cl_2); ^{1}H (400 MHz, $CDCl_3$/MeOD) δ 0.52 (6H, t, J = 6.8), 0.91–0.93 (32H, m), 1.11–1.17 (2H, m), 1.21–1.27 (2H, m), 1.88 (2H, t, J = 7.6), 2.82 (2H, t, J = 7.2), 3.35–3.49 (7H, m), 3.86 (1H, dd, J = 1.6, 3.2), 4.06 (1H, d, J = 1.6), 4.17 (1H, dd, J = 5.8, 6.6), 4.62 (1H, d, J = 4.0); ^{13}C (100 MHz, $CDCl_3$) δ 14.04, 22.62, 25.61, 26.94, 29.31, 29.36, 29.52, 29.62, 31.86, 36.44, 39.73, 51.98, 52.44, 68.17, 68.73, 69.72, 70.48, 70.87, 99.71, 169.51, 173.90; HRMS (ESI) calc. for $C_{33}H_{62}N_2O_9Na$ $[M + Na]^+$ 653.4353, found 653.4348.

_O_-α-D-Glucopyranosyl-_N_-dodecanoyl-L-serine undecylamide (CCL-34-S3)

Compound **CCL-34-S3** was obtained in 83% from **16** as white foam. R_f 0.23 (1 : 9 MeOH-CH_2Cl_2); ^{1}H (400 MHz, MeOD) δ 0.90 (6H, t, J = 6.7), 1.29 (32H, m), 1.48–1.55 (2H, m), 1.58–1.65 (2H, m), 2.27 (2H, t, J = 7.5 Hz), 3.14–3.25 (2H, m), 3.29 (1H, dd, J = 9.7 Hz), 3.42 (1H, dd, J = 3.7, 9.7 Hz), 3.53 (1H, ddd, J = 2.2, 5.5, 9.7 Hz), 3.60 (1H, dd, J = 9.7, 9.7 Hz), 3.66 (1H, dd, J = 5.5, 11.8 Hz), 3.74 (1H, dd, J = 6.0, 10.4 Hz), 3.81 (1H, dd, J = 2.2, 11.8 Hz), 3.84 (1H, dd, J = 6.0, 10.4 Hz), 4.53 (1H, dd, J = 6.0, 6.0 Hz), 4.83 (1H, d, J = 3.7 Hz); ^{13}C (100 MHz, MeOD) δ 14.48, 23.73, 26.82, 28.02, 30.37, 30.48, 30.66, 30.77, 33.07, 36.84, 40.60, 54.64, 62.56, 68.89, 71.54, 73.35, 74.00, 74.97, 100.81, 171.98, 176.22; HRMS (ESI) calc. for $C_{32}H_{63}N_2O_8$[M + H]$^+$ 603.4584, found 603.4563.

Methyl 1-(_N_-dodecanoyl undecylcarbamoyl-L-serine)-α-D-glucopyranosiduronate (CCL-34-S4)

Compound **CCL-34-S4** was obtained in 67% from **16** as white foam. R_f 0.37 (1 : 9 MeOH–CH_2Cl_2); ^{1}H (400 MHz, $CDCl_3$) δ 0.67–0.70 (6H, m), 1.07–1.11 (34H, m), 1.28–1.35 (2H, m), 1.39–1.46 (2H, m), 2.06 (2H, t, J = 8.0 Hz), 2.95–3.07 (2H, m), 3.35 (1H, dd, J = 3.6, 9.2 Hz), 3.39 (1H, dd, J = 9.2, 9.6 Hz), 3.46 (1H, dd, J = 9.2, 9.2 Hz), 3.56–3.58 (2H, m), 3.61 (3H, s), 3.89 (1H, d, J = 9.6 Hz), 4.33 (1H, dd, J = 5.2, 6.4 Hz), 4.74 (1H, d, J = 3.6 Hz); ^{13}C (100 MHz, $CDCl_3$) δ 14.10, 22.68, 25.64, 27.00, 29.36, 29.48, 29.56, 29.66, 31.92, 36.52, 39.87, 52.34, 52.70, 69.06, 71.15, 71.36, 71.77, 73.23, 99.58, 169.51, 170.59, 174.18; HRMS (ESI) calc. for $C_{33}H_{62}N_2O_9Na$ $[M + Na]^+$ 653.4353, found 653.4355.

_O_-(2,3-Di-_O_-_para_-methoxybenzyl-4,6-_O_-benzylidene-α-D-galactopyranosyl)-_N_-dodecanoyl-L-serine undecylamide (17)

Compound **17** was obtained in 53% from **8α** as white foam. R_f 0.40 (1 : 1 EtOAc–hexane); ^{1}H (400 MHz, $CDCl_3$) δ 0.86 (6H, t, J = 6.5, 7.1 Hz), 1.15–1.23 (34H, m), 1.56 (2H, br s), 2.15 (2H, t, J = 7.4 Hz), 2.54–2.61 (1H, m), 3.00–3.06 (1H, m), 3.40 (1H, dd,

J = 10.7,10.7 Hz), 3.62 (1H, br s), 3.77 (3H, s), 3.79 (3H, s), 3.85 (1H, dd, J = 3.1, 10.0 Hz), 3.88 (1H, dd, J = 3.9, 10.7 Hz), 3.96 (1H, dd, J = 1.4, 12.4 Hz), 4.09 (1H, dd, J = 3.5, 10.0 Hz), 4.15 (1H, d, J = 3.1 Hz), 4.21 (1H, dd, J = 1.0, 12.4 Hz), 4.30–4.35 (1H, m), 4.61 (1H, d, J = 10.2 Hz), 4.64 (1H, d, J = 11.8 Hz), 4.67 (1H, d, J = 11.8 Hz), 4.80 (1H, d, J = 10.2 Hz), 5.24 (1H, d, J = 3.5 Hz), 5.44 (1H, s), 6.48 (1H, d, J = 6.2 Hz), 6.82 (2H, d, J = 8.6 Hz), 6.86 (1H, d, J = 8.6 Hz), 7.07 (1H, t, J = 4.8 Hz), 7.23 (2H, d, J = 8.6 Hz), 7.30 (2H, d, J = 8.6 Hz), 7.32–7.39 (5H, m), 7.50 (1H, d, J = 1.4 Hz), 7.52 (1H, d, J = 2.1 Hz);δ_C (100 MHz, $CDCl_3$) 14.06, 22.64, 25.52, 26.85, 29.25, 29.32, 29.44, 29.58, 29.62, 31.87, 36.49, 39.42, 51.01, 55.21, 63.08, 67.55, 69.30, 71.29, 74.11, 74.69, 75.23, 76.45, 98.60, 101.12, 113.77, 113.88, 126.33, 128.12, 128.91, 129.05, 129.62, 130.29, 130.47, 137.82, 159.29, 159.60, 169.31, 172.77; HRMS (ESI) calc. for $C_{55}H_{82}N_2O_{10}Na$ $[M + Na]^+$ 953.5867, found 953.5864.

O-(2,3-Di-*O*-*para*-methoxybenzyl-α-D-galactopyranosyl)-*N*-dodecanoyl-L-serine undecylamide (18)

Compound **17** (1.27 g, 1.37 mmol) was dissolved in 10 mL of $MeCN/CH_2Cl_2/MeOH$ (15 mL/3 mL/5 mL). Vanadyl triflate (60 mg, 0.14 mol) was added at ambient temperature and the resulting mixture was stirred for 6 h. After completion of the reaction as monitored by TLC, the reaction was quenched by addition of TEA and the crude product was purified by column chromatography on silica gel to give **18** as a white foam (60 mg, 0.14 mmol). R_f 0.50 (EtOAc 100%); δ_H (400 MHz, $CDCl_3$) 0.85 (6H, t, J = 6.5, 7.1 Hz), 1.20–1.25 (34H, m), 1.55–1.62 (2H, m), 2.16 (2H, t, J = 7.9 Hz), 2.64–2.70 (1H, m), 3.05–3.11 (1H, m), 3.42 (1H, dd, J = 9.6, 11.4 Hz), 3.71–3.82 (9H, m), 3.86–3.93 (3H, m), 4.04 (1H, d, J = 2.3), 4.34 (1H, ddd, J = 4.4, 6.5, 11.4 Hz), 4.60 (1H, d, J = 10.6 Hz), 4.61 (1H, d, J = 11.2 Hz), 4.65 (1H, d, J = 11.2 Hz), 4.75 (1H, d, J = 10.6 Hz), 5.11 (1H, d, J = 3.7), 6.59 (1H, d, J = 6.5), 6.83 (2H, d, J = 8.6 Hz), 6.88 (2H, d, J = 8.6 Hz), 6.99 (1H, t, J = 5.6 Hz), 7.22 (2H, d, J = 8.6 Hz), 7.27 (2H, d, J = 8.6 Hz); δ_C (100 MHz, $CDCl_3$) 14.03, 22.60, 25.45, 26.80, 29.28, 29.42, 29.56, 31.83, 36.40, 39.46, 51.20, 55.17, 62.69, 67.76, 68.18, 70.00, 71.84, 74.29, 75.34, 77.67, 98.02, 113.88, 128.42, 128.54, 129.24, 129.48, 129.85, 130.05, 131.96, 132.06, 159.41, 159.57, 169.29, 173.12; HRMS (ESI) calc. for $C_{48}H_{79}N_2O_{10}$ $[M + H]^+$ 843.5735, found 843.5741.

O-(6-Amino-6-deoxy-2,3-di-*O*-*para*-methoxybenzyl-α-D-galactopyranosyl)-*N*-dodecanoyl-L-serine undecylamide (19)

To a solution of **18** (0.84 g, 0.99 mmol) in pyridine (10 mL), TsCl (570 mg, 2.99 mmol) was added at 0 °C. After being stirred at the same temperature for 10 min, the reaction was allowed to warm to room temperature and was stirred for another 12 h. The reaction was quenched with methanol and concentrated *in vacuo*. The reaction mixture was dissolved in EtOAc and washed with water and brine. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure to give the tosylated crude product. To a solution of the tosylated product in DMF (10 mL), sodium azide (329 mg, 5.01 mmol) was added and the resulting mixture was stirred at 80 °C for 12 h. The reaction mixture was concentrated, dissolved in EtOAc, and washed with water and brine. The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give the azide (612 mg, 0.70 mmol, 71%). The azide (523 mg, 0.60 mmol) was catalytically hydrogenated to give **19** as a white foam (435 mg, 0.52 mmol, 86%). R_f 0.12 (1 : 9 $MeOH–CH_2Cl_2$); ^1H (400 MHz, $CDCl_3$/MeOD) δ 0.77 (3H, t, J = 7.0 Hz), 0.78 (3H, t, J = 7.1 Hz), 1.13–1.24 (34H, m), 1.47–1.54 (2H, m), 2.11 (2H, t, J = 8.0 H), 2.72–2.79 (1H, m), 2.91 (1H, dd, J = 3.8, 13.3 Hz), 2.94–3.01 (1H, m), 3.04 (1H, dd, J = 6.8, 13.3 Hz), 3.49 (1H, dd, J = 9.1, 10.6 Hz), 3.64 (1H, dd, J = 3.2, 10.0), 3.69 (1H, dd, J = 5.1, 10.6 Hz), 3.70–3.72 (7H, m), 3.81 (1H, dd, J = 3.7, 10.0 Hz), 3.94 (1H, d, J = 3.2 Hz), 4.36 (1H, dd, J = 5.1, 9.1 Hz), 4.51 (1H, d, J = 10.8 Hz), 4.52 (1H, d, J = 11.2 Hz), 4.56 (1H, d, J = 11.2 Hz), 4.64 (1H, d, J = 10.8 Hz), 4.93 (1H, d, J = 3.7), 6.74 (2H, d, J = 8.6 Hz), 6.79 (2H, d, J = 8.6 Hz), 7.16 (2H, d, J = 8.6 Hz), 7.21 (2H, d, J = 8.6 Hz); ^{13}C (100 MHz, $CDCl_3$/MeOD) δ 13.33, 22.04, 25.07, 26.33, 28.73, 28.92, 29.01, 31.29, 35.55, 38.95, 41.15, 51.48, 54.48, 66.58, 67.67, 68.21, 71.11,73.35, 74.81, 97.24, 113.21, 113.28, 128.78, 129.21, 129.45, 129.63, 158.81, 159.05, 169.44, 173.75; HRMS (ESI) calc. for $C_{32}H_{64}N_3O_7$ $[M + H]^+$ 842.5895, found 842.5900.

O-(6-Amino-6-deoxy-α-D-galactopyranosyl)-*N*-dodecanoyl-L-serine undecylamide (CCL-34-S6)

To a solution of **19** (150 mg, 0.18 mmol) in CH_2Cl_2 (5 mL), trifluoroacetic acid (1 mL) was added. The reaction mixture was stirred at room temperature for 15 min, concentrated, and purified by column chromatography on silica gel to give **CCL-34-S6** as a white foam (85 mg, 0.14 mmol, 80%). R_f 0.50 (1 : 4 $MeOH–CH_2Cl_2$); ^1H (400 MHz, $CDCl_3$/MeOD) δ 0.90 (6H, t, J = 6.7 Hz), 1.25–1.35 (32H, m, CH_2), 1.49–1.54 (2H, m), 1.58–1.65 (2H, m), 2.25–2.29 (2H, m), 3.15 (1H, dd, J = 3.6, 13.2), 3.20 (1H, t, J = 7.4), 3.26 (1H, dd, J = 5.5, 13.2), 3.69 (1H, dd, J = 6.5, 10.1), 3.73 (1H, dd, J = 3.2, 10.1), 3.81 (1H, dd, J = 3.7, 10.1), 3.87–3.91 (2H, m, H-4), 3.95–3.98 (1H, m), 4.54 (1H, dd, J = 6.5, 6.5), 4.93 (1H, d, J = 3.7); ^{13}C (100 MHz, $CDCl_3$/MeOD) δ 14.43, 23.61, 26.75, 27.92, 30.23, 30.30, 30.37, 30.44, 30.59, 30.66, 32.95, 36.74, 40.52, 40.64, 41.86, 54.60, 68.21, 68.65, 69.29, 70.52, 71.55, 100.78, 172.08, 172.17, 176.29; HRMS (ESI) calc. for $C_{32}H_{64}N_3O_7$ $[M + H]^+$ 602.4744, found 602.4730.

O-(6-[(8-Phenyloctanoyl)amino]-6-deoxy-α-D-galactopyranosyl)-*N*-dodecanoyl-L-serine undecylamide (CCL-34-S7)

Compound **19** (68 mg, 0.08 mmol) was dissolved in dry CH_2Cl_2 (2 mL) and EDCI (31 mg, 0.16 mmol), HOBt (21 mg, 0.16 mmol), 8-phenyloctanoic acid (35 mg, 0.16 mmol), and DIPEA (22 μL, 0.16 mmol) were added. The reaction mixture was stirred at room temperature for 3 h. The reaction mixture was diluted with CH_2Cl_2 and washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$, concentrated, and purified by flash silica gel column chromatography to give the product of amidation. Trifluoroacetic acid (1 mL) was added to a solution of this product in CH_2Cl_2 (5 mL). The reaction mixture was stirred at room temperature for 15 min, concentrated, and purified by column chromatography on silica gel to give **CCL-34-S7** as a white foam (47 mg, 0.06 mmol, 73% for two steps). R_f 0.40 (1 : 9 $MeOH–CH_2Cl_2$); ^1H (400 MHz, $CDCl_3$/MeOD) δ 0.54 (6H, t, J = 6.7, 7.0 Hz), 0.92–1.00 (38H, m), 1.12–1.19 (2H, m), 1.22–1.30 (6H, m), 1.85–1.93 (4H, m), 2.25 (2H, t, J = 7.7), 2.78–2.95

(3H, m), 3.16–3.23 (1H, m), 3.32–3.46 (6H, m), 4.16–4.20 (1H, m), 4.51 (1H, d, J = 3.8), 6.79–6.82 (3H, m), 6.89–6.93 (2H, m), 7.38 (1H, d, J = 7.8), 7.46 (1H, t, J = 5.6), 7.55 (1H, t, J = 5.4); ^{13}C (100 MHz, $CDCl_3$/MeOD) δ 13.17, 22.02, 25.09, 25.24, 26.33, 28.51, 28.63, 28.72, 28.91, 29.00, 30.89, 31.30, 35.27, 35.47, 35.57, 39.02, 39.10, 52.31, 66.92, 68.11, 68.59, 68.71, 69.24, 98.93, 124.93, 127.56, 127.70, 142.10, 169.97, 174.23, 175.18; HRMS (ESI) calc. for $C_{46}H_{81}N_3O_8Na$ $[M + Na]^+$ 826.5921, found 826.5903.

O-(6-[(2-Hydroxydodecanoyl)amino]-6-deoxy-α-D-galactopyranosyl)-*N*-dodecanoyl-L-serine undecylamide (CCL-34-S8)

Compound **CCL-34-S8** was obtained from **19** (68 mg, 0.08 mmol) as a white foam (44 mg, 0.05 mmol, 69%). R_f 0.33 (1 : 9 MeOH–CH_2Cl_2); ^{1}H (400 MHz, $CDCl_3$/MeOD) δ 0.52 (9H, t, J = 6.7, 7.0 Hz), 0.82–1.51 (50H, m), 1.81–1.86 (2H, m), 2.69–2.82 (2H, m), 2.92–2.96 (1H, m), 3.09–3.16 (1H, m), 3.23–3.38 (6H, m), 3.60–3.66 (1H, m, H-5′), 4.08–4.11 (1H, m), 4.42–4.44 (1H, m); ^{13}C (100 MHz, $CDCl_3$/MeOD) δ 13.22, 22.05, 24.67, 24.73, 25.12, 26.36, 28.63, 28.76, 28.88, 28.95, 29.04, 31.33, 33.93, 34.08, 35.51, 38.80, 39.14, 52.32, 52.40, 66.70, 66.75, 68.14, 68.60, 68.85, 69.05, 69.34, 69.40, 71.27, 77.19, 98.80, 98.87, 169.92, 169.98, 174.26, 174.30, 176.07, 176.31; HRMS (ESI) calc. for $C_{44}H_{85}N_3O_9Na$ $[M + Na]^+$ 822.6184, found 822.6169.

O-(6-Butyrylamino-6-deoxy-α-D-galactopyranosyl)-*N*-dodecanoyl-L-serine undecylamide (CCL-34-S9)

Compound **CCL-34-S9** was obtained from **19** (35 mg, 0.04 mmol) as a white foam (22 mg, 0.03 mmol, 78%). R_f 0.37 (1 : 9 MeOH–CH_2Cl_2); ^{1}H (400 MHz, $CDCl_3$/MeOD) δ 0.52 (6H, t, J = 6.7, 7.0 Hz), 0.58 (3H, t, J = 7.4), 0.88–0.97 (32H, m), 1.11–1.17 (2H, m), 1.22–1.31 (4H, m), 1.83 (2H, t, J = 7.4), 1.89 (2H, t, J = 7.6), 2.77–2.92 (3H, m), 3.15–3.20 (1H, m), 3.30–3.44 (6H, m), 4.15 (1H, dd, J = 5.9, 5.9), 4.49 (1H, d, J = 3.7), 7.39 (1H, d, J = 7.4), 7.47 (1H, t, J = 5.6), 7.53 (1H, t, J = 5.4); ^{13}C (100 MHz, $CDCl_3$/MeOD) δ 12.46, 12.80, 18.42, 21.80, 24.90, 26.11,28.46, 28.51, 28.70, 28.79, 31.10, 35.16, 37.17, 38.82, 38.95, 39.05, 39.17, 52.26, 66.71, 67.96, 68.64, 68.83, 69.12, 98.88, 169.87, 169.96, 174.13, 174.75; HRMS (ESI) calc. for $C_{36}H_{69}N_3O_8Na$ $[M + Na]^+$ 694.4982, found 694.4989.

O-(6-[5-(2-Oxoperhydrothieno[3,4-*d*]imidazol-4-yl)pentanoylamino]-6-deoxy-α-D-galactopyranosyl)-*N*-dodecanoyl-L-serine undecylamide (CCL-34-S10)

Compound **CCL-34-S10** was obtained from **19** (68 mg, 0.11 mmol) as a white foam (65 mg, 0.08 mmol, 71%). R_f 0.13 (1 : 9 MeOH–CH_2Cl_2); ^{1}H (400 MHz, $CDCl_3$/MeOD) δ 0.86 (6H, t, J = 6.7, 7.0 Hz), 1.22–1.28 (32H, m), 1.41–1.47 (4H, m), 1.56–1.69 (6H, m), 2.22–2.27 (4H, m), 2.71 (1H, d, J = 12.8), 2.91 (1H, dd, J = 5.0, 12.8), 3.11–3.20 (3H, m), 3.26–3.30 (1H, m), 3.48 (1H, dd, J = 6.6, 13.7), 3.65–3.79 (6H, m), 4.31 (1H, dd, J = 4.5, 7.8), 4.48–4.53 (2H, m), 4.84 (1H, d, J = 3.8); ^{13}C (100 MHz, $CDCl_3$/MeOD) δ 13.04, 21.95, 24.87, 25.06, 26.28, 27.54, 27.82, 28.54, 28.66, 28.73, 28.87, 28.94, 31.24, 34.91, 35.36, 38.99, 39.05, 39.49, 52.49, 55.07, 59.73, 61.50, 66.75, 68.05, 68.49, 68.82, 69.17, 77.20, 98.86, 114.62, 117.52, 170.08, 174.38, 174.84; HRMS (ESI) calc. for $C_{42}H_{77}N_5O_9SNa$ $[M + Na]^+$ 850.5340, found 850.5341.

S-*p*-Tolyl 4-*O*-allyl-2,3,6-tri-*O*-benzyl-β-D-thiogalactopyranoside (12)

To a solution of *S*-*p*-tolyl 4,6-*O*-benzylidene-2,3-di-*O*-benzyl-β-D-thiogalactopyranoside (0.59 g, 1.07 mmol) in THF (22 mL), Me_3NBH_3 (0.32 g, 4.39 mmol), $AlCl_3$ (0.86 g, 6.45 mmol), and H_2O (0.04 mL, 2.14 mmol) were added at room temperature. After being stirred for 4 h, the reaction mixture was quenched by adding saturated aqueous HCl and extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography to give the selectively reduced product (corresponding to the 6-*O*-benzyl derivative) that was then dissolved in DMF (2.7 mL). NaH (23.4 mg, 1.56 mmol) and allyl bromide (0.076 ml, 1.25 mmol) were added at 0 °C. After being stirred for 3 h, the reaction mixture was quenched by the addition of MeOH, extracted with ethyl acetate, and washed with brine. The combined organic layers were dried over $MgSO_4$, filtered, and purified by column chromatography to give compound **12** (0.44 g, 91%). R_f 0.4 (1 : 4 EtOAc–Hexane); ^{1}H (400 MHz, $CDCl_3$) δ 2.29 (3H, s), 3.52–3.57 (2H, m), 3.66 (1H, dd, J = 5.5, 9.2 Hz), 3.72 (1H, dd, J = 9.2, 9.6 Hz), 3.83 (1H, t, J = 9.7 Hz), 3.87 (1H, d, J = 2.6 Hz), 4.10 (1H, dd, J = 5.9, 12.8 Hz), 4.38 (1H, dd, J = 5.3, 12.8 Hz), 4.49 (1H, d, J = 11.6 Hz) 4.52 (1H, d, J = 11.6 H), 4.57 (1H, d, J = 9.7), 4.67 (1H, d, J = 11.6 Hz), 4.72 (1H, d, J = 11.6 Hz), 4.73 (1H, d, J = 10.2 Hz), 4.80 (1H, d, J = 10.2 Hz), 5.13 (1H, dd, J = 1.6, 10.3 Hz), 5.23 (1H, dd, J = 1.6, 17.2 Hz), 5.89 (1H, m), 7.04 (2H, d, J = 7.9 Hz), 7.27–7.40 (15H, m), 7.46 (2H, d, J = 6.4 Hz); ^{13}C (100 MHz, $CDCl_3$) δ 21.01, 68.64, 72.57, 73.20, 73.57, 75.57, 77.32, 77.43, 83.91, 88.22, 116.43, 127.54, 127.61, 127.72, 127.85, 128.23, 128.34, 129.48, 130.36, 132.11, 135.35, 137.16, 137.85, 138.15, 138.35, 138.35. HRMS (ESI) calc. for $C_{37}H_{40}O_5SNa$ $[M + Na^+]$: 619.2494, found 619.2498.

N-(9-Fluorenylmethoxycarbonyl)-*O*-(4-*O*-allyl-2,3,6-tri-*O*-benzyl-α-D-galactopyranosyl)-L-serine allyl ester (12α)

Compound **12α** was obtained from **12** in 66% as white foam. R_f 0.38 (1 : 2 EtOAc–hexane); ^{1}H (400 MHz, $CDCl_3$) δ 3.58 (2H, d, J = 6.5 Hz), 3.76–3.82 (3H, m), 3.91–3.95 (2H, m), 4.02 (1H, dd, J = 6.2, 12.4 Hz), 4.13 (1H, t, J = 7.2 Hz), 4.18 (1H, dd, J = 3.6, 11.2 Hz), 4.27–4.35 (3H, m), 4.42 (1H, d, J = 12.0 Hz), 4.49–4.58 (5H, m), 4.65–4.74 (4H, m), 5.06–5.26 (4H, m), 5.79–5.85 (2H, m), 6.21 (1H, d, J = 8.6 Hz), 7.20–7.34 (19H, m), 7.53 (2H, d, J = 7.4 Hz), 7.70 (2H, d, J = 7.6 Hz); ^{13}C (100 MHz, $CDCl_3$) δ 47.05, 54.71, 66.05, 67.04, 68.72, 69.86, 70.31, 72.86, 73.29, 73.40, 73.93, 74.68, 76.42, 78.36, 99.57, 116.93, 118.56, 119.86, 125.11, 126.99, 127.39, 127.44, 127.58, 127.70, 128.–8, 128.28, 131.54, 135.21, 137.86, 138.50, 138.57, 141.20, 143.79, 143.84, 156.05, 169.71; HRMS (ESI) calc. for $C_{51}H_{53}NO_{10}Na$ $[M + Na]^+$ 862.3567, found 862.3566.

O-(4-*O*-Propyl)-α-D-galactopyranosyl)-*N*-dodecanoyl-L-serine undecylamide (CCL-34-S11)

Compound **CCL-34-S11** was obtained from **12α** in 43% for five steps as a white foam. R_f 0.15 (4 : 1 EtOAc–CH_2Cl_2); ^{1}H (400 MHz, $CDCl_3$) δ 0.87–0.92 (9H, m), 1.16–1.33 (32H, m), 1.46 (2H, m), 1.56–1.60 (4H, m), 2.20 (2H, t, J = 7.5 Hz), 2.51 (1H, d, J = 6.2 Hz), 2.84 (1H, bs), 3.04–3.11 (2H, m), 3.38 (1H, bs), 3.48–3.54 (1H, m), 3.63–3.88 (9H, m), 4.61 (1H, dd, J = 6.8, 12.1 Hz), 5.03 (1H, d,

J 3.4 Hz), 6.84 (1H, d, *J* = 7.5 Hz), 7.19 (1H, bs); ^{13}C (100 MHz, $CDCl_3$) δ 10.43, 14.05, 22.63, 23.35, 25.62, 26.99, 29.32, 29.61, 31.87, 36.42, 39.85, 52.31, 62.45, 68.53, 69.85, 71.17, 71.99, 75.62, 77.32, 99.48, 169.98, 174.08; HRMS (ESI) calc. for $C_{35}H_{68}N_2O_8Na$ $[M + Na]^+$ 667.4873, found 667.4868.

S-*p*-Tolyl 3-*O*-allyl-2-*O*-*para*-methoxybenzyl-4,6-*O*-benzylidene-β-D-thiogalactopyranoside (13)

A suspension of *S*-*p*-tolyl 4,6-*O*-benzylidene-β-D-thiogalactopyranoside (1 g, 2.68 mmol) and dibutyltin oxide (1 g, 4.00 mmol) in toluene (20 mL) was heated to reflux in a Dean–Stark apparatus for 4 h, after which most of the solvent was distilled off. The reaction mixture was cooled to room temperature, and the residual solvent was evaporated under reduced pressure. CsF (820 mg, 5.36 mmol), allyl bromide (0.46 ml, 5.36 mmol), tetrabutylammonium iodide (2 g, 5.36 mmol), and DMF (13 mL) were then added. The reaction mixture was heated to reflux overnight. It was then diluted with ethyl acetate, washed (sat. aq. $NaHCO_3$, brine), dried ($MgSO_4$), and concentrated. Purification by column chromatography gave the allylated product (981 mg, 2.37 mmol, 88%) as a white foam. To a solution of the allylated product and TBAI in DMF, NaH (189 mg, 4.72 mmol) was added at 0 °C. The resulting mixture was stirred for 10 min in an ice–water bath and then *p*-methoxybenzyl chloride (0.5 mL, 3.54 mmol) was added. The reaction mixture was warmed to room temperature and stirred for another 4 h until TLC analysis showed completion of the reaction. The mixture was then quenched with methanol, concentrated *in vacuo*, dissolved in EtOAc, and washed with water and brine. The organic layer was dried ($MgSO_4$), filtered, and concentrated. The resulting residue was purified by silica gel column chromatography to give **13** (853 mg, 2.05 mmol, 87%). R_f 0.25 (1 : 3 EtOAc–hexane); ^{1}H (400 MHz, $CDCl_3$) δ 2.30 (3H, s), 3.42 (1H, s), 3.52 (1H, dd, *J* = 9.2, 3.6 Hz), 3.78 (1H, dd, *J* = 9.6, 9.2 Hz), 3.79 (3H, s), 4.00 (1H, dd, *J* = 12.4, 1.6 Hz), 4.17–4.22 (3H, m), 4.37 (1H, dd, *J* = 12.4, 1.6 Hz), 4.55 (1H, d, *J* = 9.6 Hz), 4.58 (1H, d, *J* = 10.6 Hz), 4.61 (1H, d, *J* = 10.6 Hz), 5.17 (1H, dddd, *J* = 10.5, 1.7, 1.4, 1.4 Hz), 5.29 (1H, dddd, *J* = 17.2, 1.7, 1.7, 1.7 Hz), 5.52 (1H, s), 5.87–5.97 (1H, m), 6.85–6.89 (2H, m), 7.00 (2H, d, *J* = 8.0 Hz), 7.35–7.37 (5H, m), 7.47–7.49 (2H, m), δ 7.60 (2H, d, *J* = 8.4 Hz); ^{13}C (100 MHz, $CDCl_3$) δ 20.88, 54.98, 69.12, 69.44, 70.81, 73.55, 74.71, 74.91, 76.68, 77.00, 77.32, 80.94, 86.33, 100.91, 113.47, 117.03, 126.42, 127.80, 128.21, 128.67, 128.71, 129.38, 129.53, 130.57, 132.94, 134.64, 137.23, 137.76; HRMS (ESI) calc. for $C_{31}H_{34}O_6SNa$ $[M + Na]^+$ 557.1974, found 557.1981.

N-(9-Fluorenylmethoxycarbonyl)-*O*-(2-*O*-*para*-methoxybenzyl-3-*O*-allyl-4,6-*O*-benzylidene-α-D-galactopyranosyl)-L-serine allyl ester (13α)

Compound **13α** was obtained from **13** in 57% as white foam. R_f 0.13 (1 : 3 EtOAc–hexane); ^{1}H (400 MHz, $CDCl_3$) δ 3.68 (1H, s), 3.75 (3H, s), 3.78–3.86 (2H, m), 3.97 (1H, dd, *J* = 14.3, 14.3 Hz), 3.99 (1H, d, *J* = 7.4 Hz), 4.14–4.28 (6H, m), 4.30–4.45 (2H, m), 4.52 (1H, d, *J* = 11.6 Hz), 4.61 (2H, m), 4.72 (1H, d, *J* = 11.6 Hz), 4.79 (1H, d, *J* = 3.0 Hz), 5.15–5.23 (2H, m), 5.27–5.34 (2H, m), 5.51 (1H, s), 5.81–6.00 (2H, m), 6.16 (1H, NH), 6.84 (2H, d, *J* = 8.0 Hz), 7.24–7.39 (10H, m), 7.50 (2H, d, *J* = 6.8 Hz), 7.58 (2H, d, *J* = 7.4 Hz), 7.74 (2H, d, *J* = 7.7 Hz); ^{13}C (100 MHz, $CDCl_3$) δ 46.95, 54.65, 55.08, 63.28, 66.10, 67.05, 69.15, 70.32, 71.10, 73.15, 74.43, 74.85, 75.12, 100.20, 100.82, 113.66, 116.76, 118.59, 119.88, 124.90, 124.98, 126.13, 126.95, 126.98, 127.60, 127.96, 128.74, 129.40, 130.47, 131.39, 135.05, 137.65, 141.14, 143.62, 155.96, 159.15, 169.80; HRMS (ESI) calc. for $C_{45}H_{47}NO_{11}Na$ $[M + Na]^+$ 800.3047, found 800.3046.

O-(3-*O*-Allyl-α-D-galactopyranosyl)-*N*-dodecanoyl-L-serine undecylamide (CCL-34-S12)

Compound **CCL-34-S12** was obtained from **13α** in 34% for five steps as white foam. R_f 0.3 (1 : 20 MeOH–CH_2Cl_2); ^{1}H (400 MHz, $CDCl_3$) δ 0.85 (7H, m), 1.00 (1H, t, *J* = 7.2 Hz), 1.10–1.37 (37H, m), 1.37–1.70 (5H, m), 2.19 (3H, dd, *J* = 8.0, 7.2 Hz), 3.09–3.37 (4H, m), 3.52 (1H, d, *J* = 9.6 Hz), 3.62 (1H, dd, *J* = 10.4, 9.2 Hz), 3.72–3.95 (5H, m), 3.96–4.26 (5H, m), 4.56–4.59 (1H, m), 5.11 (1H, d, *J* = 3.7 Hz), 5.18 (1H, dd, *J* = 10.4, 1.7 Hz), 5.27 (1H, dd, *J* = 17.6, 1.7 Hz), 5.91 (1H, dddd, *J* = 5.2, 5.2, 5.6, 5.6 Hz), 6.90 (1H), 7.55 (1H); ^{13}C (100 MHz, $CDCl_3$) δ 14.10, 22.67, 24.22, 25.60, 26.98, 29.35, 29.49, 29.52, 29.62, 31.90, 36.54, 39.83, 51.73, 62.94, 68.00, 68.27, 70.39, 70.86, 99.38, 117.62, 134.55, 169.64, 173.81; HRMS (ESI) calc. for $C_{35}H_{66}N_2O_8Na$ $[M + Na]^+$ 665.4717, found 665.4720.

N-(9-Fluorenylmethoxycarbonyl)-*O*-(2,3,4-tri-*O*-benzyl-α-L-rhamnopyranosyl)-L-serine allyl ester (14α)

Compound **14α** was obtained from **14** in 56% yield for 2 steps as white foam. R_f 0.31 (1 : 2 EtOAc–hexane); ^{1}H (400 MHz, $CDCl_3$) δ 1.07 (3H, d, *J* = 6.5), 3.56–3.59 (2H, m), 3.74 (1H, dd, *J* = 6.4, 12.9), 3.83 (1H, dd, *J* = 2.6, 10.1), 4.01 (1H, dd, *J* = 3.6, 10.1), 4.20–4.23 (2H, m), 4.35 (1H, dd, *J* = 7.2, 10.5), 4.47 (1H, dd, *J* = 6.9, 10.5), 4.53–4.58 (1H, m), 4.61–4.64 (4H, m), 4.67 (1H, d, *J* = 3.6), 4.72 (1H, d, *J* = 11.8), 4.79 (1H, d, *J* = 12.1), 4.83 (1H, d, *J* = 11.8), 4.96 (1H, d, *J* = 11.6), 5.18 (1H, dd, *J* = 1.2, 10.3), 5.29 (1H, dd, *J* = 1.2, 17.2), 5.86 (1H, ddd, *J* = 9.0, 10.3, 17.2), 6.18 (1H, d, *J* = 9.0), 7.19–7.40 (19H, m), 7.59 (2H, t, *J* = 7.0), 7.72 (2H, d, *J* = 7.6); ^{13}C (100 MHz, $CDCl_3$) δ 16.30, 46.85, 54.28, 65.63, 66.57, 66.76, 68.80, 72.75, 73.04, 74.55, 76.01, 78.63, 98.82, 118.16, 119.67, 124.74, 124.81, 126.77, 127.25, 127.33, 127.39, 127.58, 127.72, 127.91, 128.05, 128.09, 131.36, 138.22, 138.45, 140.95, 143.44, 143.66, 156.01, 169.59; HRMS (ESI) calc. for $C_{48}H_{49}NO_9Na$ $[M + Na]^+$ 806.3305, found 806.3300.

O-α-L-Rhamnopyranosyl-*N*-dodecanoyl-L-serine undecylamide (CCL-34-S13)

Compound **CCL-34-S13** was obtained from **14α** in 57% yield for 5 steps as white foam. R_f 0.38 (1 : 9 MeOH–CH_2Cl_2); ^{1}H (400 MHz, MeOD) δ 0.90 (6H, t, *J* = 6.7), 1.19 (3H, d, *J* = 6.5), 1.28–1.36 (32H, m), 1.45–1.52 (2H, m), 1.61–1.67 (2H, m), 2.31 (2H, t, *J* = 7.5), 3.16–3.21 (2H, m), 3.48 (1H, dd, *J* = 3.3, 9.7), 3.62 (1H, d, *J* = 3.2), 3.68 (1H, dd, *J* = 3.2, 10.0), 3.77 (1H, dd, *J* = 3.7, 10.0), 3.80–3.85 (1H, m), 4.11 (1H, dd, *J* = 3.1, 9.7), 4.51–4.55 (1H, m), 4.74 (1H, d, *J* = 3.7), 7.88 (1H, t, *J* = 5.5), 8.46 (1H, d, *J* = 8.0); ^{13}C (100 MHz, $CDCl_3$/MeOD) δ 13.07, 15.12, 21.85, 24.93, 26.18, 28.56, 28.60, 28.68, 28.85, 31.13, 35.15, 38.83, 38.96, 52.31, 65.71, 67.10, 67.96, 69.70, 71.39, 98.15, 169.91, 173.91; HRMS (ESI) calc. for $C_{32}H_{62}N_2O_7Na$ $[M + Na]^+$ 609.4455, found 609.4462.

O-β-D-Galactopyranosyl-*N*-dodecanoyl-L-serine undecylamide (β-CCL-34)

Compound **β-CCL-34** was obtained from **5** in 43% yield for 5 steps as white foam. R_f 0.25 (1 : 9 MeOH–CH_2Cl_2); ^{1}H (400 MHz, $CDCl_3$/MeOD) δ 0.62 (3H, t, J = 6.6 Hz), 0.62 (3H, t, J = 7.0 Hz), 0.95–1.09 (32H, br s), 1.21–1.29 (2H, m), 1.32–1.41 (2H, m), 2.00 (2H, t, J = 7.6 Hz), 2.93 (2H, dd, J = 7.3, 13.4 Hz), 3.21–3.32 (3H, m), 3.44 (1H, dd, J = 5.2, 10.3 Hz), 3.47 (1H, dd, J = 4.7, 13.2 Hz), 3.54–3.63 (2H, m), 3.84 (1H, dd, J = 5.2, 10.3 Hz), 3.97 (1H, d, J = 7.3 Hz), 4.34 (1H, t, J = 5.2 Hz); ^{13}C (100 MHz, $CDCl_3$/MeOD) δ 13.29, 22.08, 25.12, 26.35, 28.61, 28.77, 28.84, 28.97, 29.06, 31.35, 35.56, 39.15, 52.68, 60.97, 68.47, 69.00, 70.65, 72.89, 74.80, 103.40, 169.91, 174.29; HRMS (ESI) calc. for $C_{32}H_{62}N_2O_8Na$ $[M + Na]^+$ 625.4404, found 625.4401.

O-α-D-Glucopyranosyl-*N*-dodecanoyl-L-serine undecylamide (CCL-34-S14)

Compound **CCL-34-S14** was obtained from **20** in 55% yield for 5 steps as white foam. R_f 0.23 (1 : 9 MeOH–CH_2Cl_2); ^{1}H (400 MHz, MeOD) δ 0.90 (6H, t, J = 6.7, 7.0), 1.29 (32H, br s), 1.48–1.55 (2H, m), 1.58–1.65 (2H, m), 2.27 (2H, t, J = 7.5 Hz), 3.14–3.25 (2H, m), 3.29 (1H, dd, J = 9.7 Hz), 3.42 (1H, dd, J = 3.7, 9.7 Hz), 3.53 (1H, ddd, J = 2.2, 5.5, 9.7 Hz), 3.60 (1H, dd, J = 9.7, 9.7 Hz), 3.66 (1H, dd, J = 5.5, 11.8 Hz), 3.74 (1H, dd, J = 6.0, 10.4 Hz), 3.81 (1H, dd, J = 2.2, 11.8 Hz), 3.84 (1H, dd, J = 6.0, 10.4 Hz), 4.53 (1H, dd, J = 6.0, 6.0 Hz), 4.83 (1H, d, J = 3.7 Hz); ^{13}C (100 MHz, MeOD) δ 14.48, 23.73, 26.82, 28.02, 30.37, 30.48, 30.66, 30.77, 33.07, 36.84, 40.60, 54.64, 62.56, 68.89, 71.54, 73.35, 74.00, 74.97, 100.81, 171.98, 176.22; HRMS (ESI) calc. for $C_{32}H_{63}N_2O_8$[M + H]$^+$ 603.4584, found 603.4563.

O-α-D-Mannopyranosyl-*N*-dodecanoyl-L-serine undecylamide (CCL-34-S15)

Compound **CCL-34-S15** was obtained from **22** in 51% yield for four steps as white solid. R_f 0.25 (1 : 9 MeOH–CH_2Cl_2); ^{1}H (400 MHz, $CDCl_3$/MeOD) δ 0.61 (6H, t, J = 6.7, 7.0), 0.96–1.15 (32H, m, CH_2), 1.19–1.26 (2H, m), 1.31–1.37 (2H, m), 1.98 (2H, t, J = 7.6), 2.85–2.98 (2H, m), 3.21–3.25 (1H, m), 3.37–3.58 (7H, m), 4.31 (1H, dd, J = 5.7, 5.7), 4.51 (1H, d, J = 1.1); ^{13}C (100 MHz, $CDCl_3$/MeOD) δ 13.34, 22.11,25.20, 26.41, 28.81, 28.87, 29.01, 29.09, 31.38, 35.59, 39.15, 52.48, 61.05, 66.63, 67.04, 70.03, 70.78, 72.61, 100.16, 169.72, 174.24; HRMS (ESI) calc. for $C_{32}H_{62}N_2O_8Na$ $[M + Na]^+$ 625.4404, found 625.4401.

N-(9-Fluorenylmethoxycarbonyl)-*N*-(2,2,2-trichloroethyloxycarbonyl-2-amino-2-deoxy)-*O*-(3,4,6-tri-*O*-acetoxy-β-D-glucopyranosyl)-L-serine allyl ester (24)

Compound **23** (2.9 g, 5.55 mmol) was dissolved in HBr/HOAc (14.5 ml) at 0 °C and the resulting solution was stirred for 3 h in an ice–water bath. The reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$ and extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was dried under vacuum for 10 min and then redissolved in CH_2Cl_2 (5.0 mL). The obtained solution was slowly added to a cooled solution (–4 °C) of Fmoc-Ser-OAll (1.36 g, 3.70 mmol), AgOTf (1.56 g, 6.08 mmol), and activated 4 Å MS (2.18 g) in CH_2Cl_2 (10 mL). After being stirred for 30 min at –40 °C, the reaction mixture was warmed to room temperature and stirred for another 12 h. It was then filtered over a pad of Celite and the filtrate was concentrated. The obtained residue was purified by column chromatography to give the pure product (1.3 g, 86%). R_f 0.25 (1 : 3 EtOAc–hexane); ^{1}H (400 MHz, $CDCl_3$/MeOD) δ 1.98 (3H, s), 2.00 (3H, s), 2.04 (3H, s), 3.60 (1H, dd, J = 8.7, 10.2 Hz), 3.73 (1H, m), 3.91 (1H, dd, J = 3.6, 10.3 Hz), 4.09 (1H, dd, J = 2.0, 12.4 Hz), 4.18–4.33 (4H, m), 4.44 (1H, dd, J = 5.9, 9.3 Hz), 4.49 (1H, t, J = 3.6 Hz), 4.53 (1H, d, J = 12.1 Hz), 4.58–4.71 (3H, m), 4.75 (1H, d, J = 12.1 Hz), 4.98 (1H, t, J = 10.2 Hz), 5.21 (1H, dd, J = 1.1, 10.5 Hz), 5.23 (1H, t, J = 10.2 Hz), 5.32 (1H, dd, J = 1.1, 17.2 Hz), 5.86 (1H, ddd, J = 8.0, 10.5, 17.2 Hz). 7.29–7.33 (2H, m), 7.38 (2H, t, J = 7.4 Hz), 7.63 (2H, t, J = 7.0 Hz), 7.75 (2H, d, J = 7.5 Hz); ^{13}C (100 MHz, $CDCl_3$) δ 13.76, 20.16, 20.24, 20.59, 29.21, 46.62, 53.75, 55.38, 60.03, 61.67, 65.79, 66.96, 68.35, 68.49, 71.31, 71.66, 73.89, 95.19, 100.06, 118.13, 119.66, 124.74, 124.90, 126.77, 127.41, 131.13, 140.83, 143.19, 143.49, 154.10, 155.89, 169.03, 169.10, 170.11, 170.25; HRMS (ESI) calc. for $C_{36}H_{39}N_2O_{14}NaCl_3$ $[M + Na]^+$ 851.1365, found 851.1374.

N-(2,2,2-Trichloroethyloxycarbonyl-2-amino-2-deoxy)-*O*-(3,4,6-tri-*O*-acetoxy-β-D-glucopyranosyl)-*N*-dodecanoyl-L-serine undecylamide (25)

R_f 0.28 (1 : 3 EtOAc–CH_2Cl_2); ^{1}H (400 MHz, $CDCl_3$/MeOD, mixture of two conformation isomers) δ 0.85 (6H, t, J = 6.7, 7.0 Hz), 1.18–1.35 (32H, m), 1.46–1.50 (2H, m), 1.56–1.60 (2H, m), 1.97 and 1.98 (3H, s), 2.00 and 2.01 (3H, s), 2.06 and 2.07 (3H, s), 2.22 (2H, t, J = 7.4 Hz), 3.07–3.25 (2H, m), 3.62 and 3.66 (1H, dd, J = 8.4, 10.5 and 8.4, 10.5 Hz), 3.70–3.82 (2H, m), 3.85 and 3.89 (1H, dd, J = 5.5, 10.1 and 6.0, 10.6 Hz), 4.10 and 4.13 (1H, dd, J = 2.2, 14.2 and 2.0, 14.2 Hz), 4.24–4.34 (1H, m), 4.45 and 4.53 (1H, t, J = 5.5 and 6.0 Hz), 4.54 (1H, d, J = 8.4 Hz), 4.57 and 4.58 (1H, d, J = 12.12 and 12.12 Hz), 4.82 and 4.84 (1H, d, J = 12.12 and 12.04 Hz), 4.98 and 4.99 (1H, t, J = 9.8 and 9.8 Hz), 5.18 and 5.22 (1H, dd, J = 9.8, 10.5 and 9.8, 10.5 Hz); ^{13}C (100 MHz, $CDCl_3$/MeOD) δ 14.50, 20.92, 21.03, 23.31, 26.32, 27.59, 29.85, 30.01, 30.06, 30.20, 30.29, 32.59, 36.76, 53.32, 53.51, 56.55, 62.73, 69.51, 69.73, 70.16, 72.40, 72.54, 73.10, 73.23, 75.06, 96.35, 96.44, 102.03, 155.93, 156.31, 170.65, 170.73, 171.36, 171.88, 175.38; HRMS (ESI) calc. for $C_{41}H_{70}N_3O_{12}NaCl_3$ $[M + Na]^+$ 924.3923, found 924.3916.

N-(2-Amino-2-deoxy)-*O*-(3,4,6-tri-*O*-acetoxy-β-D-glucopyranosyl)-*N*-dodecanoyl-L-serine undecylamide (26)

A solution of **25** (240 mg, 0.27 mmol) and Zn (0.7 g, 10.70 mmol) in tetrahydrofuran (4.0 mL) was stirred for 4 h at room temperature and filtered over Celite. Tetrahydrofuran was removed with a water pump and the resulting residue was purified by column chromatography to the yield the desired product (186 mg, 95%). R_f 0.06 (EtOAc 100%); ^{1}H (400 MHz, $CDCl_3$/MeOD, mixture of two conformation isomer) δ 0.89 (6H, t, J = 6.6, 7.0 Hz), 1.21–1.37 (32H, m), 1.46–1.53 (2H, m), 1.60–1.63 (2H, m), 1.98 and 2.00 (3H, s), 2.05 (3H, s), 2.06 (3H, s), 2.26–2.30 (2H, m), 2.87 (1H, dd, J = 8.3, 9.7 Hz), 3.18–3.21 (2H, m), 3.80–3.84 (1H, m), 3.82 and 3.89 (1H, dd, J = 5.0, 10.3 and 5.4, 10.3 Hz), 4.01 and 4.08 (1H, dd, J = 5.2, 10.3 and 5.0, 10.3 Hz), 4.09–4.13 (1H, m),

4.30 and 4.31 (1H, dd, J = 3.9, 8.4 and 4.5, 12.4 Hz), 4.49 and 4.54 (1H, d, J = 8.1 and 8.3 Hz), 4.59 (1H, t, J = 5.2 Hz), 4.93 and 4.95 (1H, t, J = 9.7 and 9.6 Hz), 5.10 and 5.12 (1H, dd, J = 9.7, 11.4 and 9.6, 10.1 Hz); ^{13}C (100 MHz, $CDCl_3$/MeOD) δ 14.75, 21.04, 21.06, 23.57, 26.53, 27.71, 30.06, 30.16, 30.24, 30.37, 30.44, 32.74, 36.84, 40.43, 53.00, 54.06, 56.66, 57.94, 62.98, 63.39, 69.86, 70.14, 70.26, 70.68, 71.88, 71.94, 72.75, 72.84, 73.14, 73.83, 74.07, 75.42, 103.68, 104.05, 170.97, 171.05, 171.22, 171.58, 172.04, 172.14, 173.17, 175.76; HRMS (ESI) calc. for $C_{38}H_{69}N_3O_{10}Na$ $[M + Na]^+$ 750.4881, found 750.4882.

N-(2-Acetoxy-2-amino-2-deoxy)-*O*-(3,4,6-tri-*O*-acetoxy-β-D-glucopyranosyl)-*N*-dodecanoyl-L-serine undecylamide (27)

Acetic acid (1.0 mL, 17.46 mmol) and acetic anhydride (2 mL, 21.20 mmol) were added at room temperature to a solution of **25** (91.5 mg, 0.10 mmol) and Zn (0.26 g, 3.98 mmol) in tetrahydrofuran (3.0 ml). The reaction mixture was stirred for 12 h and then filtered over Celite. Tetrahydrofuran, acetic acid, and acetic anhydride were then removed by reduced pressure. The resulting residue was purified by column chromatography to give pure **27** (55.6 mg, 72%). R_f 0.55 (1 : 9 MeOH–CH_2Cl_2); ^{1}H (400 MHz, $CDCl_3$/MeOD, mixture of two conformation isomer) δ 0.86 (6H, t, J = 6.7, 7.0 Hz), 1.19–1.36 (32H, m, CH_2), 1.47–1.51 (2H, m), 1.57–1.61 (2H, m), 1.89 and 1.90 (3H, s), 1.98 and 1.99 (3H, s), 2.01 (3H, s), 2.06 and 2.07 (3H, s), 2.17–2.30 (2H, m), 3.01–3.28 (2H, m), 3.70– 3.75 (4H, m), 4.13 (1H, dd, J = 2.2, 9.8 Hz), 4.30 (1H, dd, J = 6.1, 12.4 Hz), 4.50 and 4.52 (1H, t, J = 5.8 and 6.1 Hz), 4.63 and 4.67 (1H, d, J = 8.5 and 8.5 Hz), 4.99 and 4.99 (1H, t, J = 9.4 and 9.4 Hz), 5.14 and 5.17 (1H, dd, J = 9.4, 10.5 and 9.4, 10.4 Hz); ^{13}C (100 MHz, $CDCl_3$/MeOD) δ 29.92, 30.06, 30.12, 30.26, 30.34, 32.65, 36.78, 40.38, 40.47, 40.60, 48.56, 48.78, 48.99, 49.20, 49.41, 49.84, 53.63, 53.70, 54.49, 54.70, 62.85, 69.56, 69.87, 72.50, 72.61, 3.35, 73.56, 78.08, 78.71, 78.73, 101.98, 102.10, 170.75, 170.84, 171.01, 171.54, 171.89, 171.94, 172.80, 173.17, 175.44, 175.54; HRMS (APCI) calc. for $C_{40}H_{71}N_3O_{11}Na$ $[M + Na]^+$ 792.4986, found 792.4992.

N-(2-Amino-2-deoxy)-*O*-β-D-glucopyranosyl-*N*-dodecanoyl-L-serine undecylamide (CCL-34-S16)

NaOMe (3.0 mg, 0.06 mmol) was added at room temperature to a solution of **26** (105 mg, 0.14 mmol) in MeOH (3.0 mL) and CH_2Cl_2 (1.0 mL). The reaction mixture was stirred for 30 min, neutralized with IR-120, filtered, concentrated, and purified by column chromatography to give pure **CCL-34-S16** (48.6 mg, 60%). R_f 0.38 (1 : 6 MeOH–CH_2Cl_2); ^{1}H (400 MHz, $CDCl_3$/MeOD) δ 0.88 (3H, t, J = 7.0 Hz), 0.88 (3H, t, J = 7.0 Hz), 1.21–1.40 (32H, m), 1.46–1.55 (2H, m), 1.56–1.67 (2H, m), 2.26 (2H, t, J = 7.4 Hz), 2.56 (1H, t, J = 8.4 Hz), 3.18 (2H, t, J = 6.4 Hz), 3.21–3.28 (3H, m), 3.67 (1H, dd, J = 5.3, 11.7 Hz), 3.75 (1H, dd, J = 5.2, 10.3 Hz), 3.88 (1H, d, J = 11.7 Hz), 4.07 (1H, dd, J = 5.5, 10.3 Hz), 4.25 (1H, d, J = 8.4 Hz), 4.56 (1H, t, J = 5.3 Hz); ^{13}C (100 MHz, $CDCl_3$/MeOD) δ 14.60, 23.66, 26.77, 27.90, 30.27, 30.39, 30.47, 30.59, 30.67, 32.97, 36.92, 40.59, 54.70, 54.88, 57.97, 62.55, 70.21, 70.56, 71.53, 71.69, 76.94, 78.00, 103.79, 104.24, 171.70, 176.22; HRMS (ESI) calc. for $C_{32}H_{64}N_3O_7Na$ $[M + H]^+$ 602.4744, found 602.4736.

N-(2-Dodecanoyl-2-amino-2-deoxy)-*O*-β-D-glucopyranosyl-*N*-dodecanoyl-L-serine undecylamide (CCL-34-S17)

NEt_3 (0.02 mL, 0.16 mmol) was added at room temperature to a solution of **26** (56 mg, 0.08 mmol), lauric acid (31 mg, 0.16 mmol), EDCI (29 mg, 0.16 mmol), and HOBt (21 mg, 0.16 mmol) in CH_2Cl_2 (0.8 mL). The reaction mixture was stirred for 12 h. After removal of the solvent, the resulting residue was directly purified by column chromatography to give a product (38 mg, 54%) that was then hydrolyzed by NaOMe (0.7 mg, 0.013 mmol) in MeOH (0.4 mL) and CH_2Cl_2 (0.1 mL) at room temperature for 30 min. The mixture was neutralized with IR-120, filtered, and concentrated. The resulting residue was purified by column chromatography to give **CCL-34-S17** (19.6 mg, 60%). R_f 0.15 (1 : 15 MeOH–CH_2Cl_2); ^{1}H (400 MHz, $CDCl_3$/MeOD, mixture of two conformation isomer) δ 0.86 (9H, t, J = 6.7, 7.0 Hz), 1.19–1.38 (48H, m), 1.48 (2H, bs), 1.60 (4H, bs), 2.18–2.27 (4H, m), 3.06–3.19 (2H, m), 3.22–3.28 (2H, m), 3.36–3.42 (1H, m), 3.59–3.69 (2H, m), 3.69–3.73 (1H, m), 3.81–3.98 (2H, m), 4.32 and 4.36 (1H, d, J = 8.4 and 8.3 Hz), 4.47–4.51 (1H, m); ^{13}C (100 MHz, $CDCl_3$/MeOD) δ 14.63, 23.72, 26.79, 26.90, 26.98, 27.97, 28.03, 30.26, 30.31, 30.40, 30.45, 30.55, 30.65, 30.67, 30.70, 30.74, 30.76, 30.80, 33.04, 36.98, 37.00, 37.54, 40.67, 40.74, 54.66, 54.74, 56.71, 56.82, 69.52, 69.81, 72.01, 72.17, 75.82, 77.79, 78.68, 79.01, 79.33, 102.55, 103.01, 171.83, 171.97, 176.03, 176.22, 177.06, 177.10; HRMS (ESI) calc. for $C_{44}H_{85}N_3O_8Na$ $[M + Na]^+$ 806.6234, found 806.6238.

N-(2-Acetoxy-2-amino-2-deoxy)-*O*-β-D-glucopyranosyl-*N*-dodecanoyl-L-serine undecylamide (CCL-34-S18)

NaOMe (1.2 mg, 0.02 mmol) was added at room temperature to a solution of **27** (55 mg, 0.07 mmol) in MeOH (0.4 mL) and CH_2Cl_2 (0.1 mL). The reaction mixture was stirred for 30 min, neutralized with IR-120, filtered, and concentrated. The resulting residue was purified by column chromatography to give **CCL-34-S18** (37.7 mg, 82%). R_f 0.13 (1 : 9 MeOH–CH_2Cl_2); ^{1}H (400 MHz, $CDCl_3$/MeOD, mixture of two conformation isomer) δ 0.87 (6H, t, J = 6.7, 7.0 Hz), 1.17–1.45 (32H, m), 1.45–1.49 (2H, m), 1.58–1.62 (2H, m), 1.97 and 1.99 (3H, s), 2.21–2.25 (2H, m), 3.16 (2H, t, J = 7.2 Hz), 3.26–3.29 (2H, m), 3.39–3.44 (1H, m), 3.59–3.68 (2H, m), 3.73 (1H, dd, J = 5.9, 10.3 Hz), 3.83–3.89 (1H, m), 3.94 (1H, dd, J = 5.2 and 10.3 Hz), 4.31 and 4.37 (1H, d, J = 8.3 and 8.3 Hz), 4.48–4.51 (1H, m); ^{13}C (100 MHz, $CDCl_3$/MeOD) δ 14.45, 23.41, 26.48, 27.68, 29.95, 30.11, 30.19, 30.31, 30.39, 32.70, 36.83, 40.45, 54.17, 56.75, 62.53, 69.25, 71.79, 75.58, 77.9, 102.06, 102.60, 171.46, 173.79, 175.67; HRMS (ESI) calc. for $C_{34}H_{65}N_3O_8Na$ $[M + Na]^+$ 666.4669, found 806.4674.

N-Dodecanoyl-L-serine undecylamide (CCL-34-S19)

CCL-34-S19 was obtained from commercial Fmoc-Ser-OH by coupling with undecylamine, deprotection of the Fmoc group, and coupling with lauric acid in 66% yield over 3 steps. ^{1}H (400 MHz, $CDCl_3$) δ 0.85 (3H, t, J = 6.7 Hz), 0.85 (3H, t, J = 7.0 Hz), 1.19–1.31 (H, br s), 1.42–1.49 (2H, m), 1.54–1.65 (2H, m), 2.22 (1H, t, J = 7.5), 2.23 (1H, t, J = 7.5), 3.19 (1H, td, J = 7.1), 3.20 (1H, td, J = 5.6, 7.1), 3.56 (1H, dd, J = 4.6, 11.5), 4.09 (1H, dd, J = 3.0, J = 11.5), 4.34–4.39 (1H, ddd, J = 3.0, 4.6, 7.1), 6.69 (1H, d, J = 7.1), 6.92 (1H, t, J = 5.6); ^{13}C (100 MHz, $CDCl_3$) δ 14.05, 22.63, 25.59,

26.84, 29.20, 29.30, 29.46, 29.51, 29.57, 31.86, 36.48, 39.53, 53.76, 62.90, 170.89, 174.33. HRMS (ESI) calc. for $C_{26}H_{53}N_2O_3[M + H]^+$441.4056, found 441.4051.

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