# Sulfated Galactocerebrosides as Potential Antiinflammatory Agents

Anne Marinier,*,‡ Alain Martel,‡ Jacques Banville,‡ Carol Bachand,‡ Roger Remillard,‡ Philippe Lapointe,‡ Brigitte Turmel,‡ Marcel Menard,‡ William E. Harte, Jr.,† J. J. Kim Wright,† Gordon Todderud,▽ Kenneth M. Tramposch,▽ Jürgen Bajorath,§ Diane Hollenbaugh,§ and Alejandro Aruffo§

*Departments of Chemistry, Dermatological Disease, and Inflammatory Disease, Bristol-Myers Squibb Pharmaceutical Research Institute, Candiac, Quebec, Canada, Wallingford, Connecticut, Buffalo, New York, and Seattle, Washington*

*Received October 7, 1996*⊗

Native sulfatides, as well as many sulfated glycolipids, have been shown to avidly bind to the selectin receptors. *In vivo*, native sulfatides significantly block activity in selectin-dependent inflammatory responses. The fact that nonsulfated galactocerebrosides did not inhibit selectin-mediated adhesion identified a critical role for the anionic sulfate residue. We therefore initiated a program to evaluate the activity of position isomers. This study showed a binding selectivity for the positions 2 and 3 of the sulfate group on the carbohydrate ring as well as enhanced activity for the disulfated analogs. Furthermore, it was discovered that the attachment of lipophilic substituents on the carbohydrate ring was tolerated, consistent with the presence of a lipophilic pocket in the binding cavity. This resulted in compounds with a 6-fold increased potency.

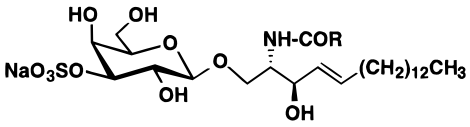
## Introduction

The adhesion of leukocytes to endothelial cells constitutes an early and essential step in inflammatory cell extravasation. One class of molecules that mediates these interactions is the selectin family which includes three known members: E-, P-, and L-selectins.[1a] These receptors are type I membrane proteins and have a homologous extracellular domain structure, including an N-terminal lectin domain and an epidermal growth factor-related domain, and a variable number of complement regulatory repeat elements. P-Selectin (CD-62), whose expression is upregulated by thrombin and other mediators, is found on the cell surface of platelets and endothelial cells. E-Selectin is expressed by the vascular endothelial cells after cytokine activation associated with inflammation. L-Selectin is expressed on most leukocytes.[1]

Extravasation of leukocytes into sites of inflammation is in part dependent on the initial interaction with endothelial P-selectin. This is supported by the finding of *in vivo* antiinflammatory activity of P-selectin-blocking antibodies.[2] P-Selectin is thus a novel antiinflammatory target, and small molecular weight antagonists may have useful antiinflammatory activity.

A terminal moiety composed of sialyl Lewis x ($SLe^x$) on the surface of leukocytes was recognized as one ligand involved in selectin-dependent cell adhesion.[3] The myeloid cell line HL-60, which expresses the $SLe^x$ antigen on its surface, was found to adhere strongly to both P- and E-selectins. A second class of selectin ligand, the sulfatides **1**, was also identified.[4] These native sulfated galactocerebrosides were found to strongly bind to P- and L-selectin IgG chimeras. In addition sulfatides were shown to block the binding of HL-60 cells to P- and E-selectin Ig fusion proteins. Sulfatides were recently shown to have antiinflammatory activity *in vivo*.[5] After intravenous administration sulfatides caused a marked reduction in the vascular permeability and cell infiltration in the rat dermal reverse passive Arthus reaction. They also demonstrated significant protective effects in neutrophil- and selectin-dependent models of lung injury in rats. In addition, they were recently reported as suppressors of the $CCl_4$-induced liver inflammation in rats by inhibiting the attachment of L-selectin-expressing lymphocytes to their native sugar ligands.

**Chart 1.** Sulfatide Structure[a]




**1**

[a] **a**, R = $(CH_2)_{13}CH{=}CH(CH_2)_7CH_3$ (nervonic); **b**, R = $CHOH(CH_2)_{12}CH{=}CH(CH_2)_7CH_3$ (α-hydroxynervonic); **c**, R = $(CH_2)_{22}CH_3$ (lignoceric); **d**, R = $(CHOH(CH_2)_{21}CH_3$ (α-hydroxylignoceric); **e**, R = $(CH_2)_{14}CH_3$ (palmitic).

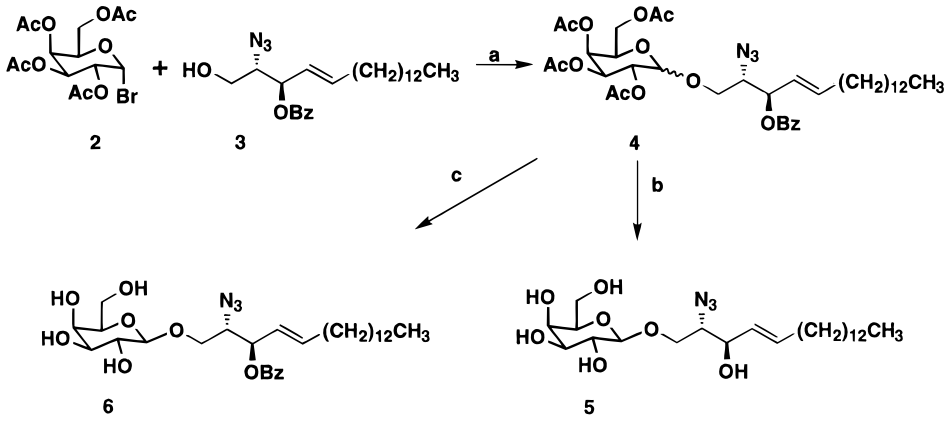
The sulfatides are a family of sulfated galactocerebrosides that differ only in the composition of the fatty acid residue that acylates the amino group of the sphingosine (Chart 1, **1**). In sulfatides prepared from bovine brain, the fatty acid component consists mainly of nervonic and α-hydroxynervonic acids with a smaller percentage of the corresponding saturated α-hydroxylated and non-hydroxylated lignoceric acids.

Molecular models of E-selectin[6] and P-selectin[7] have been constructed based on the X-ray structure of the rat mannose-binding protein (MBP), a type C-lectin with homology to the selectins in core regions and the lectin domain. A shallow depression, close to the calcium ion and solvent accessible, was found after examination of the models. Site-specific mutagenesis of the residues located in this groove showed the importance of the region for the binding of HL-60 cells. In P-selectin, critical residues within this groove include Lys 113, Tyr 48, and Tyr 94. These residues are conserved in E- and L-selectins. The recently published crystal structure of

* To whom correspondence should be addressed: Bristol-Myers Squibb Pharmaceutical Research Institute, 100 Boul. de l'Industrie, Candiac, Quebec, Canada, J5R 1J1.
‡ Department of Chemistry, Quebec.
† Department of Chemistry, CT.
▽ Department of Dermatological Disease, NY.
§ Department of Inflammatory Disease, WA.
⊗ Abstract published in *Advance ACS Abstracts,* August 15, 1997.

S0022-2623(96)00696-6 CCC: $14.00 

**Scheme 1**[a]




[a] (a) $Hg(CN)_2/CH_3NO_2$/80−85 °C; (b) MeONa/MeOH/rt; (c) MeONa/MeOH/−50 °C.

the lectin and EGF domains of E-selectin has corroborated these previous models.[8]

Mutagenesis studies using sulfatides as the binding entity to P-selectin[7b,9] revealed that sulfatides and the cellular ligand on HL-60 cells bind to an overlapping but not identical set of residues in P-selectin. Lys 113 remains critical for binding of P-selectin to both sulfatides and the cellular ligand. In contrast, Tyr 94 and Tyr 48 are not crucial for binding to sulfatides, while Lys 111, which was not critical for binding to myeloid cells, is as important as Lys 113 for binding to sulfatides. In a model of sulfatides binding to P-selectin,[9] the negatively charged group in sulfatides should make an ionic interaction with Lys 113 and/or Lys 111.

The relative chemical simplicity of the sulfatides coupled to their antiinflammatory activity prompted us to initiate a synthetic program aimed at further understanding of the key elements required for biological activity and the augmentation of this activity. Careful examination of the putative binding cavity revealed a lipophilic pocket delimitated by the side chains of Arg 85 and Lys 84. Attachment of nonpolar substituents at specific positions on the carbohydrate ring should provide additional lipophilic contacts with the receptor that could result in potency gain. Furthermore, the presence of two positively charged residues in the binding cavity (Lys 113 and Lys 111) encouraged the preparation of polysulfated derivatives that could make additional interactions with these residues. Here we report some preliminary data on molecular modification of sulfatides and the effect on the ability to bind to P-selectin. Specifically we determine the optimum position for sulfation and the effect of disulfation. We also explore the incorporation of lipophilic substituents on the galactose ring and their issue on the potency of the compounds.

## Chemistry

The pure $\beta$-anomer **4** was obtained from *O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)trichloroacetimidate and **3** using Schmidt's methodology.[10,11] Alternatively, glycosidation of D-*erythro*-azidosphingosine[12] (**3**) with tetra-*O*-acetyl-α-D-galactosyl bromide[13] (**2**) under Koenigs−Knorr conditions[14] catalyzed with mercuric cyanide was also performed and gave a mixture of $\beta$- and α-anomeric glycoside **4** in 76% and 9.5% yields, respectively (Scheme 1). The two anomers could be conveniently separated at this stage.

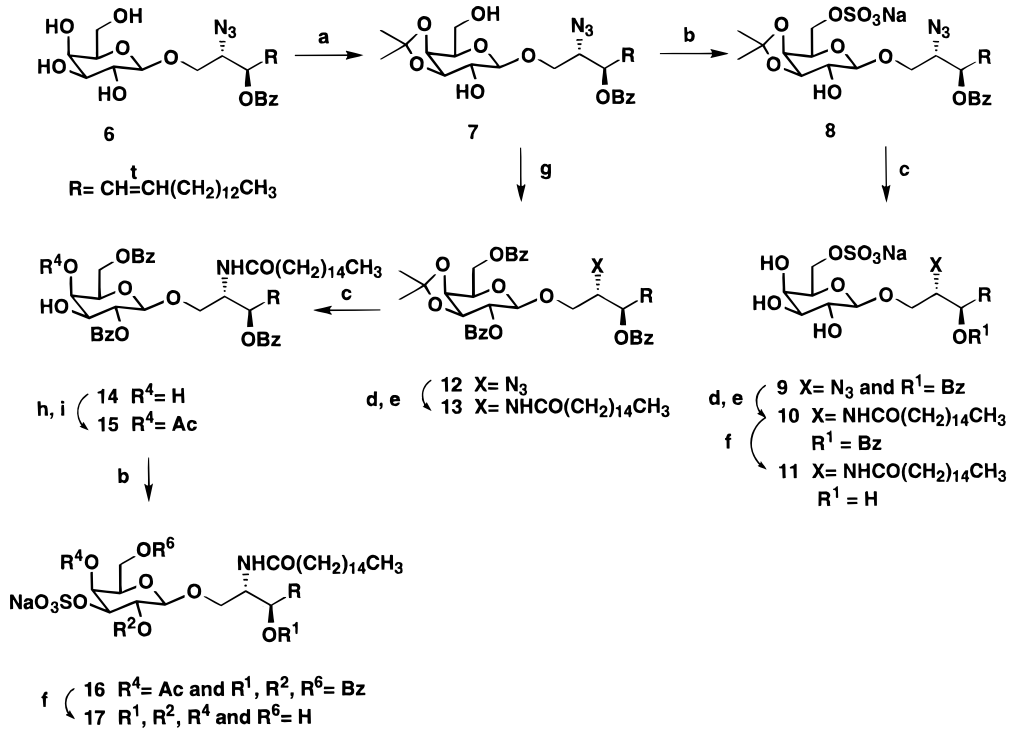
**Monosulfated Analogs.** Starting with the $\beta$-glycoside intermediate **5** or **6** standard carbohydrate protection−deprotection strategies were used for the preparation of the 2-, 3-, 4-, and 6-monosulfated analogs as shown in Schemes 2 and 3. Hence, protection of compound **6** with 2,2-dimethoxypropane gave the corresponding 3,4-*O*-isopropylidene derivative **7** which was used to synthesize the 3- and 6-monosulfated analogs. Selective monosulfation at the primary hydroxyl group followed by removal of the 3,4-*O*-isopropylidene protecting group produced azido triol **9** which was then reduced and acylated as described by Schmidt et al.[12] to give compound **10**. The 6-monosulfated compound **11** was obtained after a final debenzoylation. On the other hand, complete benzoylation at positions 2 and 6 of the 3,4-*O*-isopropylidene **7** followed by attachment of the palmitoyl side chain on the reduced derivative afforded the fully protected intermediate **13**. This compound was then hydrolyzed to give the corresponding 3,4-diol **14**. Introduction of an acetate in the axial position 4 was accomplished as described by Lemieux,[15] and the free 3-hydroxyl group of compound **15** was then sulfated. Basic hydrolysis gave the 3-sulfated galactocerebroside **17**.

The coupling of the palmitoic acid moiety could also be achieved at the beginning of the synthetic sequence as illustrated for the preparation of the 2-sulfated analog **23** in Scheme 3. Thus, unprotected glycoside **6** was reduced and acylated, and the 3 and 4 positions of the resulting galactocerebroside **18** were protected as an isopropylene ketal. The primary hydroxyl group at position 6 of diol **19** was then selectively blocked by treatment with pivaloyl chloride. Sulfation of the resulting alcohol **20** followed by protecting group cleavage gave the 2-sulfated galactocerebroside **23**.

Finally, from the key intermediate **5**, the 4 and 6 positions on the carbohydrate were protected by formation of the benzylidene acetal **24**. Complete benzoylation followed by acidic treatment produced diol **26** where the primary 6-hydroxyl group was subsequently blocked as a pivaloyl ester. After reduction of the azido group and acylation, alcohol **28** was sulfated and hydrolyzed to afford the 4-sulfated galactocerebroside **30**.

**Disulfated Analogs.** The preparation of the disulfated analogs followed similar synthetic sequences as described in Schemes 4 and 5. The 3,4-*O*-isopropylidenegalactocerebroside **19** was first bis-sulfated and then submitted to an acidic treatment to remove the

**Scheme 2.** 3- and 6-Monosulfated Compounds[a]




[a] PTSA/$CH_3C(OCH_3)_2CH_3$; (b) $SO_3$·$N(CH_3)_3$/DMF or Py·$SO_3$/pyridine; (c) TFA (90%); (d) $H_2S$/pyridine/$H_2O$; (e) $CH_3(CH_2)_{14}COCl$/NaOAc/THF; (f) NaOMe/MeOH; (g) BzCl/pyridine; (h) $CH_3C(OEt)_3$/PTSA/toluene; (i) HOAc/$H_2O$.

isopropylidene ketal group. Debenzoylation gave the 2,6-disulfated glycoside **32**.

The synthesis of the 3,6-disulfated analog **41** started with the 3,4-*O*-isopropylideneglycoside **33** which was then selectively silylated at position 6. After benzoylation of the free hydroxyl groups, the acylamino side chain was introduced as before. Compound **36** was then hydrolyzed, and the resulting diol **37** was submitted to Lemieux's sequence.[15] This afforded, after treatment with fluoride ions in the presence of acetic acid to avoid acetate migration at position 6, the diol **39** which was bis-sulfated. Basic hydrolysis provided the 3,6-sulfated galactocerebroside **41**.

The preparation of the 2,3- and 4,6-disulfated analogs required the same intermediate **42** originating from unprotected glycoside **6** (Scheme 5). The usual formation of the cerebroside side chain (reduction and acylation) was followed by sulfation of the free hydroxyl groups in positions 2 and 3. Hydrolysis of the benzoyl protecting group in compound **49** gave the 2,3-disulfated galactocerebroside **50**. On the other hand, bis-benzoylation at positions 2 and 3 of the 4,6-*O*-benzylidene acetal **42** and subsequent azido reduction and acylation provided the fully protected derivative **43**. The preparation of the 4,6-disulfated glycoside **46** was completed by acidic cleavage of the benzylidene acetal, bis-sulfation at positions 4 and 6 of the resulting diol **44**, and final debenzoylation.

## Biology

***In Vitro* Cell-Free Binding Assay.** The assay used to determine the ability of compounds to inhibit the binding of P-selectin has employed a truncated soluble P-selectin protein containing the lectin, EGF, and two complement repeat domains fused to an immunoglobulin tail, termed receptor globulin (Rg), as previously described.[1,16] The P-selectin Rg was allowed to bind to a 96-well ELISA plate coated with sulfatides (Sigma). The P-selectin was mixed with HRP-conjugated goat anti-human IgG, and this immunocomplex was incubated on the antigen-coated plate in the presence or absence of the test compounds. The bound complexes were detected by addition of buffer containing substrate and 3,3′,5,5′-tetramethylbenzidine. Color development was monitored, and following termination of the assay, the absorbance at 450 nm was determined. The test compounds were compared to sulfatides (positive control) or solvent (negative control). The compounds were initially dissolved in DMSO and diluted in PBS so that the final assay conditions contained 0.5% DMSO. Dose−response curves were constructed for each compound using eight concentrations in 2-fold serial dilutions. The mean of duplicate determinations was used for each data point. The $IC_{50}$ values reported were interpolated from the linear portion of the log dose−response curves. The data are reported in Tables 1 and 2.

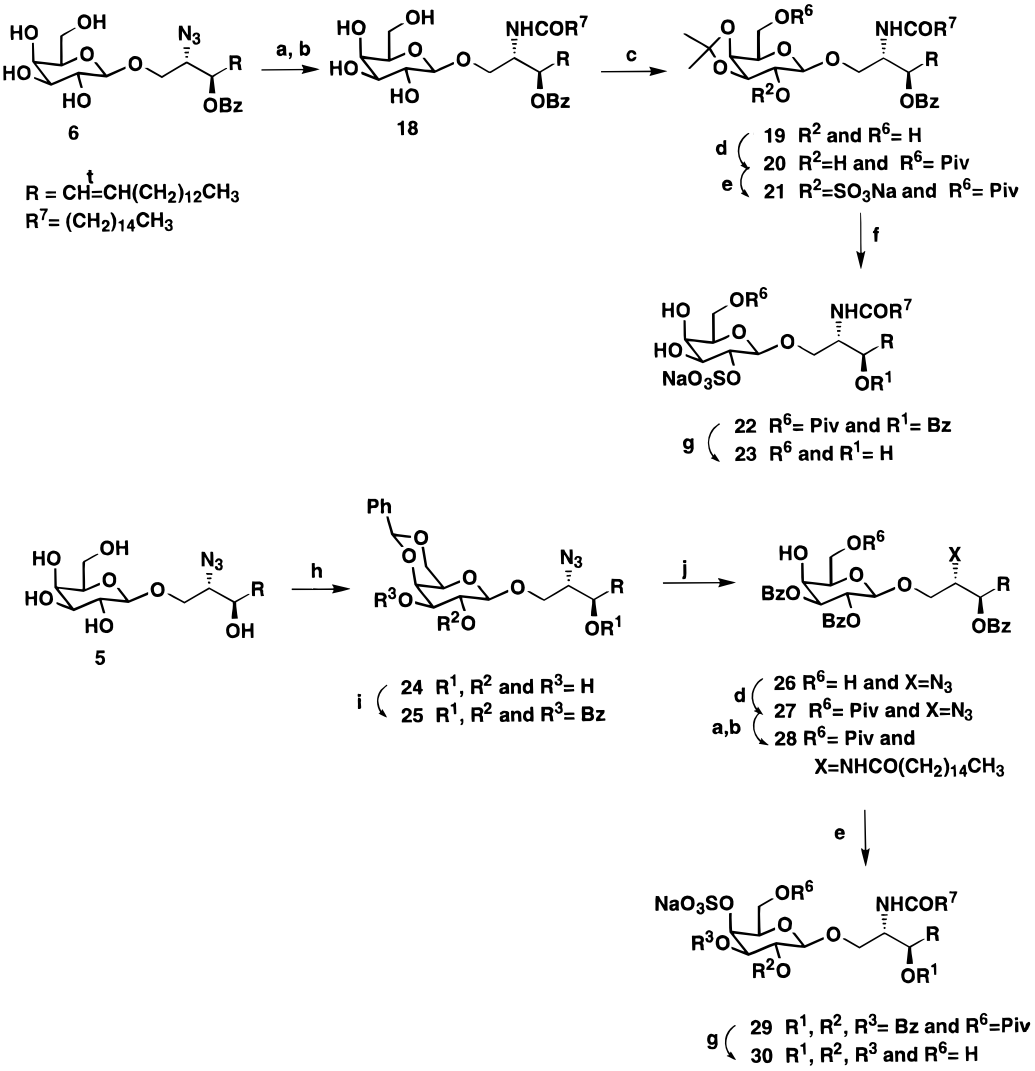
## Results

Table 1 clearly shows that sulfatides strongly inhibit the binding of P-selectin to sulfatide-coated plates. In compound **17** the natural fatty acid side chain is replaced by palmitic acid. This change had no effect on the inhibition of binding. Therefore, all further analogs were prepared as palmitates. The sulfate group was absolutely required for inhibition since galactosyl ceramide was completely inactive at 50 $\mu$M.

In the case of monosulfates the 3 position appears to be optimum for inhibitory activity. The 3-sulfated analog **17** was found to be 4-fold more potent than the 2-sulfated analog **23** (Table 1). The 4- and 6-monosulfated derivatives **30** and **11** are much less active with 20-fold decreased potencies compared to **17**.

Sulfation of more than one galactose hydroxyl group significantly enhances the ability to inhibit P-selectin

**Scheme 3.** 2- and 4-Monosulfated Compounds[a]




[a] (a) $H_2S$/pyridine/$H_2O$; (b) $CH_3(CH_2)_{14}COCl$/NaOAc/THF; (c) PTSA/$CH_3C(OCH_3)_2CH_3$; (d) $C_4H_9COCl$/pyridine; (e) Py·$SO_3$/pyridine or $NMe_3$·$SO_3$/DMF; (f) TFA (90%); (g) MeONa/MeOH; (h) PhCHO/$HCO_2H$; (i) BzCl/pyridine; (j) TFA (50%)/$CH_2Cl_2$.

**Table 1.** *In Vitro* Results of Various Sulfatide Derivatives as Inhibitors of P-Selectin

| no. | position(s) of sulfate(s) | cell-free assay $IC_{50}$ ($\mu$M) |
|---|---|---|
| commercial sulfatides (Sigma) | 3 | 0.64 |
| **11** | 6 | 12 |
| **17** | 3 | 0.6 |
| **23** | 2 | 2.5 |
| **30** | 4 | 12.5 |
| **32** | 2, 6 | 1.2 |
| **41** | 3, 6 | 2.4 |
| **46** | 4, 6 | 1.7 |
| **50** | 2, 3 | 0.1 |
| galactosyl ceramide | no sulfate | >50 |

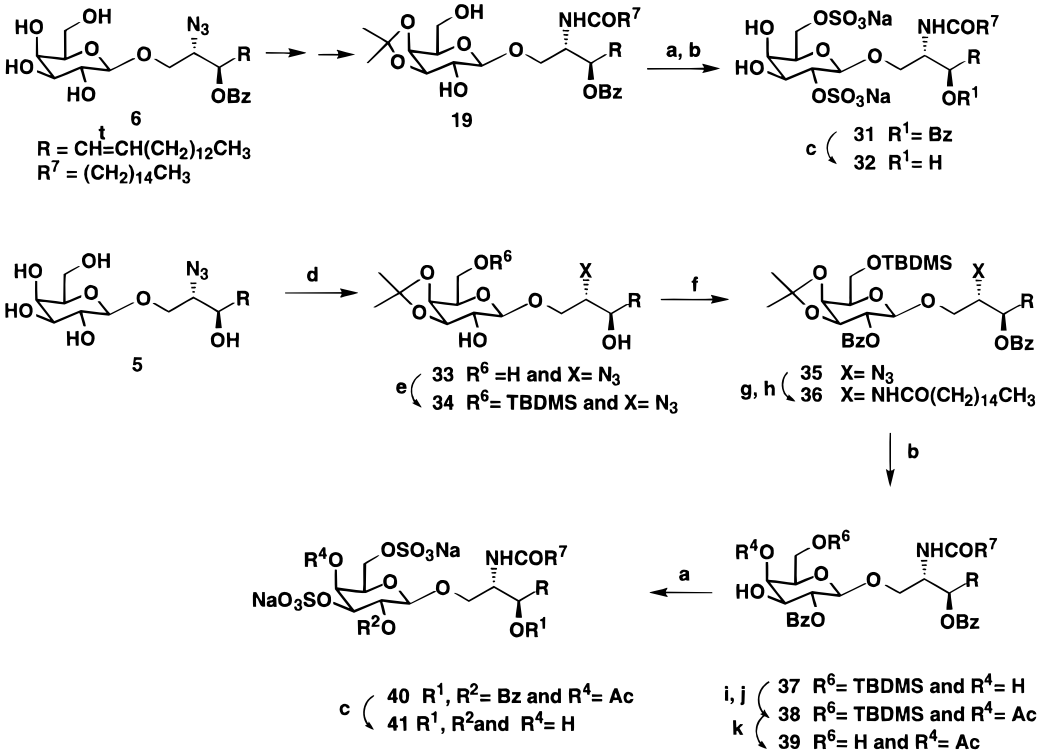
**Table 2.** *In Vitro* Results of Various Substituted Sulfatide Derivatives as Inhibitors of P-Selectin

| no. | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^6$ | cell-free assay $IC_{50}$ ($\mu$M) |
|---|---|---|---|---|---|---|
| **10** | Bz | H | H | H | $SO_3Na$ | 0.4 |
| **16** | Bz | Bz | $SO_3Na$ | Ac | Bz | 4.3 |
| **31** | Bz | $SO_3Na$ | H | H | $SO_3Na$ | 0.9 |
| **40** | Bz | Bz | $SO_3Na$ | Ac | $SO_3Na$ | 1.3 |
| **45** | Bz | Bz | Bz | $SO_3Na$ | $SO_3Na$ | 0.1 |
| **48** | Bz | $SO_3Na$ | $SO_3Na$ | −CHPh− | −CHPh− | 0.1 |
| **49** | Bz | $SO_3Na$ | $SO_3Na$ | H | H | 0.1 |
| sulfatides (Sigma) | H | H | $SO_3Na$ | H | H | 0.64 |

binding. The 2,6-disulfate (**32**) was found to be 10 times more potent than the 6-monosulfate and 2 times more potent than the 2-monosulfate. In general, all of the disulfated analogs are more active than their monosulfated counterparts. The 2,3-disulfate compound **50** is at least 10-fold more active than the other disulfates. Moreover, **50** is 6-fold more potent than sulfatides.

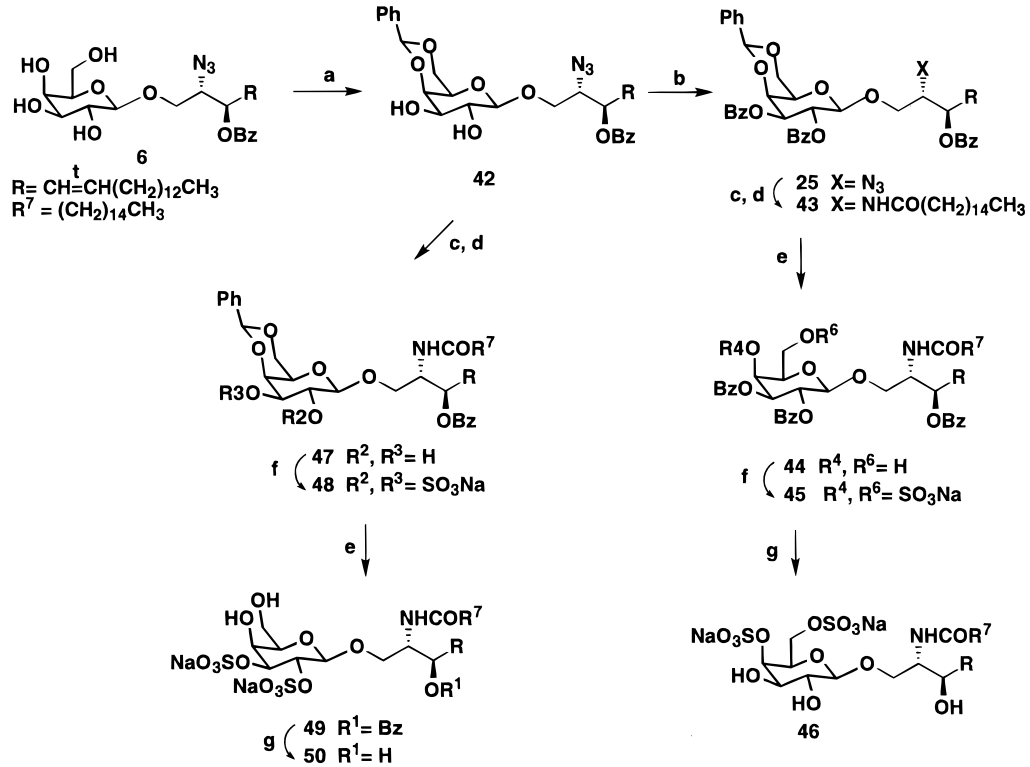
We also evaluated a number of synthetic intermediates for inhibition of P-selectin binding (Table 2). We were particularly interested in determining the effect of replacing hydroxyl groups with lipophilic substituents. In compound **10**, the hydroxyl group in the aglycone of this 6-monosulfate was protected by a benzoyl group. This change resulted in a 30-fold improvement in activity relative to the parent compound. When all of the hydroxyl groups were protected, as in the 3-sulfated compound **16**, there was a 7-fold decrease in potency. This limited exploration of the hydrophobic pocket suggested that lipophilic groups on both the galactose and aglycone moieties could be tolerated. The incorporation of a benzoyl function into the aglycone was also tolerated in the disulfate analogs.

**Scheme 4.** 2,6- and 3,6-Disulfated Compounds[a]




[a] (a) $SO_3 \cdot N(CH_3)_3$/DMF or $SO_3$·py/pyridine; (b) TFA (90%); (c) $NaOCH_3/CH_3OH$; (d) PTSA/$CH_3C(OCH_3)_2CH_3$; (e) TBDMSCl/pyridine; (f) BzCl/pyridine; (g) $H_2S$/pyridine/$H_2O$; (h) $CH_3(CH_2)_{14}COCl$/NaOAc/THF; (i) PTSA/$CH_3C(OEt)_3$/toluene; (j) HOAc, $H_2O$; (k) TBAF/AcOH/THF.

**Scheme 5.** 2,3- and 4,6-Disulfated Compounds[a]




[a] (a) PhCHO/HCOOH; (b) BzCl/pyridine; (c) $H_2S$/pyridine/$H_2O$; (d) $CH_3(CH_2)_{14}COCl$/NaOAc/THF; (e) TFA (90%)/$CH_2Cl_2$; (f) $NMe_3 \cdot SO_3$/DMF or Py·$SO_3$/pyridine; (g) NaOMe/MeOH.

The benzoylated 2,6-disulfate **31** and the 2,3-disulfate **49** had potencies equivalent to those of the parent compounds **32** and **50**. As in the monosulfate series, derivatization of all remaining hydroxyl groups was tolerated as exemplified by compounds **40** and **48**. The 3,6-disulfated derivative **40** was 2-fold more potent than the parent compound, and **48** was equiactive. In the case of the polybenzoylated 4,6-disulfate **45**, a 17-fold improvement in inhibitory activity was observed over the parent compound **46**.

## Discussion

This study shows that the position of the sulfate on the galactose ring is important for optimal interaction with P-selectin. The 3 position is most favored. The rank order of potency was found to be 3 > 2 > 4 = 6. Surprisingly, despite the critical importance of the sulfate residue for interaction with P-selectin (as exemplified by the lack of activity of galactosyl ceramide) all of the positional isomers retain binding affinity to P-selectin. These results are similar to the findings described by Suzuki and co-workers.[4b] They reported the positional selectivity of the sulfate group in a series of synthetic sulfatide analogs evaluated for the ability to bind to L-selectin. Their rank order for the galactose sulfate was 3 > 6 > 2. Therefore, the 3-sulfate appears to be favored in the interaction of galactosyl-based compounds with both P- and L-selectins. Our finding that P-selectin prefers a 2-monosulfate over a 6-monosulfate is not similar to Suzuki's results. It is possible that there may be subtle differences in the binding pockets which can account for this apparent selectivity. However, it must be noted that the assays used were quite different. We evaluated the ability to inhibit P-selectin binding to sulfatide-coated plates. The L-selectin study evaluated the ability of the protein to bind to plates coated with the test compound.

The finding that the sulfate group can be at different positions on the pyranose ring and still retain significant activity tends to indicate that the position of the carbohydrate ring in the protein groove is not as critical as we first thought. The ionic interaction of Lys 113 and/or Lys 111 with the sulfate entity can still be accommodated to some extent in the different monosulfates, despite a required rotation or translation of the galactose ring. The high flexibility of the lipophilic ceramide side chain can probably permit slight modifications in its direction and tilt. This means that different binding modes are likely tolerated, depending on the position of the sulfate group.

The good potency of the disulfated analogs is consistent with the importance of both Lys 111 and Lys 113 as described by Bajorath et al.[7b,9] Therefore, it can be presumed that the two sulfate groups can interact to a certain extent with both positive residues. The importance of polysulfation was also observed by Suzuki[4b] in that L-selectin binding was strongest to a 3,4,6-trisulfate. As we observed for the monosulfated analogs, the position of these two negatively charged residues in the galactose ring appears to be fairly specific. It has been shown by Lemieux[17] that specificity in the recognition of oligosaccharides by proteins involves clusters of hydroxyl groups in these oligosaccharides. These clusters are usually essential to complex formation and have been termed "polar key" by Lemieux. By analogy, the current biological results tend to demonstrate that a "polar key" located at positions 2 and 3 or 4 and 6 of the galactose residue is preferred for binding activity, as shown by compounds **48** and **45**. Ionic groups to nonadjacent positions like in compound **40** seem to be less favored.

A benzoate group in the ceramide aglycone appears to improve the activity of sulfated compounds at position 6 (cf. compounds **10** and **31**). The same trend is noticed for the 4,6- and 3,6-disulfated analogs **45** and **40**, although benzoate groups are also present in the sugar. Since this behavior cannot be ruled out from the more active series (3- or 2,3-sulfated analogs), the contribution of the benzoate group in ceramide aglycone in terms of lipophilicity gain or protein interactions cannot yet be assessed with certainty. It seems however that most of the less active sulfated series (4,6- and 3,6-disulfated) benefit from the presence of nonpolar substituents in the carbohydrate ring as shown by compounds **45** and **40**. Despite no significant activity improvement in compound **48**, the presence of a benzylidene group at positions 4 and 6 of this 2,3-disulfated derivative indicates also that lipophilic substituents are well-tolerated. These results could be explained by the presence of a lipophilic pocket in the binding cavity, delimited by the carbon side chains of Lys 84 and Arg 85.[18]

## Conclusion

In this study we have shown that modifications of sulfatides can produce compounds with enhanced binding affinity for P-selectin. Previous work using antibodies in animal models demonstrated that the selectins appear to play an important role in inflammatory cell infiltration. In addition, sulfatides have shown to block cell infiltration in rats, albeit high doses of compound were required. Compounds with enhanced potency for inhibiting P-selectin-dependent cell adhesion are desired as potential therapeutic agents in the treatment of acute inflammatory reactions.

The high flexibility of these analogs, nevertheless, does not permit so far to unambiguously establish the general binding features. Furthermore, the physical properties of this family of compounds in terms of formation of vesicles or micelles have to be more deeply explored in order to elaborate a more precise molecular binding model. Additional studies are underway to further probe the sulfatide structural requirements for P-selectin-dependent adhesion to provide insight on the design of more potent and specific inhibitors.

## Experimental Section

**Materials and Methods.** Analytical grade solvents were used for reactions and chromatographies. Flash column chromatographies were performed on Merck silica gel 60 (230−400 Mesh), and Merck silica gel 60 $F_{254}$ 0.5 mm plates were used. All melting points were determined on a Gallenkamp melting point apparatus and are not corrected. $^1$H NMR spectra were measured on a Bruker AC200 (200 MHz) or a Bruker AMX400 (400 MHz) instrument. Chemical shifts are reported in $\delta$ units using the solvent as internal standard. The signals are described as s (singlet), d (doublet), t (triplet), qa (quartet), qi (quintet), m (multiplet), and br (broad). Infrared spectra were recorded on a Perkin-Elmer 781, and optical rotations were measured on a Perkin-Elmer 241 apparatus. Elemental analyses were performed at the Analytical Center of Bristol-Myers Squibb in Syracuse, NY.

**Key Intermediates. (2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-[(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)oxy]-4-octadecene and (2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-[(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)oxy]-4-octadecene (4). Procedure A:** A solution of (2*S*,3*R*,4*E*)-2-azido-3-(benzoyloxy)-4-octadecen-1-ol[4] (**3**) (2.9 g, 6.75 mmol) in dry benzene (100 mL) and nitromethane (100 mL) was heated under reflux. Benzene was distilled, and the solution was concentrated under vacuum to 50−60 mL. To this solution were added 2,3,4,6-tetra-*O*-acetyl-α-D-galactosyl bromide[5] (**2**) (5.0 g, 12.16 mmol) and mercury(II) cyanide (3.0 g, 12.16 mmol) at 22 °C and under argon, and the resulting mixture was heated up to 80−85 °C for 15−20 min. The reaction was then cooled down

to 5 °C and diluted with ethyl ether/water (1:1, 100 mL). Hydrogen sulfide was bubbled in, and the resulting black precipitate was filtered on Celite and washed with ethyl ether (3 × 25 mL). The organic phases were washed with cold aqueous sodium bicarbonate solution (1 M, 4 × 25 mL), water (25 mL), and brine (25 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated. The black resulting residue was purified by chromatography on silica gel (250 g, 0−30% ethyl acetate/hexane) and afforded the β-anomer (3.90 g, 76%) and the α-anomer (0.49 g, 9.5%) of the title compound as colorless oils.

**Procedure B (modification of Schmidt's procedure):** (2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-4-octadecen-1-ol (3.93 g, 9.14 mmol) and *O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)-trichloroacetimidate (6.30 g, 12.78 mmol) in a mixture of dry dichloromethane (50 mL) and hexane (90 mL) were stirred with crushed 4 Å molecular sieves (3 g) for 20 min. A solution of tin(IV) chloride in dichloromethane (1.8 mL, 1 M) was then added dropwise over 50 min. The mixture was stirred for another 1 h after the addition ended. The sieves were filtered and washed with ethyl acetate, and the filtrate was diluted with ethyl acetate (300 mL). The solution was washed with water, saturated sodium bicarbonate, and brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by silica gel chromatography (toluene/ethyl acetate) to afford the β-anomer (5.30 g, 76%). Only traces of (2*S*,3*R*,4*E*)-2-azido-3-(benzoyloxy)-4-octadecen-1-yl acetate were obtained using this method, while, in our hands, up to 40% of this side product was obtained using Schmidt's original procedure.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$) α-anomer: 3050, 2930 (C−H), 2100 (−$N_3$), 1750 (C═O). IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$) β-anomer: 3050, 2930, 2955 (C−H), 2130 ($N_3$), 1750 (C═O). $^1$H NMR (400 MHz, $CDCl_3$) δ α-anomer: 0.89 (3H, t, $J$ = 7.0 Hz, -$CH_3$), 1.25 (20H, br s, -$(CH_2)_{10}$-), 1.39 (2H, m, -$CH_2$-), 2.00, 2.01, 2.09, 2.15 (4 × 3H, 4s, 4 × -OCO$CH_3$), 2.09 (2H, m, ═CH-C$H_2$-), 3.52 (1H, dd, $J$ = 10.7, 7.7 Hz, H-1), 3.88 (1H, dd, $J$ = 10.7, 3.5 Hz, H-1), 3.91−3.95 (1H, m, H-2), 4.09−4.10 (2H, m, H-6′), 4.24 (1H, td, $J$ = 6.5, 1.1 Hz, H-5′), 5.14−5.17 (2H, m, H-1′, H-2′), 5.34−5.39 (1H, m, H-3′), 5.49 (1H, dd, $J$ = 3.3, 1.1 Hz, H-4′), 5.53−5.60 (2H, m, H-3, H-4), 5.93−5.99 (1H, m, H-5), 7.45−8.06 (5H, 3m, -$C_6H_5$). $^1$H NMR (400 MHz, $CDCl_3$) δ β-anomer: 0.89 (3H, t, $J$ = 7.0 Hz, -$CH_3$), 1.25 (20H, br s, -$(CH_2)_{10}$-), 1.39 (2H, m, -$CH_2$-), 2.00, 2.03, 2.11, 2.16 (4 × 3H, 4s, 4 × -OCO$CH_3$), 2.09 (2H, m, ═CH-C$H_2$), 3.58−3.63 (1H, m, H-1), 3.89−3.97 (3H, m, H-1, H-5′, H-2), 4.11 (1H, dd, $J_{AB}$ = 11.2, $J_{AX}$ = 6.7 Hz, H-6′), 4.14 (1H, dd, $J_{AB}$ = 11.2, $J_{BX}$ = 6.7 Hz, H-6′), 4.51 (1H, d, $J$ = 7.9 Hz, H-1′), 5.02 (1H, dd, $J$ = 10.5, 3.4 Hz, H-3′), 5.42 (1H, dd, $J$ = 10.5, 7.9 Hz, H-2′), 5.39 (1H, d, $J$ = 3.4 Hz, H-4′), 5.53−5.62 (2H, m, H-3, H-4), 5.94 (1H, dt, $J$ = 14.3, 6.9 Hz, H-5), 7.45−8.08 (5H, 3m, -$C_6H_5$).

**(2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-(β-D-galactopyranosyloxy)-4-octadecene (6).** A solution of (2*S*,3*R*,4*E*)-2-azido-3-(benzoyloxy)-1-[(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)oxy]-4-octadecene (**4**) (4.0 g, 5.26 mmol) in dichloromethane (20 mL) was added slowly to a freshly prepared solution of sodium (2.44 g, 106 mmol) in methanol (120 mL) at −70 °C and under argon. The temperature of the cooling bath was allowed to reach −50 °C during 3 h. The reaction mixture was cooled down to −70 °C and neutralized with a solution of acetic acid (6.0 mL, 106 mmol) in dichloromethane (10 mL). The mixture was concentrated under vacuum, giving a residue which was dissolved in dichloromethane (50 mL). The residual solid (sodium acetate) was filtered on Celite and washed with dichloromethane (5 × 10 mL). The combined filtrate and washings were evaporated, and the residue was purified by silica gel chromatography (200 g, 0−12% methanol/dichloromethane) and afforded the title compound (2.77 g, 89%) as a white solid.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3700−3200 (O−H), 3060, 2930, 2860 (C−H), 2110 (−$N_3$), 1720 (C═O). $^1$H NMR (400 MHz, DMSO-$d_6$) δ: 0.85 (3H, t, $J$ = 6.8 Hz, -$CH_3$), 1.20−1.65 (22H, m, -$(CH_2)_{11}$-), 2.04 (2H, m, ═CH-C$H_2$-), 3.23−3.33 (3H, m, H-5′, H-3′, H-2′), 3.44 (1H, dd, $J$ = 10.6, 5.7 Hz, H-6′), 3.51 (1H, dd, $J$ = 10.6, 6.1 Hz, H-6′), 3.59 (1H, dd, $J$ = 10.5, 5.3 Hz, H-1), 3.61 (1H, d, $J$ = 2.1 Hz, H-4′), 3.78 (1H, dd, $J$ = 10.5, 7.5 Hz, H-1), 4.13 (1H, d, $J$ = 7.5 Hz, H-1′), 4.16−4.20 (1H, m, -$CHN_3$-), 4.91 (1H, br d, $J$ = 3.8 Hz, -OH), 4.55 (1H, ap t, -OH), 4.75 (1H, br s, -OH), 4.91 (1H, br d, $J$ = 3.6 Hz, -OH), 5.56 (1H, dd, $J$ = 15.3, 7.6 Hz, H-4), 5.65 (1H, dd, $J$ = 7.6, 3.7 Hz, H-3), 5.88 (1H, dt, $J$ = 15.3, 6.8 Hz, H-5), 7.53−8.00 (5H, 3m, -$C_6H_5$).

**Monosulfated Compounds. Synthesis of (2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-hydroxy-1-[[6-*O*-(sodium oxysulfonyl)-β-D-galactopyranosyl]oxy]-4-octadecene (11). (2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-[(3,4-*O*-isopropylidene-β-D-galactopyranosyl)oxy]-4-octadecene (7).** A solution of (2*S*,3*R*,4*E*)-2-azido-3-(benzoyloxy)-1-(β-D-galactopyranosyloxy)-4-octadecene (**6**) (0.955 g, 0.161 mmol) in 2,2-dimethoxypropane (50 mL) was treated with *p*-toluenesulfonic acid (0.050 g), and the resulting mixture was stirred at 22 °C for 18 h. Water (5 mL) was added followed by *p*-toluenesulfonic acid (0.045 g), and the mixture was stirred for another 1.5 h. Triethylamine (3 drops) was then added, and the mixture was evaporated under vacuum. The residue was dissolved in ethyl acetate (400 mL), and the organic phase was washed with a saturated solution of sodium bicarbonate and brine, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by silica gel chromatography (60 g, 20−30% acetone/toluene) and afforded the title compound (0.600 g, 60%).

$[\alpha]^{22}_D$: −17.3° ($c$ = 0.98, $CHCl_3$). IR (NaCl, film) $\nu_{max}$ ($cm^{-1}$): 3650−3100 (O−H), 2930, 2855 (C−H), 2105 (−$N_3$), 1720 (C═O ester). $^1$H NMR (200 MHz, $CDCl_3$) δ: 0.87 (3H, t, $J$ = 6.3 Hz, -$CH_3$), 1.24−1.35 (22H, m, -$(CH_2)_{11}$-), 1.35 and 1.52 (2 × 3H, 2s, $(CH_3)_2$-C-), 2.03−2.13 (2H, m, ═CH-C$H_2$-), 2.33−2.38 (1H, m, -OH-6′), 2.55 (1H, d, $J$ = 2.4 Hz, -OH-2′), 3.57 (1H, ddd, $J$ = 8.3, 8.3, 2.4 Hz, H-2′), 3.65−4.17 (8H, m, -$CHN_3$-, H-1, H-3′, H-4′, H-5′, H-6′), 4.22 (1H, d, $J$ = 8.3 Hz, H-1′), 5.58 (1H, dd, $J$ = 15.0, 8.0 Hz, H-4), 5.71 (1H, dd, $J$ = 8.0, 4.0 Hz, H-3), 5.97 (1H, dt, $J$ = 15.0, 6.7 Hz, H-5), 7.39−8.08 (5H, 3m, -$C_6H_5$).

**(2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-[[3,4-*O*-isopropylidene-6-*O*-(sodium oxysulfonyl)-β-D-galactopyranosyl]oxy]-4-octadecene (8).** A solution of (2*S*,3*R*,4*E*)-2-azido-3-(benzoyloxy)-1-[(3,4-*O*-isopropylidene-β-D-galactopyranosyl)-oxy]-4-octadecene (**7**) (0.550 g, 0.87 mmol) in dry pyridine was treated with sulfur trioxide−pyridine complex (0.207 g, 1.28 mmol), and the resulting mixture was stirred at 22 °C for 2.5 h. Water (5 mL) and solid sodium bicarbonate (0.50 g) were added, and the mixture was stirred for 10 more minutes and evaporated under vacuum. The residue was coevaporated with toluene and purified by silica gel chromatography (chloroform/methanol, 95:5−8:2) and afforded the title compound (0.532 g, 83%) as a white glassy solid.

$[\alpha]^{22}_D$: 0° ($c$ = 0.8, MeOH, 95%). IR (Nujol) $\nu_{max}$ ($cm^{-1}$): 3700−3100 (br, O−H), 2900 (br, C−H), 2110 (−$N_3$), 1715 (C═O ester). $^1$H NMR (400 MHz, DMSO-$d_6$) δ: 0.85 (3H, t, $J$ = 6.7 Hz, -$CH_3$), 1.20−1.32 (22H, m, -$(CH_2)_{11}$-), 1.26 and 1.39 (2 × 3H, 2s, -C$(CH_3)_2$), 2.04 (2H, qa, $J$ = 6.8 Hz, ═CH-C$H_2$-), 3.22 (1H, br qa, H-2′), 3.61 (1H, dd, $J$ = 10.3, 5.1 Hz, H-1), 3.80 (1H, dd, $J$ = 10.3, 8.0 Hz, H-1), 3.86 (2H, d, $J$ = 6.1 Hz, H-6′), 3.95 (1H, br t, H-3′), 4.00 (1H, br td, H-5′), 4.10 (1H, dd, $J$ = 5.6, 1.8 Hz, H-4′), 4.17 (1H, m, H-2), 4.21 (1H, d, $J$ = 8.0 Hz, H-1′), 5.30 (1H, d, $J$ = 5.3 Hz, -OH), 5.57 (1H, dd, $J$ = 15.1, 7.4 Hz, H-4), 5.64 (1H, dd, $J$ = 7.4, 3.6 Hz, H-3), 5.88 (1H, dt, $J$ = 15.1, 6.8 Hz, H-5), 7.54−7.58, 7.65−7.69, and 7.97−7.99 (5H, 3m, aromatic H).

**(2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-[[6-*O*-(sodium oxysulfonyl)-β-D-galactopyranosyl]oxy]-4-octadecene (9).** A solution of (2*S*,3*R*,4*E*)-2-azido-3-(benzoyloxy)-1-[[3,4-*O*-isopropylidene-6-*O*-(sodium oxysulfonyl)-β-D-galactopyranosyl]oxy]-4-octadecene (**8**) (0.42 g, 0.57 mmol) in methanol (60 mL) was treated with Dowex $H^+$ resin (1 g) for 45 min. The mixture was filtered and the resin washed with chloroform/methanol (7:3, 20 mL). The filtrate was treated with Rexyn $Na^+$ resin (∼2 g) until the solution became basic. The mixture was filtered and evaporated, and the residue was purified by silica gel chromatography (20−30% methanol/chloroform) and afforded the title compound (0.358 g, 90%) as a waxy solid.

IR (Nujol) $\nu_{max}$ ($cm^{-1}$): 3700−3100 (br, O-H), 2915, 2850 (C−H), 2110 (−$N_3$), 1720 (C═O ester). $^1$H NMR (400 MHz, DMSO-$d_6$) δ: 0.84 (3H, t, $J$ = 6.8 Hz, -$CH_3$), 1.19−1.31 (22H, m,

-$(CH_2)_{11}$-), 2.03 (2H, br qa, =CH-C$H_2$-), 3.26−3.30, 3.54−3.60, and 3.74−3.79 (2H, 3H, 2H, 3 sets of m, H-2′, H-3′, H-4′, H-5′, H-6′, H-1), 3.83 (1H, dd, $J$ = 10.6, 6.2 Hz, H-1 or H-6′), 4.13 (1H, d, $J$ = 7.0 Hz, H-1′), 4.12−4.17 (1H, m, H-2), 4.50 (1H, d, $J$ = 4.7 Hz, -OH), 4.66 (1H, d, $J$ = 5.3 Hz, -OH), 4.84 (1H, d, $J$ = 4.5 Hz, -OH), 5.55 (1H, dd, $J$ = 15.3, 7.5 Hz, H-4), 5.63 (1H, dd, $J$ = 7.5, 3.6 Hz, H-3), 5.87 (1H, dt, $J$ = 15.3, 7.2 Hz, H-5), 7.53−7.56, 7.64−7.68, and 7.96−7.98 (5H, 3 sets of m, aromatic H).

**(2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[[6-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (10).** A solution of (2*S*,3*R*,4*E*)-2-azido-3-(benzoyloxy)-1-[[6-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (**9**) (0.034 g, 0.049 mmol) in a mixture of pyridine (2.5 mL) and water (2.5 mL) was saturated with hydrogen sulfide and stirred at 22 °C for 18 h. The solvent was evaporated under vacuum, and the last traces of pyridine were coevaporated with toluene. The residual solid was then dissolved in tetrahydrofuran (6 mL) and treated with aqueous sodium acetate (50%, 5 mL) and palmitoyl chloride (0.016 g, 0.058 mmol). The aqueous phase was extracted with tetrahydrofuran (2 × 10 mL). The combined organic layers were evaporated in vacuum, and the solid residue was purified by silica gel chromatography (20−30% methanol/chloroform) to give the title material (0.037 g, 84%) as a white glassy solid.

$[\alpha]^{22}_D$: +4° ($c$ = 0.5, $CHCl_3$/MeOH, 7:3). IR (KBr) $\nu_{max}$ ($cm^{-1}$): 3700−3150 (br, O−H, N−H), 2930, 2860, (C−H), 1725, 1640 (C=O ester, amide). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$: 0.85 (6H, t, $J$ = 6.8 Hz, 2 × -$CH_3$), 1.21−1.35 (46H, m, -$(CH_2)_{10}$-, -$(CH_2)_{13}$-), 1.47 (2H, m, -$CH_2$-), 1.97−2.13 (4H, m, =CH-C$H_2$-, -NHCOC$H_2$-), 3.28−3.31 (2H, m, H-2′, H-3′), 3.48 (1H, dd, $J$ = 10.2, 5.0 Hz, H-1), 3.54 (1H, br t, H-5′), 3.59 (1H, br t, H-4′), 3.74 (1H, dd, $J_{AB}$ = 10.6 Hz, $J_{AX}$ = 6.3 Hz, H-6′), 3.81 (1H, dd, $J_{AB}$ = 10.6 Hz, $J_{BX}$ = 5.9 Hz, H-6′), 3.89 (1H, dd, $J$ = 10.2, 5.8 Hz, H-1), 4.07 (1H, d, $J$ = 7.1 Hz, H-1′), 4.34 (1H, m, H-2), 4.49 (1H, d, $J$ = 4.7 Hz, -OH), 4.66 (1H, br s, -OH), 4.92 (1H, d, $J$ = 2.9 Hz, -OH), 5.45 (1H, dd, $J$ = 7.6, 5.8 Hz, H-3), 5.52 (1H, dd, $J$ = 15.1, 7.7 Hz, H-4), 5.79 (1H, dt, $J$ = 15.1, 6.8 Hz, H-5), 7.48−7.52, 7.61−7.65, 7.93−7.95 (5H, 3 sets of m, aromatic H), 7.84 (1H, d, $J$ = 9.1 Hz, -NH-).

**(2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-1-[[6-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (11).** A solution of (2*S*,3*R*,4*E*)-2-(hexadecanoylamino)-3-(benzoyloxy)-1-[[6-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (**10**) (0.402 g, 0.444 mmol) in methanol (25 mL) and dichloromethane (25 mL) was treated with sodium methoxide (0.2 M, 3.0 mL, 0.6 mmol) at 22 °C. The mixture was stirred for 18 h. Resin Dowex $H^+$ 50W-X8 was then added, and this mixture was stirred until the pH became neutral. The mixture was filtered, and the resin was washed with dichloromethane/methanol, 1:1. The filtrate was then treated with resin Rexyn 102 ($Na^+$) and stirred for 15 min. The mixture was filtered, the resin was washed with dichloromethane/methanol (1:1), and the filtrate was concentrated. The residue was purified by silica gel chromatography (20% methanol/chloroform) and afforded the title compound (0.257 g, 72%) as a white solid.

$[\alpha]^{22}_D$: −6.5° ($c$ = 1.0, $CHCl_3$/MeOH, 7:3). IR (KBr) $\nu_{max}$ ($cm^{-1}$): 3700−3050 (br, O−H, *N*−H), 2920, 2850 (C−H), 1630 (C=O amide). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$: 0.85 (6H, t, $J$ = 6.8 Hz, 2 × -$CH_3$), 1.23 (46H, m, -$(CH_2)_{13}$-, -$(CH_2)_{10}$-), 1.44 (2H, m, -$CH_2$-), 1.92 (2H, m, =CH-C$H_2$-), 2.02 (2H, t, $J$ = 7.4 Hz, -NHCOC$H_2$-), 3.28 (2H, m, H-2′, H-3′), 3.38 (1H, dd, $J$ = 9.9, 3.5 Hz, H-1), 3.54 (1H, t, $J$ = 6.1 Hz, H-5′), 3.59 (1H, br s, H-4′), 3.75−3.88 (4H, m, H-2, H-3, H-6′), 3.97 (1H, dd, $J$ = 9.9, 4.8 Hz, H-1), 4.03 (1H, d, $J$ = 7.0 Hz, H-1′), 4.49 (1H, d, $J$ = 4.7 Hz, -OH), 4.66 (1H, d, $J$ = 5.2 Hz, -OH), 4.87 (1H, d, $J$ = 3.3 Hz, -OH), 4.89 (1H, d, $J$ = 5.6 Hz, -OH), 5.34 (1H, dd, $J$ = 15.3, 7.0 Hz, H-4), 5.52 (1H, dt, $J$ = 15.3, 6.6 Hz, H-5), 7.52 (1H, d, $J$ = 9.0 Hz, -NH-).

**Synthesis of (2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-hydroxy-1-[[3-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (17). (2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-[(3,4-*O*-isopropylidene-2,6-di-*O*-benzoyl-*β*-D-galactopyranosyl)oxy]-4-octadecene (12).** A solution of (2*S*,3*R*,4*E*)-2-azido-3-(benzoyloxy)-1-[(3,4-*O*-isopropylidene-*β*-D-galactopyranosyl)oxy]-4-octadecene (**7**) (0.900 g, 1.42 mmol) in pyridine (15 mL) was treated with benzoyl chloride (0.66 mL, 5.68 mmol) at 5 °C. The mixture was stirred overnight at 5 °C; then methanol (∼2 mL) was added to this cold mixture which was stirred for 1 more hour. The mixture was diluted with ethyl acetate (60 mL) and washed with 1 M aqueous sodium bicarbonate (2 × 15 mL), water (2 × 15 mL), and brine (15 mL). The organic phase was dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by silica gel chromatography (0−16% ethyl acetate/hexane) to give the title material (1.14 g, 96%) as a yellow oil.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3050, 2990, 2930, 2855 (C−H), 2110 (−$N_3$), 1725 (C=O ester). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$: 0.88 (3H, m, -$CH_3$), 1.20−1.30 (22H, m, -$(CH_2)_{11}$-), 1.37 and 1.64 (2 × 3H, 2s, -C$(CH_3)_2$), 1.90 (2H, m, =CH-C$H_2$-), 3.57 and 3.84−3.98 (1H, 2H, 2 sets of m, H-1, H-2), 4.21 (2H, br t, H-5′), 4.32 (1H, dd, $J$ = 5.5, 1.9 Hz, H-4′), 4.41 (1H, br t, H-3′), 4.58 (1H, d, $J$ = 7.9 Hz, H-1′), 4.56−4.73 (2H, m, H-6′), 5.28 (1H, br t, H-2′), 5.44 (1H, dd, $J$ = 14.9, 8.0 Hz, H-4), 5.55 (1H, dd, $J$ = 8.0, 3.3 Hz, H-3), 5.71 (1H, dt, $J$ = 14.9, 6.6 Hz, H-5), 7.37−7.57 and 7.98−8.09 (15H, 2 sets of m, aromatic H).

**(2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[(3,4-*O*-isopropylidene-2,6-di-*O*-benzoyl-*β*-D-galactopyranosyl)oxy]-4-octadecene (13).** (2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-[(3,4-*O*-isopropylidene-2,6-di-*O*-benzoyl-*β*-D-galactopyranosyl)oxy]-4-octadecene (**12**) (1.0 g, 1.19 mmol) was reacted by the procedure used to synthesize compound **10** and afforded the title compound (1.16 g, 93%) as a white solid. IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3680 (N−H), 3050, 2990, 2930, 2855 (C−H), 1725, 1670 (C=O ester, amide). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$: 0.89 (6H, 2 t, $J$ = 6.7, 6.8 Hz, 2 × -$CH_3$), 1.12−1.35 (46H, m, -$(CH_2)_{13}$-, -$(CH_2)_{10}$-), 1.38 and 1.64 (2 × 3H, 2s, -C$(CH_3)_2$), 1.38−1.47 (2H, m, -$CH_2$-), 1.80 (2H, t, $J$ = 7.6 Hz, -NHCOC$H_2$-), 1.97 (2H, qa, $J$ = 6.9 Hz, =CH-C$H_2$-), 3.62 (1H, dd, $J$ = 10.0, 4.0 Hz, H-1), 4.13 (1H, dd, $J$ = 10.0, 3.2 Hz, H-1), 4.17 (1H, m, H-5′), 4.31 (1H, dd, $J$ = 5.5, 2.1 Hz, H-4′), 4.41 (1H, dd, $J$ = 7.0, 5.5 Hz, H-3′), 4.39−4.45 (1H, m, H-2), 4.48 (1H, dd, $J$ = 11.6, 7.4 Hz, H-6′), 4.51 (1H, d, $J$ = 7.9 Hz, H-1′), 4.63 (1H, dd, $J$ = 11.6, 4.9 Hz, H-6′), 5.24 (1H, br t, H-2′), 5.45 (1H, dd, $J$ = 15.2, 7.2 Hz, H-4), 5.53 (1H, br t, H-3), 5.75 (1H, d, $J$ = 9.1 Hz, -NH-), 5.80 (1H, dt, $J$ = 15.2, 6.9 Hz, H-5), 7.39−7.46, 7.50−7.60, and 7.99−8.05 (15H, 3 sets of m, aromatic H).

**(2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[(2,6-di-*O*-benzoyl-*β*-D-galactopyranosyl)oxy]-4-octadecene (14).** A solution of (2*S*,3*R*,4*E*)-2-(hexadecanoylamino)-3-(benzoyloxy)-1-[(3,4-*O*-isopropylidene-2,6-di-*O*-benzoyl-*β*-D-galactopyranosyl)oxy]-4-octadecene (**13**) (1.15 g, 1.09 mmol) in dichloromethane (40 mL) was treated with aqueous trifluoroacetic acid (90%, 1 mL) at 5 °C. The mixture was stirred at 22 °C for 1 h, then diluted with ethyl acetate (100 mL), and washed with 1 M aqueous sodium bicarbonate (2 × 20 mL), water (3 × 20 mL), and brine (20 mL). The organic phase was dried over anhydrous magnesium sulfate, filtered, and evaporated to give the title compound (1.06 g, 95% crude).

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3700-3450 (N−H, O−H), 3050, 2990, 2930, 2860 (C−H), 1725, 1670 (C=O ester, amide). $^1$H NMR (400 MHz, $CDCl_3$ + $D_2O$) $\delta$: 0.89 (6H, m, 2 × -$CH_3$), 1.15−1.40 (48H, m, -$(CH_2)_{13}$-, -$(CH_2)_{11}$-), 1.83 (2H, t, $J$ = 7.6 Hz, -NHCOC$H_2$-), 1.98 (2H, qa, $J$ = 6.9 Hz, =CH-C$H_2$-), 3.62 (1H, dd, $J$ = 9.4, 3.2 Hz, H-3′), 3.80−3.83 (2H, m, H-1, H-5′), 3.98 (1H, d, $J$ = 3.2 Hz, H-4′), 4.13 (1H, d, $J$ = 9.9 Hz, H-1), 4.21 (1H, dd, $J$ = 11.4, 6.5 Hz, H-6′), 4.44 (1H, m, H-2), 4.52−4.56 (1H, m overlapped by H-1′, H-6′), 4.53 (1H, d, $J$ = 7.7 Hz, H-1′), 5.26 (1H, br t, H-2′), 5.46 (1H, dd, $J$ = 15.2, 7.9 Hz, H-4), 5.59 (1H, br t, H-3), 5.81 (1H, d, $J$ = 9.0 Hz, -NH-), 5.85 (1H, dt, $J$ = 15.2, 6.9 Hz, H-5), 7.39−7.47, 7.51−7.61, and 8.01−8.05 (15H, 3 sets of m, aromatic H).

**(2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[(2,6-di-*O*-benzoyl-4-*O*-acetyl-*β*-D-galactopyranosyl)oxy]-4-octadecene (15).** A suspension of (2*S*,3*R*,4*E*)-2-(hexadecanoylamino)-3-(benzoyloxy)-1-[(2,6-di-*O*-benzoyl-*β*-D-galactopyranosyl)oxy]-4-octadecene (**14**) (1.06 g, 1.05 mmol) in dry benzene (25 mL) and triethyl orthoacetate (25 mL) was treated with *p*-toluenesulfonic acid (25 mg) at 22 °C. The mixture was stirred for 1 h, and then triethylamine (∼1 mL) was added

followed by cold water (20 mL). The aqueous phase was extracted with ethyl acetate (4 × 50 mL), and these combined extracts were washed with 1 M aqueous sodium bicarbonate (3 × 40 mL), water (2 × 40 mL), and brine (40 mL). The organic phase was dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue was dissolved in dichloromethane (∼5 mL) and treated with 80% aqueous acetic acid (10 mL). The mixture was stirred at 22 °C for ∼ 15 min. Toluene was added, and the mixture was coevaporated under vacuum (3x). The residue was purified by silica gel chromatography (0−40% ethyl acetate/hexane) and afforded the title compound (1.1 g, 100%) as a white solid.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3700−3450 (N−H, O−H), 3050, 2930, 2860 (C−H), 1725, 1670 (C═O ester, amide). $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$: 0.89 (6H, m, 2 × -$CH_3$), 1.11−1.41 (48H, m, -$(CH_2)_{13}$-, -$(CH_2)_{11}$-), 1.81 (2H, br t, -NHCOC$H_2$-), 1.97 (2H, qa, $J$ = 6.9 Hz, ═CH-C$H_2$-), 2.25 (3H, s, -OAc), 2.55 (1H, br s, -OH), 3.66 (1H, dd, $J$ = 9.9, 3.8 Hz, H-1), 3.99 (1H, t, $J$ = 6.6 Hz, H-5′), 4.05 (1H, dd, $J$ = 10.0, 3.6 Hz, H-3′), 4.15 (1H, dd, $J$ = 9.9, 3.2 Hz, H-1), 4.25 (1H, dd, $J_{AB}$ = 11.3 Hz, $J_{AX}$ = 6.5 Hz, H-6′), 4.30 (1H, dd, $J_{AB}$ = 11.3 Hz, $J_{BX}$ = 6.7 Hz, H-6′), 4.45 (1H, m, H-2), 4.50 (1H, d, $J$ = 7.9 Hz, H-1′), 5.27 (1H, dd, $J$ = 10.0, 7.9 Hz, H-2′), 5.45 (1H, dd, $J$ = 15.2, 7.5 Hz, H-4), 5.47 (1H, br d, H-4′), 5.52 (1H, br t, H-3), 5.68 (1H, d, $J$ = 9.2 Hz, -NH-), 5.82 (1H, dt, $J$ = 15.2, 6.9 Hz, H-5), 7.39−7.47, 7.52−7.61, and 7.97−8.05 (15H, 3 sets of m, aromatic H).

**(2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[[2,6-di-*O*-benzoyl-4-*O*-acetyl-3-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (16).** A solution of (2*S*,3*R*,4*E*)-2-(hexadecanoylamino)-3-(benzoyloxy)-1-[(2,6-di-*O*-benzoyl-4-*O*-acetyl-*β*-D-galactopyranosyl)oxy]-4-octadecene (**15**) (1.1 g, 1.04 mmol) in dry dimethylformamide (40 mL) was treated with sulfur trioxide-trimethylamine complex (0.723 g, 5.20 mmol) and heated to 80−85 °C for 1.5 h. The mixture was cooled down to 5 °C, and 1 M aqueous sodium bicarbonate (15 mL) and solid sodium bicarbonate were added to saturation. The mixture was stirred for 1 h and then concentrated under vacuum. The residue was in dichloromethane, and this mixture was filtered. The filtrate was evaporated and gave a residue which was purified by silica gel chromatography (0−12% methanol/chloroform) to afford the title material (1.09 g, 90%).

IR (Nujol) $\nu_{max}$ ($cm^{-1}$): 3700−3350 (N−H), 2930, 2860 (C−H), 1725, 1660 (C═O ester, amide). $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$: 0.83 (6H, t, $J$ = 6.7 Hz, 2 × -$CH_3$), 1.10−1.39 (48H, m, -$(CH_2)_{13}$-, -$(CH_2)_{11}$-), 1.74−1.96 (4H, m, ═CH-C$H_2$-, -NHCOC$H_2$-), 2.09 (3H, s -OAc), 3.52 (1H, dd, $J$ = 9.9, 7.1 Hz, H-1), 3.72 (1H, dd, $J$ = 9.9, 6.6 Hz, H-1), 4.16 (1H, dd, $J$ = 11.0, 7.1 Hz, H-6′), 4.24 (1H, br t, H-5′), 4.27−4.35 (2H, m, H-2, H-6′), 4.65 (1H, dd, $J$ = 10.3, 3.4 Hz, H-3′), 4.83 (1H, d, $J$ = 8.0 Hz, H-1′), 5.15 (1H, dd, $J$ = 10.3, 8.0 Hz, H-2′), 5.31 (1H, dd, $J$ = 7.4, 4.7 Hz, H-3), 5.38 (1H, dd, $J$ = 15.0, 7.3 Hz, H-4), 5.46 (1H, dt, $J$ = 15.0, 6.3 Hz, H-5), 5.59 (1H, d, $J$ = 3.3 Hz, H-4′), 7.41−7.51, 7.56−7.65, 7.84−7.86, and 7.93−7.98 (16H, 4 sets of m, aromatic H, -NH-). MS (CI, $NH_3$): 1132 $(M - Na)^-$.

**(2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-hydroxy-1-[[3-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (17).** (2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[[2,6-di-*O*-benzoyl-4-*O*-acetyl-3-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (**16**) (0.689 g, 0.59 mmol) was reacted by the procedure used to synthesize compound **11** and afforded the title compound (0.316 g, 67%) as a white solid.

IR (Nujol) $\nu_{max}$ ($cm^{-1}$): 3700−3050 (N−H), 2930, 2860 (C−H), 1740, 1650 (C═O ester, amide). $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$: 0.82 (6H, t, $J$ = 6.8 Hz, 2 × -$CH_3$), 1.20−1.25 (46H, m, -$(CH_2)_{13}$-, -$(CH_2)_{11}$-), 1.40 (2H, m, -$CH_2$-), 1.89 (2H, m, ═CH-C$H_2$-), 1.99 (2H, t, $J$ = 7.4 Hz, -NHCOC$H_2$-), 3.33−3.56 and 3.91−3.95 (5H, 3H, 2 sets of m, H-1, H-2′, H-3′, H-4′, H-3, H-6′), 3.73 (1H, m, H-2), 3.85 (1H, t, $J$ = 7.8 Hz, H-5′), 4.13 (1H, d, $J$ = 7.7 Hz, H-1′), 4.42 (1H, d, $J$ = 4.7 Hz, -OH), 4.58 (1H, t, $J$ = 5.5 Hz, -OH-6′), 4.84 (1H, d, $J$ = 5.4 Hz, -OH), 5.07 (1H, d, $J$ = 2.4 Hz, -OH), 5.30 (1H, dd, $J$ = 15.4, 7.3 Hz, H-4), 5.50 (1H, dt, $J$ = 15.4, 6.7 Hz, H-5), 7.55 (1H, d, $J$ = 9.0 Hz, -NH-).

**Synthesis of (2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-hydroxy-1-[[2-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]-oxy]-4-octadecene (23). (2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-(*β*-D-galactopyranosyloxy)-4-octadecene (18).** (2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-(*β*-D-galactopyranosyloxy)-4-octadecene (**6**) (250 mg, 0.42 mmol) was reacted by the procedure used to synthesize compound **10** and afforded the title compound (260 mg, 77%) as a white solid.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3700−3100 (O−H, N−H), 3050, 2930, 2860 (C−H), 1720 (C═O ester), 1670 (C═O amide). $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$: 0.87−0.90 (6H, ≈t, 2 × -$CH_3$), 1.24−1.63 (48H, br m, -$(CH_2)_{13}$-, -$(CH_2)_{11}$-), 2.04 (2H, m, ═CH-C$H_2$-), 2.17−2.22 (2H, m, -NHCOC$H_2$-), 3.43 (1H, br t, H-5′), 3.53 (1H, dd, $J$ = 9.5, 3.3 Hz, H-3′), 3.66 (1H, dd, $J$ = 9.5, 7.7 Hz, H-2′), 3.71 (1H, dd, $J$ = 12.3, 3.9 Hz, H-1), 3.78−3.85 (2H, m, H-6′), 3.99−4.03 (2H, m, H-4′, H-1), 4.29 (1H, d, $J$ = 7.7 Hz, H-1′), 4.57−4.60 (1H, m, H-2), 5.50 (1H, dd, $J$ = 15.3, 7.4 Hz, H-4), 5.65 (1H, t, $J$ = 7.4 Hz, H-3), 5.92 (1H, dt, $J$ = 15.3, 6.9 Hz, H-5), 6.16 (1H, d, $J$ = 6.16 Hz, -NH-), 7.45−8.04 (5H, 3 sets of m, -$C_6H_5$).

**(2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[(3,4-*O*-isopropylidene-*β*-D-galactopyranosyl)oxy]-4-octadecene (19).** (2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-(*β*-D-galactopyranosyloxy)-4-octadecene (**18**) (0.170 g, 0.22 mmol) was reacted by the procedure used to synthesize compound **7** and afforded the title compound (0.160 g, 90%) as a white amorphous solid.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3680, 3600, 3425 (O−H, N−H), 3050, 2930, 2850 (C−H), 1720 (C═O ester), 1640 (C═O amide). $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$: 0.89 (6H, t, $J$ = 6.7 Hz, 2 × -$CH_3$), 1.25−1.35 (46H, m, -$(CH_2)_{13}$-, -$(CH_2)_{10}$-), 1.35 and 1.51 (2 × 3H, 2s, -C$(CH_3)_2$-), 1.57−1.66 (2H, m, -$CH_2$-), 2.02−2.08 and 2.18−2.21 (2 × 2H, 2 sets of m, -NHCOC$H_2$-, ═CH-C$H_2$-), 3.51 (1H, dd, $J$ = 7.1, 8.3 Hz, H-2′), 3.76−3.86 (3H, m, H-1, H-6′, H-5′), 3.95 (1H, dd, $J$ = 11.5, 7.1 Hz, H-1), 3.98 (1H, dd, $J$ = 11.2, 5.5 Hz, H-6′), 4.08 (1H, dd, $J$ = 7.1, 5.6 Hz, H-3′), 4.13 (1H, dd, $J$ = 5.6, 2.1 Hz, H-4′), 4.21 (1H, d, $J$ = 8.3 Hz, H-1′), 4.55 (1H, m, H-2), 5.52 (1H, ddt, $J$ = 15.4, 7.2, 1.3 Hz, H-4), 5.62 (1H, br t, H-3), 5.90 (1H, dt, $J$ = 15.4, 6.6 Hz, H-5), 5.97 (1H, d, $J$ = 9.2 Hz, -NH-), 7.44−7.53, 7.57−7.61, and 8.03−8.05 (5H, 3 sets of m, aromatic H).

**(2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[(3,4-*O*-isopropylidene-6-*O*-pivaloyl-*β*-D-galactopyranosyl)oxy]-4-octadecene (20).** A solution of (2*S*,3*R*,4*E*)-2-(hexadecanoylamino)-3-(benzoyloxy)-1-[(3,4-*O*-isopropylidene-*β*-D-galactopyranosyl)oxy]-4-octadecene (**19**) (80 mg, 0.1 mmol) in pyridine (2 mL) was treated with pivaloyl chloride (0.015 mL, 0.12 mmol) and 4-(dimethylamino)pyridine (∼5−10 mg). The mixture was stirred at 22 °C overnight, then diluted with ethyl acetate (10 mL), and washed with water (3 × 5 mL), 1 M aqueous sodium bicarbonate (3 × 5 mL), water (3 × 5 mL), and brine (5 mL). The organic phase was dried over anhydrous magnesium sulfate, filtered, and evaporated. The residue was purified by silica gel plates (50% ethyl acetate/hexane) and afforded the title compound (64 mg, 73%) as a white amorphous solid.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3690, 3500, 3430 (O−H, N−H), 3050, 2930, 2850 (C−H), 1725 (C═O ester), 1665 (C═O amide). $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$: 0.89 (6H, t, $J$ = 6.8 Hz, 2 × -$CH_3$), 1.18 (9H, s, -OCOtBu), 1.25−1.37 (46H, m, -$(CH_2)_{13}$-, -$(CH_2)_{10}$-), 1.33 and 1.49 (2 × 3H, 2s, -C$(CH_3)_2$-), 1.57−1.63 (2H, m, -$CH_2$-), 2.04 (2H, qa, $J$ = 7.0 Hz, ═CH-C$H_2$-), 2.17−2.19 (2H, m, -NHCOC$H_2$-), 3.2 (1H, br s, -OH), 3.48 (1H, dd, $J$ = 7.0, 7.2 Hz, H-2′), 3.76 (1H, dd, $J$ = 11.1, 3.8 Hz, H-1), 3.96 (1H, ddd, $J$ = 7.3, 5.8, 2.2 Hz, H-5′), 4.02 (1H, dd, $J$ = 11.1, 6.8 Hz, H-1), 4.07 (1H, dd, $J$ = 6.9, 5.5 Hz, H-3′), 4.11 (1H, dd, $J$ = 5.5, 2.1 Hz, H-4′), 4.18 (1H, d, $J$ = 8.2 Hz, H-1′), 4.26 (1H, dd, $J_{AB}$ = 11.4 Hz, $J_{AX}$ = 7.3 Hz, H-6′), 4.31 (1H, dd, $J_{AB}$ = 11.4 Hz, $J_{BX}$ = 5.7 Hz, H-6′), 4.52 (1H, m, H-2), 5.49 (1H, ddt, $J$ = 15.0, 7.1, 1.3 Hz, H-4), 5.56 (1H, dd, $J$ = 7.1, 5.5 Hz, H-3), 3.88 (1H, dt, $J$ = 15.0, 6.9 Hz, H-5), 6.01 (1H, d, $J$ = 9.1 Hz, -NH-), 7.44−7.48, 7.53−7.61, and 8.02−8.04 (5H, 3 sets of m, aromatic H).

**(2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[[3,4-*O*-isopropylidene-6-*O*-pivaloyl-2-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (21).** (2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[(3,4-*O*-

isopropylidene-6-*O*-pivaloyl-β-D-galactopyranosyl)oxy]-4-octadecene (**20**) (61 mg, 0.066 mmol) was reacted by the procedure used to synthesize compound **16** and afforded the title compound (47 mg, 69%) as a white solid.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3680 (N−H), 3050, 2930, 2850 (C−H), 1725 (C═O ester), 1670 (C═O amide). $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$: 0.89 (6H, br t, 2 × -$CH_3$), 1.17 (9H, s, -OCOtBu), 1.17−1.29 (48H, m, -$(CH_2)_{13}$-, -$(CH_2)_{11}$-), 1.29 and 1.54 (2 × 3H, 2s, -C$(CH_3)_2$-), 1.96 (2H, br qa, ═CH-C$H_2$-), 2.22 (2H, m, -NHCOC$H_2$-), 3.6−4.6 (10H, br dd, s, br t, 6 sets of m, H-2, H-1, H-1′, H-2′, H-3′, H-4′, H-5′, H-6′), 5.45 (1H, dd, $J$ = 15.3, 7.1 Hz, H-4), 5.60 (1H, t, $J$ = 7.1 Hz, H-3), 5.88 (1H, dt, $J$ = 15.3, 6.4 Hz, H-5), 6.66 (1H, br s, -NH-), 7.34−7.43, 7.53−7.56, 8.00−8.02 (5H, 3 sets of m, aromatic H).

**(2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[[6-*O*-pivaloyl-2-*O*-(sodium oxysulfonyl)-β-D-galactopyranosyl]oxy]-4-octadecene (22).** (2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[[3,4-*O*-isopropylidene-6-*O*-pivaloyl-2-*O*-(sodium oxysulfonyl)-β-D-galactopyranosyl]oxy]-4-octadecene (**21**) (52 mg, 0.05 mmol) was reacted by the procedure used to synthesize compound **14** and afforded the title compound (∼50 mg, crude) which was used for the next step without purification.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3680-3200 (N−H, O−H), 3050, 2930, 2860 (C−H), 1725 (C═O ester), 1650 (C═O amide). $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$: 0.9 (6H, br t, 2 × -$CH_3$), 1.0 (9H, s, -OCOtBu), 1.2 (46H, m, -$(CH_2)_{13}$-, -$(CH_2)_{10}$-), 1.5 (2H, m, -$CH_2$-), 1.9 and 2.2 (2 × 2H, 2 sets of m, -NHCOC$H_2$-, ═CH-C$H_2$-), 3.4−4.6 (10H, 5 sets of m, H-2, H-1, H-1′, H-2′, H-3′, H-4′, H-5′, H-6′), 5.4−6.0 (4H, 3 sets of m, H-5, H-4, H-3, -NH-), 7.4−7.6 and 8.01−8.04 (5H, 3 sets of m, aromatic H).

**(2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-hydroxy-1-[[2-*O*-(sodium oxysulfonyl)-β-D-galactopyranosyl]oxy]-4-octadecene (23).** (2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[[6-*O*-pivaloyl-2-*O*-(sodium oxysulfonyl)-β-D-galactopyranosyl]oxy]-4-octadecene (**22**) (50 mg, 0.05 mmol) was reacted by the procedure used to synthesize compound **11** and gave the title compound (30 mg, 75%) as a beige solid.

IR (Nujol) $\nu_{max}$ ($cm^{-1}$): 3700−3100 (N−H, O−H), 2920, 2850 (C−H), 1635 (C═O amide). $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$: 0.85 (6H, t, $J$ = 6.8 Hz, 2 × -$CH_3$), 1.23−1.31 (46H, m, -$(CH_2)_{13}$-, -$(CH_2)_{10}$-), 1.41 (2H, m, -$CH_2$-), 1.90 (2H, m, ═CH-C$H_2$-), 2.08 (2H, m, -NHCOC$H_2$-), 3.25−3.39 and 3.46−3.53 (2H, 3H, 2 sets of m, H-4′ or H-5′, H-6′, H-1), 3.66 (1H, br t, H-4′ or H-5′), 3.71 (1H, dt, $J$ = 9.0, 3.0 Hz, H-2), 3.86 (1H, br qa, H-3), 4.11 (1H, dd, $J$ = 9.5, 7.6 Hz, H-2′), 4.13 (1H, dd, $J$ = 9.3, 2.8 Hz, H-3′), 4.23 (1H, d, $J$ = 7.6 Hz, H-1′), 4.56 (1H, d, $J$ = 3.8 Hz, -OH), 4.61 (1H, t, $J$ = 5.6 Hz, -OH-6′), 4.81 (1H, d, $J$ = 5.6 Hz, -OH), 4.99 (1H, d, $J$ = 1.4 Hz, -OH-3′), 5.31 (1H, dd, $J$ = 15.3, 7.2 Hz, H-4), 5.49 (1H, dt, $J$ = 15.3, 6.6 Hz, H-5), 7.39 (1H, d, $J$ = 9.2 Hz, -NH-). MS (CI, $NH_3$): 778 ($M - Na$)$^-$.

**Synthesis of (2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-hydroxy-1-[[4-*O*-(sodium oxysulfonyl)-β-D-galactopyranosyl]oxy]-4-octadecene (30). (2*S*,3*R*,4*E*)-2-Azido-1-[(4,6-*O*-benzylidene-β-D-galactopyranosyl)oxy]-4-octadecene (24).** A solution of (2*S*,3*R*,4*E*)-2-azido-3-(benzoyloxy)-1-[(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)oxy]-4-octadecene (**4**) (1.0 g, 1.3 mmol) was treated as described by Schmidt[13] to give (2*S*,3*R*,4*E*)-2-azido-1-(β-D-galactopyranosyloxy)-4-octadecene (**5**). This crude material was then dissolved in formic acid (5 mL) and treated with benzaldehyde (5 mL), and this mixture was stirred at 22 °C for 0.75 h. The mixture was then diluted with ethyl acetate (50 mL), cooled down to 5 °C, and neutralized with solid sodium bicarbonate and 1 M aqueous sodium bicarbonate. The organic phases were separated, and the aqueous phase was extracted with ethyl acetate (2 × 30 mL). The combined organic extracts were washed with 1 M aqueous sodium bicarbonate (30 mL), water (30 mL), and brine (30 mL). The organic phase was dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by silica gel chromatography (0−90% ethyl acetate/hexane) and afforded the title compound (0.418 g, 56%) as a white solid.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3600−3400 (O−H), 3050, 2930, 2860 (C−H), 2100 (−$N_3$). $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$: 0.89 (3H, t, $J$ = 6.8 Hz, -$CH_3$), 1.27−1.35 (20H, m, -$(CH_2)_{10}$-), 1.40 (2H, m, -$CH_2$-), 2.08 (2H, qa, $J$ = 6.8 Hz, ═CH-C$H_2$-), 2.49 (1H, br s, -OH), 2.53 (1H, d, $J$ = 8.9 Hz, -OH-3′), 2.69 (1H, br s, -OH), 3.51 (1H, d, $J$ = 1.0 Hz, H-5′), 3.57 (1H, m, H-2), 3.70 (1H, ddd, $J$ = 9.4, 8.9, 3.7 Hz, H-3′), 3.80 (1H, dd overlapped by H-1, $J$ = 9.2, 8.1 Hz, H-2′), 3.81 (1H, dd, $J$ = 10.7, 3.9 Hz, H-1), 4.09 (1H, dd, $J$ = 12.5, 1.8 Hz, H-6′), 4.16 (1H, dd, $J$ = 10.6, 5.5 Hz, H-1), 4.22 (1H, dd, $J$ = 3.6, 0.8 Hz, H-4′), 4.30 (1H, br t, H-3), 4.34 (1H, d, $J$ = 12.5, 1.4 Hz, H-6′), 4.37 (1H, d, $J$ = 7.6 Hz, H-1′), 5.53 (1H, ddt, $J$ = 15.4, 7.3, 1.2 Hz, H-4), 5.56 (1H, s, -OCHO-), 5.83 (1H, dt, $J$ = 15.4, 6.8 Hz, H-5), 7.36−7.40 and 7.49−7.52 (5H, 2 sets of m, aromatic H).

**(2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-[(2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)oxy]-4-octadecene (25).** (2*S*,3*R*,4*E*)-2-Azido-1-[(4,6-*O*-benzylidene-β-D-galactopyranosyl)oxy]-4-octadecene (**24**) (0.597 g, 1.03 mmol) was reacted by the procedure used to synthesize compound **12** and gave the title compound (1.21 g, crude, quantitive) which was used as such for the next reaction without any further purification.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3050, 2930, 2860 (C−H), 2110 (−$N_3$), 1730 (C═O), 1265 (C−O). $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$: 0.89 (3H, t, $J$ = 6.8 Hz, -$CH_3$), 1.23−1.33 (22H, m, -$(CH_2)_{11}$-), 1.93 (2H, m, ═CH-C$H_2$-), 3.69−3.74 (2H, m, H-1, -$CHN_3$-), 3.97−4.02 (2H, m, H-1, H-5′), 4.15 (1H, dd, $J$ = 12.4, 1.5 Hz, H-6′), 4.42 (1H, dd, $J$ = 12.4, 1.3 Hz, H-6′), 4.61 (1H, d, $J$ = 3.4 Hz, H-4′), 4.83 (1H, d, $J$ = 8.0 Hz, H-1′), 5.40 (1H, dd, $J$ = 10.4, 3.4 Hz, H-3′), 5.46−5.56 (2H, m overlapping -O-CH-O-, H-4, H-3), 5.56 (1H, s, -O-CH-O-), 5.73 (1H, dt, $J$ = 15.2, 6.7 Hz, H-5), 5.91 (1H, dd, $J$ = 10.4, 8.0 Hz, H-2′), 7.27−8.04 (20 H, 2m, 4 × -$C_6H_5$).

**(2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-[(2,3-di-*O*-benzoyl-β-D-galactopyranosyl)oxy]-4-octadecene (26).** A solution of (2*S*,3*R*,4*E*)-2-azido-3-(benzoyloxy)-1-[(2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)oxy]-4-octadecene (**25**) (1.21 g, 1.03 mmol, crude) in dichloromethane (50 mL) was treated with 50% aqueous trifluoroacetic acid (10 mL) at 22 °C. The resulting mixture was stirred for 3 h, then cooled down to 5 °C, and neutralized with 1 M aqueous sodium bicarbonate and solid sodium bicarbonate. The aqueous phase was extracted with ethyl acetate (3 × 100 mL), and the combined extracts were washed with 1 M aqueous sodium bicarbonate (2 × 25 mL), water (2 × 25 mL), and brine (25 mL). The organic phase was dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by silica gel chromatography (0−50% ethyl acetate/hexane) and afforded the title compound (0.729 g, 88%) as a yellow oil.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3700−3400 (O−H), 3050, 2930, 2860 (C−H), 2110 (−$N_3$), 1730 (C═O). $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$: 0.89 (3H, t, $J$ = 6.9 Hz, -$CH_3$), 1.23−1.34 (22H, m, -$(CH_2)_{11}$-), 2.01 (2H, qa, $J$ = 6.9 Hz, ═CH-C$H_2$-), 3.71−3.75 and 4.00−4.06 (2 × 2H, 2 sets of m, H-1, H-2, H-5′, H-6′), 3.87 (1H, dd, $J$ = 10.9, 6.2 Hz, H-1), 3.95 (1H, dd, $J$ = 12.3, 3.8 Hz, H-6′), 4.45 (1H, br d, H-4′), 4.78 (1H, d, $J$ = 7.9 Hz, H-1′), 5.29 (1H, dd, $J$ = 10.3, 3.2 Hz, H-3′), 5.54 (1H, ddt, $J$ = 15.5, 8.1, 1.3 Hz, H-4), 5.76 (1H, dd, $J$ = 8.1, 4.2 Hz, H-3), 5.85 (1H, dd, $J$ = 10.3, 7.9 Hz, H-2′), 5.88 (1H, dt, $J$ = 15.5, 6.9 Hz, H-5), 7.35−7.39, 7.44−7.53, 7.56−7.61, 7.95−8.01, and 8.04−8.10 (15H, 5 sets of m, aromatic H).

**(2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-[(2,3-di-*O*-benzoyl-6-*O*-pivaloyl-β-D-galactopyranosyl)oxy]-4-octadecene (27).** (2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-[(2,3-di-*O*-benzoyl-β-D-galactopyranosyl)oxy]-4-octadecene (**26**) (0.711 g, 0.89 mmol) was reacted by the procedure used to synthesize compound **20** and afforded the title compound (0.254 g, 32%) as a colorless oil along with (2*S*,3*R*,4*E*)-2-azido-3-(benzoyloxy)-1-[(2,3-di-*O*-benzoyl-4,6-di-*O*-pivaloyl-β-D-galactopyranosyl)oxy]-4-octadecene (0.460 g, 53%) as a yellow oil.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3700−3400 (O−H), 3050, 2930, 2860 (C−H), 2110 (−$N_3$), 1730 (C═O). $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$: 0.89 (3H, t, $J$ = 6.9 Hz, -$CH_3$), 1.17−1.32 (31H, m, -$(CH_2)_{11}$-, -OCOtBu), 1.95 (2H, qa, $J$ = 6.7 Hz, ═CH-C$H_2$-), 2.42 (1H, br s, -OH), 3.64 and 3.91−3.97 (1H, 3H, qa, m, H-1, H-2, H-5′), 4.24 (1H, br s, H-4′), 4.32 (1H, dd, $J_{AB}$ = 11.4, $J_{AX}$ = 6.5 Hz, H-6′), 4.40 (1H, dd, $J_{AB}$ = 11.4, $J_{BX}$ = 6.4 Hz, H-6′), 4.74 (1H, d, $J$ = 7.9 Hz, H-1′), 5.33 (1H, dd, $J$ = 10.3, 3.3 Hz, H-3′), 5.48 (1H, dd, $J$ = 15.3, 8.0 Hz, H-4), 5.57 (1H, dd, $J$ = 8.1, 3.6 Hz, H-3), 5.72−5.79 (1H, m overlapped by H-2′, H-5), 5.77 (1H,

dd, $J$ = 10.3, 7.9 Hz, H-2′), 7.35−7.59 and 7.96−8.04 (15H, 2 sets of m, aromatic H).

**(2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[(2,3-di-*O*-benzoyl-6-*O*-pivaloyl-β-D-galactopyranosyl)oxy]-4-octadecene (28).** (2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-[(2,3-di-*O*-benzoyl-6-*O*-pivaloyl-β-D-galactopyranosyl)oxy]-4-octadecene (**27**) (0.250 g, 0.28 mmol) was reacted by the procedure used to synthesize compound **10** and afforded the title compound (0.092 g, 30%) as a white solid.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3700−3400 (O−H, N−H), 3050, 2930, 2860 (C−H), 1730, 1670 (C═O). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$: 0.89 (6H, t, $J$ = 6.8 Hz, 2 × -$CH_3$), 1.12−1.44 (46H, m, -$(CH_2)_{13}$-, -$(CH_2)_{10}$-), 1.16 (9H, s, -OCOC$(CH_3)_3$), 1.58−1.68 (2H, m, -$CH_2$-), 1.81 (2H, t, $J$ = 7.7 Hz, -NHCOC$H_2$-), 2.01 (2H, qa, $J$ = 6.9 Hz, ═CH-C$H_2$-), 3.63 (1H, dd, $J$ = 9.8, 3.8 Hz, H-1), 3.85 (1H, t, $J$ = 6.4 Hz, H-5′), 4.06 (1H, dd, $J$ = 11.4, 6.4 Hz, H-6′), 4.17 (1H, dd, $J$ = 9.8, 3.0 Hz, H-1), 4.18 (1H, br s, H-4′), 4.28 (1H, dd, $J$ = 11.4, 6.5 Hz, H-6′), 4.44 (1H, m, H-2), 4.64 (1H, d, $J$ = 7.8 Hz, H-1′), 5.33 (1H, dd, $J$ = 10.4, 3.1 Hz, H-3′), 5.48 (1H, dd, $J$ = 15.3, 7.4 Hz, H-4), 5.58 (1H, br t, H-3), 5.70 (1H, dd, $J$ = 10.4, 7.8 Hz, H-2′), 5.85 (1H, dt, $J$ = 15.3, 6.9 Hz, H-5), 7.36−7.59, 7.94−8.00, and 8.04−8.06 (16H, 3 sets of m, aromatic H, -NH-).

**(2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[[2,3-di-*O*-benzoyl-6-*O*-pivaloyl-4-*O*-(sodium oxysulfonyl)-β-D-galactopyranosyl]oxy]-4-octadecene (29).** (2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[(2,3-di-*O*-benzoyl-6-*O*-pivaloyl-β-D-galactopyranosyl)oxy]-4-octadecene (**28**) (0.085 g, 0.078 mmol) was reacted by the procedure used to synthesize compound **16** and afforded the title compound (0.072 g, 77%) as a white solid.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3700−3400 (N−H), 3050, 2930, 2860 (C−H), 1725, 1670 (C═O). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$: 0.88 (6H, br t, 2 × -$CH_3$), 1.00 (9H, s, -OCOtBu), 1.03−1.37 (48H, m, -$(CH_2)_{13}$-, -$(CH_2)_{10}$-), 1.68 (2H, t, $J$ = 7.3 Hz, -NHCOC$H_2$-), 1.95 (2H, m, ═CH-C$H_2$-), 3.59, 3.95, 4.08−4.10, and 4.40−4.49 (1H, 1H, 2H, 2H, br d, br s, 2 sets of m, H-5′, H-6′, H-2, H-1), 4.66 (1H, d, $J$ = 7.7 Hz, H-1′), 5.13 (1H, br s, H-4′), 5.35 (1H, br d, H-3′), 5.44 (1H, dd, $J$ = 15.1, 7.4 Hz, H-4), 5.55 (1H, t, $J$ = 7.2 Hz, H-3), 5.70 (1H, dd, $J$ = 10.0, 7.7 Hz, H-2′), 5.80 (1H, dt, $J$ = 15.1, 6.7 Hz, H-5), 7.35−7.42, 7.49−7.53, and 7.96−8.02 (16H, 3 sets of m, aromatic H, -NH-).

**(2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-hydroxy-1-[[4-*O*-(sodium oxysulfonyl)-β-D-galactopyranosyl]oxy]-4-octadecene (30).** (2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[[2,3-di-*O*-benzoyl-6-*O*-pivaloyl-4-*O*-(sodium oxysulfonyl)-β-D-galactopyranosyl]oxy]-4-octadecene (**29**) (0.070 g, 0.058 mmol) was reacted by the procedure used to synthesized compound **11** and gave the title compound (12 mg, 26%) as a beige solid.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3700−3050 (N−H, O−H), 2930, 2850 (C−H), 1640 (C═O). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$: 0.85 (6H, t, $J$ = 6.7 Hz, 2 × -$CH_3$), 1.23−1.27 (46H, m, -$(CH_2)_{13}$-, -$(CH_2)_{10}$-), 1.44 (2H, m, -$CH_2$-), 1.92−2.04 (4H, m, -NHCOC$H_2$-, ═CH-C$H_2$-), 3.23 (1H, dd, $J$ = 9.3, 7.6 Hz, H-2′), 3.29−3.52 (5H, m, H-1, H-3′, H-5′, H-6′), 3.75 (1H, m, H-2), 3.89 (1H, br t, H-3), 3.98 (1H, dd, $J$ = 9.9, 4.4 Hz, H-1), 4.05 (1H, d, $J$ = 7.6 Hz, H-1′), 4.38 (1H, d, $J$ = 3.1 Hz, H-4′), 4.45 (1H, br s, -OH), 4.69 (1H, d, $J$ = 6.1 Hz, -OH), 4.90 and 5.03 (2H, 2br s, 2 × -OH), 5.34 (1H, d, $J$ = 15.3, 7.1 Hz, H-4), 5.52 (1H, dt, $J$ = 15.3, 6.7 Hz, H-5), 7.51 (1H, d, $J$ = 9.0 Hz, -NH-). MS (CI, $NH_3$): 778 (M − Na)$^-$.

**Disulfated Compounds. Synthesis of (2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-hydroxy-1-[[2,6-bis-*O*-(sodium oxysulfonyl)-β-D-galactopyranosyl]oxy]-4-octadecene (32). (2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[[2,6-bis-*O*-(sodium oxysulfonyl)-β-D-galactopyranosyl]oxy]-4-octadecene (31).** (2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-(benzoyloxy)-1-[(3,4-*O*-isopropylidene-β-D-galactopyranosyl)oxy]-4-octadecene (**19**) (160 mg, 0.19 mmol) was reacted by the procedure used to synthesize compounds **16** and **14** and gave the title compound (115 mg, 60%) as a white solid.

IR (Nujol) $\nu_{max}$ ($cm^{-1}$): 3700−3100 (O−H, N−H), 2930, 2860 (C−H), 1715 (C═O ester), 1650 (C═O amide), 1270, 1010 (S═O). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$: 0.85 (6H, t, $J$ = 6.8 Hz, 2 × -$CH_3$), 1.21−1.44 (48H, br m, -$(CH_2)_{13}$-, -$(CH_2)_{11}$-), 1.97 (2H, m, ═CH-C$H_2$-), 2.02−2.21 (2H, m, -NHCOC$H_2$-), 3.45−3.51 (2H, m, H-1, H-3′), 3.58 (1H, br t, $J$ = 6.1 Hz, H-5′), 3.62 (1H, t, $J$ = 3.9 Hz, H-4′), 3.74 (1H, dd, $J$ = 10.6, 6.3 Hz, H-6′), 3.82 (1H, dd, $J$ = 10.6, 5.7 Hz, H-6′), 3.97 (1H, dd, $J$ = 9.8, 4.5 Hz, H-1), 4.15 (1H, dd, $J$ = 9.4, 7.8 Hz, H-2′), 4.24−4.28 (1H, m, H-2), 4.27 (1H, d, $J$ = 7.6 Hz, H-1′), 4.69 (1H, d, $J$ = 3.9 Hz, -OH), 5.09 (1H, d, $J$ = 1.4 Hz, -OH), 5.39 (1H, t, $J$ = 7.6 Hz, H-3), 5.45 (1H, dd, $J$ = 15.0, 7.6 Hz, H-4), 5.76 (1H, dt, $J$ = 15.0, 6.8 Hz, H-5), 7.73 (1H, d, $J$ = 8.9 Hz, -NH-), 7.48−7.98 (5H, 3m, -$C_6H_5$).

**(2*S*,3*R*,4*E*)-2-(Hexadecanoylamino)-3-hydroxy-1-[[2,6-bis-*O*-(sodium oxysulfonyl)-β-D-galactopyranosyl]oxy]-4-octadecene (32).** (2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[[2,6-bis-*O*-(sodium oxysulfonyl)-β-D-galactopyranosyl]oxy]-4-octadecene (**31**) (0.243 g, 0.24 mmol) was reacted by the procedure used to synthesize compound **11** and afforded the title compound (0.17 g, 78%) as a pale beige solid.

IR (Nujol) $\nu_{max}$ ($cm^{-1}$): 3700−3100 (O−H, N−H), 2920, 2860 (C−H), 1650 (C═O amide). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$: 0.85 (6H, t, $J$ = 6.8 Hz, 2 × -$CH_3$), 1.23−1.43 (48H, br m, -$(CH_2)_{13}$-, -$(CH_2)_{11}$-), 1.89 (2H, m, ═CH-C$H_2$-), 2.00−2.16 (2H, m, -NHCOC$H_2$-), 3.27 (1H, dd, $J$ = 9.3, 3.3 Hz, H-1), 3.47 (1H, dd, $J$ = 9.6, 3.1 Hz, H-3′), 3.58 (1H, br t, H-5′), 3.63 (1H, d, $J$ = 3.1 Hz, H-4′), 3.70 (1H, m, H-3), 3.76−3.86 (1H, m overlapping H-6′, H-2), 3.79 (1H, dd, $J$ = 10.6, 6.5 Hz, H-6′), 3.84 (1H, dd, $J$ = 10.6, 5.6 Hz, H-6′), 4.09 (1H, dd, $J$ = 9.6, 7.7 Hz, H-2′), 4.15 (1H, dd, $J$ = 9.3, 2.7 Hz, H-1), 4.24 (1H, d, $J$ = 7.7 Hz, H-1′), 4.68 (1H, br s, -OH), 4.87 (1H, d, $J$ = 3.8 Hz, -OH), 4.95 (1H, br s, -OH), 5.30 (1H, dd, $J$ = 15.4, 7.2 Hz, H-4), 5.48 (1H, dt, $J$ = 15.4, 6.6 Hz, H-5), 7.41 (1H, d, $J$ = 9.2 Hz, -NH-).

**Synthesis of (2*S*,3*R*,4*E*)-3-Hydroxy-2-(hexadecanoylamino)-1-[[3,6-bis-*O*-(sodium oxysulfonyl)-β-D-galactopyranosyl]oxy]-4-octadecene (41). (2*S*,3*R*,4*E*)-2-Azido-3-hydroxy-1-[(3,4-*O*-isopropylidene-β-D-galactopyranosyl)oxy]-4-octadecene (33).** (2*S*,3*R*,4*E*)-2-Azido-3-hydroxy-1-(β-D-galactopyranosyloxy)-4-octadecene (**5**) (0.50 g, 1.07 mmol) was reacted by the procedure used to synthesize compound **7** and afforded the title compound (0.425 g, 75%).

$^1$H NMR (200 MHz, $CDCl_3$) $\delta$: 0.88 (3H, t, $J$ = 6.8 Hz, -$CH_3$), 1.25 (22H, m, -$(CH_2)_{11}$-), 1.35 and 1.53 (2 × 3H, 2s, $(CH_3)_2$-C-), 1.64−2.13 (5H, m, ═CH-C$H_2$-, 3 × -OH), 3.44 (1H, m, H-2), 3.59 (1H, t, $J$ = 7.4 Hz, H-1), 3.81−4.35 (9H, m, H-1′, H-2′, H-3′, H-4′, H-5′, H-6′, H-1, H-3), 5.53 (1H, m, H-4), 5.86 (1H, m, H-5).

**(2*S*,3*R*,4*E*)-2-Azido-3-hydroxy-1-[[3,4-*O*-isopropylidene-6-*O*-(*tert*-butyldimethylsilyl)-β-D-galactopyranosyl]oxy]-4-octadecene (34).** *tert*-Butyldimethylsilyl chloride (425 mg, 2.82 mmol) was added to a stirred solution of (2*S*,3*R*,4*E*)-2-azido-3-hydroxy-1-[(3,4-*O*-isopropylidene-β-D-galactopyranosyl)oxy]-4-octadecene (**33**) (425 mg, 0.805 mmol) in pyridine (20 mL) at −20 °C and under argon. The reaction mixture was stirred at −20 °C overnight; then methanol was added. The mixture was stirred again for 2 more hours at 22 °C. The reaction mixture was then poured into water and diluted with ethyl acetate (150 mL). The organic layer was washed with water (5×) and brine, dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by silica gel chromatography and afforded the title compound (537 mg, 100%).

$^1$H NMR (200 MHz, $CDCl_3$) $\delta$: 0.08 (6H, s, -Si$(CH_3)_2$), 0.88 (3H, t, $J$ = 6.7 Hz, -$CH_2$-C$H_3$), 0.90 (9H, s, -C$(CH_3)_3$), 1.25 (22H, m, -$(CH_2)_{11}$-), 1.34 and 1.53 (2 × 3H, 2s, $(CH_3)_2$-C-), 1.66−2.11 (4H, m, ═CH-C$H_2$-, 2 × -OH), 3.45 (1H, m, H-2), 3.57 (1H, t, H-1), 3.80−4.32 (9H, m, H-1′, H-2′, H-3′, H-4′, H-5′, H-6′, H-1, H-3), 5.53 (1H, m, H-4), 5.84 (1H, m, H-5).

**(2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-[[2-*O*-benzoyl-3,4-*O*-isopropylidene-6-*O*-(*tert*-butyldimethylsilyl)-β-D-galactopyranosyl]oxy]-4-octadecene (35).** (2*S*,3*R*,4*E*)-2-Azido-3-hydroxy-1-[[3,4-*O*-isopropylidene-6-*O*-(*tert*-butyldimethylsilyl)-β-D-galactopyranosyl]oxy]-4-octadecene (**34**) (537 mg, 0.837 mmol) was reacted by the procedure used to synthesize compound **12** and afforded the title compound (572 mg, 80%).

$^1$H NMR (200 MHz, $CDCl_3$) $\delta$: 0.09 (6H, s, -Si$(CH_3)_2$), 0.84−0.94 (3H, m overlapping -C$(CH_3)_3$, -$CH_2$-C$H_3$), 0.90 (9H, s, -C$(CH_3)_3$), 1.25 (22H, m, -$(CH_2)_{11}$-), 1.34 and 1.57 (2 × 3H, 2s,

$(CH_3)_2$-C-), 1.92 (2H, m, =CH-C$H_2$-), 3.54 (1H, m, H-2), 3.86−3.95 and 4.26−4.38 (7H, 2m, H-3′, H-4′, H-5′, H-6′, H-1), 4.51 (1H, d, $J$ = 8.1 Hz, H-1′), 5.22−5.78 (4H, m, H-3, H-4, H-5, H-2′), 7.30−8.08 (10H, 2m, 2 × -$C_6H_5$).

**(2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[[2-*O*-benzoyl-3,4-*O*-isopropylidene-6-*O*-(*tert*-butyldimethylsilyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (36).** (2*S*,3*R*,4*E*)-2-azido-3-(benzoyloxy)-1-[[2-*O*-benzoyl-3,4-*O*-isopropylidene-6-*O*-(*tert*-butyldimethylsilyl)-*β*-D-galactopyranosyl]-oxy]-4-octadecene (**35**) (572 mg, 0.673 mmol) was reacted by the procedure used to synthesize compound **10** and afforded the title compound (575 mg, 96%).

$^1$H NMR (200 MHz, $CDCl_3$) $\delta$: 0.02 and 0.04 (2 × 3H, 2s, -Si$(CH_3)_2$), 0.85−0.91 (6H, m overlapping -C$(CH_3)_3$, 2 × -$CH_2$-C$H_3$), 0.86 (9H, s, -C$(CH_3)_3$), 1.13−1.38 (48H, m, -$(CH_2)_{11}$-, -$(CH_2)_{13}$-), 1.34 and 1.60 (2 × 3H, 2s, (C$H_3$)$_2$-C-), 1.74 (2H, ap t, $J$ = 7.5 Hz, =CH-C$H_2$-), 1.98 (2H, m, -C$H_2$CONH-), 3.57 (1H, dd, $J$ = 3.9, 9.9 Hz, H-1), 3.69−3.89 (3H, m, H-6′, H-5′), 4.11 (1H, dd, $J$ = 3.1, 9.9 Hz, H-1), 4.25−4.36 (3H, m, H-2, H-3′, H-4′), 4.41 (1H, d, $J$ = 8.1 Hz, H-1′), 5.19 (1H, dd, $J$ = 7.1, 8.0 Hz, H-3), 5.40−5.52 (2H, m, H-2′, H-4), 5.71 (1H, d overlapping H-5, $J$ = 9.3 Hz, -NH-), 5.77 (1H, dt, $J$ = 14.3, 6.9 Hz, H-5), 7.39 (10H, 3m, 2 × -$C_6H_5$).

**(2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[[2-*O*-benzoyl-6-*O*-(*tert*-butyldimethylsilyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (37).** Trifluoroacetic acid (90%, ≈4 mL) was added to a stirred solution of (2*S*,3*R*,4*E*)-3-(benzoyloxy)-2-(hexadecanoylamino)-1-[[2-*O*-benzoyl-3,4-*O*-isopropylidene-6-*O*-(*tert*-butyldimethylsilyl)-*β*-D-galactopyranosyl]-oxy]-4-octadecene (**36**) (575 mg, 0.649 mmol) in dichloromethane (75 mL) at 22 °C. The reaction mixture was stirred at 22 °C and monitored by TLC. The solvents were evaporated, and the residue was dissolved in ethyl acetate. The organic layer was washed with a 10% aqueous solution of sodium bicarbonate, water, and brine, dried over anhydrous magnesium sulfate, filtered, and concentrated.

The residue was dissolved in pyridine (25 mL) and treated with *tert*-butyldimethylsilyl chloride (425 mg, 2.82 mmol) at −15 °C. The reaction mixture was stirred at −15 °C overnight; then methanol was added. The mixture was stirred again for 2 more hours at 22 °C. The reaction mixture was then poured into water and diluted with ethyl acetate (150 mL). The organic layer was washed with water (5x) and brine, dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by silica gel chromatography and afforded the title compound.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$: 0.01 and 0.03 (2 × 3H, 2s, -Si$(CH_3)_2$), 0.86 (9H, s overlapping -$CH_3$, -C$(CH_3)_3$), 0.86−0.90 (6H, m, 2 × -$CH_2$-C$H_3$), 1.10−1.26 (46H, m, -$(CH_2)_{10}$-, -$(CH_2)_{13}$-), 1.64 (2H, m, -$CH_2$-), 1.78 (2H, t, $J$ = 7.6 Hz, =CH-C$H_2$-), 1.98 (2H, m, -C$H_2$CONH-), 3.48 (1H, t, H-5′), 3.60 (1H, dd, $J$ = 9.4, 3.4 Hz, H-1), 3.66 (1H, dd, $J$ = 10.5, 4.3 Hz, H-6′), 3.75−3.81 (2H, m, H-6′, H-3′), 4.07 (1H, d, $J$ = 3.1 Hz, H-4′), 4.13 (1H, d, H-1), 4.42 (1H, m, H-2), 4.48 (1H, d, $J$ = 7.8 Hz, H-1′), 5.25 (1H, dd, $J$ = 8.8, 8.8 Hz, H-2′), 5.44 (1H, dd, $J$ = 15.3, 7.6 Hz, H-4), 5.53 (1H, dd, $J$ = 7.4, 7.4 Hz, H-3), 5.77 (1H, d, $J$ = 9.2 Hz, -NH-), 5.84 (1H, dt, $J$ = 15.3, 6.7 Hz, H-5), 7.43−8.06 (10H, 3m, 2 × -$C_6H_5$).

**(2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[[2-*O*-benzoyl-4-*O*-acetyl-6-*O*-(*tert*)-butyldimethylsilyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (38).** The title compound was prepared from **37** according to the procedure used to synthesize compound **15**.

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$: −0.03 and −0.01 (2 × 3H, 2s, -Si$(CH_3)_2$), 0.82 (9H, s overlapping -$CH_3$, -C$(CH_3)_3$), 0.82−0.85 (6H, m, 2 × -$CH_2$-C$H_3$), 1.13−1.35 (48H, m, -$(CH_2)_{11}$-, -$(CH_2)_{13}$-), 1.76−1.94 (4H, m, =CH-C$H_2$-, -C$H_2$CONH-), 2.07 (3H, s, $CH_3$CO-), 3.47−3.56 (3H, m, H-6′, H-1), 3.72 (1H, dd, $J$ = 10.0, 6.5 Hz, H-1), 3.81 (1H, t, H-5′), 3.94−3.99 (1H, m, H-3′), 4.29 (1H, m, H-2), 4.62 (1H, d, $J$ = 8.0 Hz, H-1′), 5.01 (1H, dd, $J$ = 9.9, 8.0 Hz, H-2′), 5.24 (1H, d, $J$ = 3.4 Hz, H-4′), 5.30 (1H, dd, $J$ = 7.2, 4.7 Hz, H-3), 5.37−5.43 (2H, m, H-4, -NH-), 5.48 (1H, dt, $J$ = 15.2, 6.3 Hz, H-5), 7.44−7.95 (10H, 4m, 2 × -$C_6H_5$).

**(2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[(2-*O*-benzoyl-4-*O*-acetyl-*β*-D-galactopyranosyl)oxy]-4-octadecene (39).** A solution of (2*S*,3*R*,4*E*)-3-(benzoyloxy)-2-(hexadecanoylamino)-1-[[2-*O*-benzoyl-4-*O*-acetyl-6-*O*-(*tert*-butyldimethylsilyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (**38**) (430 mg, 0.484 mmol) in tetrahydrofuran (40 mL) was treated with tetrabutylammonium fluoride (1 M solution in tetrahydrofuran, 5 mL, 0.5 mmol) at −15 °C. The reaction mixture was stirred for 36 h at 0 °C, then diluted with ethyl acetate, and washed with water (4x), 10% aqueous sodium bicarbonate solution (3x), and water with solid sodium bicarbonate (3x). The organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated. The resulting white solid was used for the next reaction without further purification.

$^1$H NMR (400 MHz, $CDCl_3$) $\delta$: 0.89 (6H, m, 2 × -$CH_3$), 1.19−1.41 (48H, m, -$(CH_2)_{11}$-, -$(CH_2)_{13}$-), 1.44 (2H, br s, 2 × -OH), 1.90 (2H, t, $J$ = 7.7 Hz, -C$H_2$CONH-), 2.00 (2H, m, =CH-C$H_2$-), 2.26 (3H, s, $CH_3$CO-), 3.41 (1H, dd, $J$ = 11.9, 5.8 Hz, H-6′), 3.58 (1H, dd, $J$ = 11.9, 6.6 Hz, H-6′), 3.64−3.70 (2H, m, H-5′, H-3′), 3.99 (1H, dd, $J$ = 10.0, 3.6 Hz, H-1), 4.03 (1H, dd, $J$ = 10.0, 2.8 Hz, H-1), 4.47 (1H, m, H-2), 4.55 (1H, d, $J$ = 7.9 Hz, H-1′), 5.26 (1H, dd, $J$ = 10.0, 7.9 Hz, H-2′), 5.29 (1H, d, $J$ = 3.8 Hz, H-4′), 5.48 (1H, dd, $J$ = 15.3, 7.7 Hz, H-4), 5.60 (1H, dd, $J$ = 7.7, 7.7 Hz, H-3), 5.71 (1H, d, $J$ = 9.3 Hz, -NH-), 5.87 (1H, dt, $J$ = 15.3, 6.8 Hz, H-5), 7.43−8.06 (10H, 3m, 2 × -$C_6H_5$).

**(2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[[2-*O*-benzoyl-4-*O*-acetyl-3,6-bis-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (40).** (2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[(2-*O*-benzoyl-4-*O*-acetyl-*β*-D-galactopyranosyl)oxy]-4-octadecene (**39**) (100 mg, 0.105 mmol) was reacted by the procedure used to synthesize compound **8** and afforded the title compound (94 mg, 77%) as a white solid.

IR (Nujol) $\nu_{max}$ (cm$^{-1}$): 3700−3150 (N−H), 2730, 2860 (C−H), 1725 (C=O ester), 1645 (C=O amide). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$: 0.85 (6H, m, 2 × -$CH_3$), 1.10−1.40 (48H, m, -$(CH_2)_{11}$-, -$(CH_2)_{13}$-), 1.74 (2H, m, =CH-C$H_2$-), 1.94 (2H, m, -C$H_2$CONH-), 2.08 (3H, s, -$CH_3$CO-), 3.47 (1H, dd, $J$ = 9.3, 7.8 Hz, H-1), 3.61 (1H, dd, $J$ = 11.1, 7.7 Hz, H-6′), 3.74−3.78 (2H, m, H-1, H-6′), 4.07 (1H, dd, $J$ = 7.7, 3.7 Hz, H-5′), 4.27 (1H, m, H-2), 4.57 (1H, dd, $J$ = 10.3, 3.3 Hz, H-3′), 4.72 (1H, d, $J$ = 8.0 Hz, H-1′), 5.09 (1H, dd, $J$ = 10.3, 8.0 Hz, H-2′), 5.29 (1H, dd, $J$ = 6.9, 4.3 Hz, H-3), 5.34−5.43 (2H, m, H-4, H-5), 5.46 (1H, d, $J$ = 3.3 Hz, H-4′), 7.41−7.99 (10H, 4m, 2 × -$C_6H_5$), 7.67 (1H, d, $J$ = 9.0 Hz, -NH-).

**(2*S*,3*R*,4*E*)-3-Hydroxy-2-(hexadecanoylamino)-1-[[3,6-bis-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (41).** (2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[[2-*O*-benzoyl-4-*O*-acetyl-3,6-bis-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (**40**) (100 mg, 0.087 mmol) was reacted by the procedure used to synthesize compound **11** and afforded the title compound (43 mg, 55%) as a white solid.

IR (Nujol) $\nu_{max}$ (cm$^{-1}$): 3700−3100 (O−H, N−H), 2730, 2860 (C−H), 1640 (C=O amide). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$: 0.84 (6H, t, $J$ = 6.7 Hz, 2 × -$CH_3$), 1.22−1.43 (48H, m, -$(CH_2)_{11}$-, -$(CH_2)_{13}$-), 1.91 (2H, m, =CH-C$H_2$-), 2.01 (2H, t, $J$ = 7.3 Hz, -C$H_2$CONH-), 3.41−3.50 (2H, m, H-1, H-6′), 3.58 (1H, ∼t, $J$ = 5.9 Hz, H-5′), 3.73−3.87 (5H, m, H-1, H-6′, H-2′, H-4′, H-3), 3.94 (1H, dd overlapping H-2, $J$ = 9.8, 3.3 Hz, H-3′), 3.93−3.96 (1H, m, H-2), 4.15 (1H, d, $J$ = 7.7 Hz, H-1′), 4.56, 4.86, 5.09 (3H, 3s, 3 × -OH), 5.34 (1H, dd, $J$ = 15.3, 6.9 Hz, H-4), 5.51 (1H, dt, $J$ = 15.3, 6.6 Hz, H-5), 7.48 (1H, d, $J$ = 8.9 Hz, -NH-). MS (CI, $NH_3$): 903 (M − H)$^-$.

**Synthesis of (2*S*,3*R*,4*E*)-3-Hydroxy-2-(hexadecanoylamino)-1-[[4,6-bis-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (46). (2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-[(4,6-*O*-benzylidene-*β*-D-galactopyranosyl)-oxy]-4-octadecene (42).** Benzaldehyde (5 mL) was added to a solution of (2*S*,3*R*,4*E*)-2-azido-3-(benzoyloxy)-1-(*β*-D-galactopyranosyloxy)-4-octadecene (**6**) (450 mg, 0.76 mmol) in formic acid (5 mL) at 22 °C and under argon. This mixture was stirred for 0.75 h, then cooled down to 5 °C, and diluted with ethyl acetate (25 mL) and water (10 mL). The two-phase solution was neutralized by adding solid sodium bicarbonate and a solution of sodium bicarbonate (1 M). The aqueous phase was then extracted with ethyl acetate (2 × 25 mL). The combined organic layers were washed with a cold solution of sodium bicarbonate (1 M, 25 mL), water (25 mL), and brine

(25 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by silica gel chromatography (20 g, 10% acetone/ethyl acetate) and afforded the title compound (233 mg, 45%) as a pale yellow oil.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3580 (O−H), 3060, 2930, 2860 (C−H), 2110 (−$N_3$), 1720 (C=O), 1265 (C−O). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$: 0.89 (3H, t, $J$ = 6.9 Hz, -$CH_3$), 1.25 (20H, br s, -$(CH_2)_{10}$-), 1.39 (2H, qi, $J$ = 6.9 Hz, -C$H_2$-$CH_3$), 2.09 (2H, m, =CH-C$H_2$-), 3.49 (1H, d, $J$ = 0.9 Hz, H-5′), 3.69−3.74 (2H, m, -$CHN_3$-, H-1), 3.80 (1H, dd, $J$ = 9.6, 7.6 Hz, H-1), 3.99−4.05 (2H, m, H-2′, H-3′), 4.08 (1H, dd, $J$ = 12.5, 1.8 Hz, H-6′), 4.23 (1H, dd, $J$ = 3.5, 0.9 Hz, H-4′), 4.33 (1H, dd, overlapping H-1′, $J$ = 12.5, 1.3 Hz, H-6′), 4.35 (1H, d, $J$ = 7.5 Hz, H-1′), 5.56 (1H, s, -O-CH-O-), 5.61 (1H, ddt, $J$ = 15.2, 8.0, 1.2 Hz, H-4), 5.69 (1H, dd, $J$ = 8.0, 4.0 Hz, H-3), 5.97 (1H, dt, $J$ = 15.2, 6.8 Hz, H-5), 7.34−8.12 (10H, 4m, 2 × -$C_6H_5$).

**(2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[(2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-*β*-D-galactopyranosyl)oxy]-4-octadecene (43).** (2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-[(2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-*β*-D-galactopyranosyl)oxy]-4-octadecene (**25**) (250 mg, 0.28 mmol) was reacted by the procedure used to synthesize compound **10** and afforded the title compound (266 mg, 86%) as a white solid.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3060, 2930, 2860 (C−H), 1725 (C=O ester), 1675 (C=O amide), 1265 (C−O). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$: 0.89 (6H, t, $J$ = 6.8 Hz, 2 × -$CH_3$), 1.14−1.43 (48H, m, -$(CH_2)_{11}$-, -$(CH_2)_{13}$-), 1.83 (2H, t, $J$ = 7.6 Hz, -$COCH_2$-), 1.99 (2H, m, =CH-C$H_2$-), 3.67 (1H, br s, H-5′), 3.81 (1H, dd, $J$ = 10.4, 4.1 Hz, H-1), 4.11 (1H, d, $J$ = 12.4, 1.4 Hz, H-6′), 4.17 (1H, dd, $J$ = 10.4, 4.0 Hz, H-1), 4.30 (1H, dd, $J$ = 12.4, 1.1 Hz, H-6′), 4.42−4.47 (1H, m, H-2), 4.58 (1H, d, $J$ = 3.5 Hz, H-4′), 4.74 (1H, d, $J$ = 8.0 Hz, H-1′), 5.38 (1H, dd, $J$ = 10.4, 3.5 Hz, H-3′), 5.50 (1H, dd, $J$ = 15.3, 7.0 Hz, H-4), 5.55 (1H, s, -O-CH-O-), 5.60 (1H, dd, $J$ = 7.0 Hz, H-3), 5.77−5.87 (1H, m, overlapping H-2′, H-5), 5.85 (1H, dd, $J$ = 10.4, 8.0 Hz, H-2′), 7.35−7.99 (20 H, 4m, 4 × -$C_6H_5$), 8.04 (1H, d, $J$ = 8.5 Hz, -NH-).

**(2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[(2,3-di-*O*-benzoyl-*β*-D-galactopyranosyl)oxy]-4-octadecene (44).** Trifluoroacetic acid (90%, 0.5 mL) was added to a stirred solution of (2*S*,3*R*,4*E*)-3-(benzoyloxy)-2-(hexadecanoylamino)-1-[(2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-*β*-D-galactopyranosyl)oxy]-4-octadecene (**43**) (258 mg, 0.23 mmol) in dichloromethane (15 mL) at 5 °C. The mixture was stirred for 0.5 h at 5 °C and at 22 °C for 1 h. Trifluoroacetic acid (same quantity) was added again, and the reaction mixture was stirred for 1 more hour at 22 °C. The mixture was diluted with ethyl acetate (30 mL) and washed with a cold aqueous solution of sodium bicarbonate (1 M, 2 × 15 mL), water (2 × 15 mL), and brine (15 mL). The organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue was purified by silica gel chromatography (15 g, 0−60% ethyl acetate/hexane) and afforded the title compound (193 mg, 83%) as a white solid.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3060, 2930, 2860 (C−H), 1730 (C=O ester), 1670 (C=O amide), 1265 (C−O). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$: 0.89 (6H, t, $J$ = 6.8 Hz, 2 × -$CH_3$), 1.25−1.57 (48H, m, -$(CH_2)_{11}$-, -$(CH_2)_{13}$-), 1.97−2.04 (4H, m, -$COCH_2$-, =CH-C$H_2$-), 3.53 (1H, t overlapping -OH-6′, $J$ = 3.0 Hz, H-5′), 3.53−3.58 (1H, m, -OH-6′), 3.67−3.71 (2H, m, H-1, H-6′), 3.86 (1H, dd, $J$ = 12.6, 3.5 Hz, H-6′), 4.01 (1H, dd, $J$ = 9.7, 1.8 Hz, H-1), 4.25 (1H, br s, H-4′), 4.49−4.54 (1H, m, H-2), 4.66 (1H, d, $J$ = 7.8 Hz, H-1′), 5.27 (1H, dd, $J$ = 10.4, 2.9 Hz, H-3′), 5.51 (1H, dd, $J$ = 15.4, 8.2 Hz, H-4), 5.73−5.86 (2H, m, H-3, H-2′), 5.96 (1H, dt, $J$ = 15.3, 7.0 Hz, H-5), 7.36−8.07 (15H, 5m, 3 × -$C_6H_5$), 8.06 (1H, d, $J$ = 8.4 Hz, -NH-).

**(2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[[2,3-di-*O*-benzoyl-4,6-bis-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (45).** (2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[(2,3-di-*O*-benzoyl-*β*-D-galactopyranosyl)oxy]-4-octadecene (**44**) (182 mg, 0.18 mmol) was reacted by the procedure used to synthesize compound **16** and afforded the title compound (117 mg, 54%) as a white solid.

IR (Nujol) $\nu_{max}$ ($cm^{-1}$): 3700−3200 (O−H), 2930, 2860 (C−H), 1725 (C=O ester), 1650 (C=O amide), 1460 (S=O). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$: 0.83 (6H, 2t, $J$ = 6.9 Hz, 2 × -$CH_3$), 1.14−1.50 (48H, m, -$(CH_2)_{11}$-, -$(CH_2)_{13}$-), 1.75−2.00 (4H, m, -$COCH_2$-, =CH-C$H_2$-), 3.57−3.61 (1H, m, H-5′), 3.82−3.88 and 4.08−4.12 (2 × 2H, 2m, H-6′, H-1), 4.07−4.13 (1H, m, H-2), 4.66 (1H, d, $J$ = 3.3 Hz, H-4′), 4.80 (1H, d, $J$ = 7.7 Hz, H-1′), 5.27−5.54 (5H, m, H-3, H-3′, H-2′, H-5, H-4), 7.35−7.88 (15H, 3m, 3 × -$C_6H_5$), 7.76 (1H, d, $J$ = 8.9 Hz, NH-).

**(2*S*,3*R*,4*E*)-3-Hydroxy-2-(hexadecanoylamino)-1-[[4,6-bis-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (46).** (2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[[2,3-di-*O*-benzoyl-4,6-bis-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (**45**) (1.0 g, 0.82 mmol) was reacted by the procedure used to synthesize compound **11** and afforded the title compound (212 mg, 20%) as an off-white solid.

IR (Nujol) $\nu_{max}$ ($cm^{-1}$): 3700−3100 (O−H, N−H), 2930, 2860 (C−H), 1640 (C=O amide). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$: 0.84 (6H, t, $J$ = 6.7 Hz, 2 × -$CH_3$), 1.05−1.26 (46H, br s, -$(CH_2)_{10}$-, -$(CH_2)_{13}$-), 1.43 (2 H, m, -$CH_2$-), 1.91 (2H, m, =CH-C$H_2$-), 2.02 (2H, t, $J$ = 7.4 Hz, -C$H_2$-CONH-), 3.21 (1H, dd, $J$ = 9.6, 7.7 Hz, H-2′), 3.36−3.41 (2H, m, H-3′, H-5′), 3.67−3.78 (3H, m, H-6′, H-1, H-2), 3.83−3.95 (2H, m, H-1, H-3), 4.00 (1H, dd, $J$ = 9.8, 4.9 Hz, H-6′), 4.05 (1H, d, $J$ = 7.7 Hz, H-1′), 4.33 (1H, d, $J$ = 3.0 Hz, H-4′), 5.30 (1H, dd, $J$ = 15.3, 7.2 Hz, H-4), 5.51 (1H, dt, $J$ = 15.3, 6.6 Hz, H-5), 7.54 (1H, d, $J$ = 9.1 Hz, -NH-).

**Synthesis of (2*S*,3*R*,4*E*)-3-Hydroxy-2-(hexadecanoylamino)-1-[[2,3-bis-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (50). (2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[(4,6-*O*-benzylidene-*β*-D-galactopyranosyl)oxy]-4-octadecene (47).** (2*S*,3*R*,4*E*)-2-Azido-3-(benzoyloxy)-1-[(4,6-*O*-benzylidene-*β*-D-galactopyranosyl)oxy]-4-octadecene (**42**) (235 mg, 0.34 mmol) was reacted by the procedure used to synthesize compound **10** and afforded the title compound (230 mg, 76%) as a white solid.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3055, 2930, 2860 (C−H), 1720 (C=O ester), 1640 (C=O amide). $^1$H NMR (400 MHz, $CDCl_3$) $\delta$: 0.88 (6H, t, $J$ = 6.3 Hz, 2 × -$CH_3$), 1.24 (44H, br s, -$(CH_2)_{10}$-, -$(CH_2)_{12}$-), 1.60 (4H, br s, 2 × -$CH_2$-), 2.03 (2H, m, =CH-$CH_2$-), 2.19 (2H, t, $J$ = 7.5 Hz, -C$H_2$CONH-), 3.48−4.34 (9H, m, H-1, H-1′, H-2′, H-3′, H-4′, H-5′, H-6′), 4.52 (1H, m, H-2), 5.44−5.63 (3H, m, H-3, H-4, -O-CH-O-), 5.88 (1H, dt, $J$ = 14.8, 6.7 Hz, H-5), 6.21 (1H, d, $J$ = 9.2 Hz, -NH-), 7.34−8.05 (10H, 2m, 2 × -$C_6H_5$).

**(2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[[2,3-bis-*O*-(sodium oxysulfonyl)-4,6-*O*-benzylidene-*β*-D-galactopyranosyl]oxy]-4-octadecene (48).** (2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[(4,6-*O*-benzylidene-*β*-D-galactopyranosyl)oxy]-4-octadecene (**47**) (66 mg, 0.074 mmol) was reacted by the procedure used to synthesize compound **16** and afforded the title compound (70 mg, 86%) as a white solid.

IR ($CH_2Cl_2$) $\nu_{max}$ ($cm^{-1}$): 3700−3150 (N−H), 2925, 2860 (C−H), 1725 (C=O ester), 1650 (C=O amide), 1265 (C−O, S=O). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$: 0.84 (6H, t, $J$ = 6.9 Hz, 2 × -$CH_3$), 1.18−1.27 (46H, br s, -$(CH_2)_{11}$-, -$(CH_2)_{12}$-), 1.42 (2H, m, -$CH_2$-), 1.93 (2H, m, =CH-C$H_2$-), 2.00−2.19 (2H, m, -C$H_2$-CONH-), 3.40 (1H, dd, $J$ = 10.0, 3.5 Hz, H-1), 3.50 (1H, s, H-5′), 3.86 (1H, d, $J_{AB}$ = 11.1 Hz, H-6′), 3.96 (1H, d, $J_{AB}$ = 11.1 Hz, H-6′), 4.09−4.14 (1H, m overlapping H-1, H-3′), 4.13 (1H, dd, $J$ = 10.0, 3.3 Hz, H-1), 4.25 (1H, m, H-2), 4.31 (1H, dd, $J$ = 9.9, 7.8 Hz, H-2′), 4.37 (1H, d, $J$ = 7.8 Hz, H-1′), 4.57 (1H, d, $J$ = 3.3 Hz, H-4′), 5.38−5.48 (3H, m, -O-CH-O-, H-3, H-4), 5.71 (1H, dt, $J$ = 14.5, 7.7 Hz, H-5), 7.30−7.99 (10H, 4m, 2 × -$C_6H_5$), 8.30 (1H, d, $J$ = 9.0 Hz, -NH-).

**(2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[[2,3-bis-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]-oxy]-4-octadecene (49).** (2*S*,3*R*,4*E*)-3-(Benzoyloxy)-2-(hexadecanoylamino)-1-[[2,3-bis-*O*-(sodium oxysulfonyl)-4,6-*O*-benzylidene-*β*-D-galactopyranosyl]oxy]-4-octadecene (**48**) (140 mg, 0.128 mmol) was reacted by the procedure used to synthesize compound **44** and afforded the title compound (70.5 mg, 55%) as a white solid.

IR (Nujol) $\nu_{max}$ ($cm^{-1}$): 3700−3150 (O−H, N−H), 2920, 2855 (C−H), 1720 (C=O ester), 1650 (C=O amide), 1265 (C−O, S=O). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$: 0.82 (6H, t, $J$ = 6.9 Hz, 2 × -$CH_3$), 1.18−1.24 (46H, m, -$(CH_2)_{11}$-, -$(CH_2)_{12}$-), 1.41

(2H, m, -$CH_2$-), 1.92 (2H, m, =CH-C$H_2$-), 1.98−2.16 (2H, m, -C$H_2$CONH-), 3.27−3.33 (3H, m, H-1, H-5′, H-6′), 3.41 (1H, dd, $J$ = 8.3, 4.4 Hz, H-6′) 3.90 (1H, m, H-2), 4.06 (1H, d, $J$ = 8.3 Hz, H-1), 4.19−4.22 (4H, m, H-1′, H-2′, H-3′, H-4′), 4.51 (2H, br s, 2 × -OH), 5.33 (1H, t, $J$ = 7.6 Hz, H-3), 5.38 (1H, dd, $J$ = 14.6, 7.6 Hz, H-4), 5.69 (1H, dt, $J$ = 14.6, 7.0 Hz, H-5), 7.48−7.97 (5H, 3m, -$C_6H_5$), 8.37 (1H, d, $J$ = 9.2 Hz, -NH-). MS (CI, $NH_3$): 962 ($M - 2Na + H)^-$.

**(2*S*,3*R*,4*E*)-3-Hydroxy-2-(hexadecanoylamino)-1-[[2,3-bis-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (50).** A solution of (2*S*,3*R*,4*E*)-3-(benzoyloxy)-2-(hexadecanoylamino)-1-[[2,3-bis-*O*-(sodium oxysulfonyl)-*β*-D-galactopyranosyl]oxy]-4-octadecene (**49**) (46 mg, 0.045 mmol) was reacted by the procedure used to synthesize compound **11** and afforded the title compound (26 mg, 64%) as a white solid.

IR (Nujol) $\nu_{max}$ ($cm^{-1}$): 3700−3150 (O−H, N−H), 2925, 2855 (C−H), 1650 (C=O amide). $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$: 0.84 (6H, t, $J$ = 6.8 Hz, 2 × -$CH_3$), 1.22−1.46 (48H, m, -$(CH_2)_{11}$-, -$(CH_2)_{13}$-), 1.88 (2H, m, =CH-C$H_2$-), 1.93−2.11 (2H, m, -C$H_2$-CONH-), 3.09 (1H, dd, $J$ = 9.2, 2.7 Hz, H-1), 3.35 (1H, dd, t, $J$ = 6.2 Hz, H-5′), 3.45 (1H, dd, $J$ = 10.8, 6.2 Hz, H-6′), 3.51 (1H, dd, $J$ = 10.8, 6.2 Hz, H-6′), 3.67 (1H, br t, H-3), 3.84−3.92 (2H, m, H-2, H-1), 4.11 (1H, d, $J$ = 3.9 Hz, -OH), 4.18−4.25 (4H, m, H-1′, H-2′, H-3′, H-4′), 4.62 (1H, t, $J$ = 5.7 Hz, -OH-6′), 4.77 (1H, d, $J$ = 5.8 Hz, -OH), 5.29 (1H, dd, $J$ = 15.4, 7.1 Hz, H-4), 5.45 (1H, dt, $J$ = 15.4, 6.6 Hz, H-5), 8.06 (1H, d, $J$ = 9.4 Hz, -NH-).

**Acknowledgment.** The authors offer their sincere appreciation to Dr. Stephen Klohr from BMS-PRI, Wallingford, CT, for performing mass spectral analysis. We would also like to acknowledge the contributions of Mr. Gilles Lacasse, Dr. Christian Coté, Ms. Danielle Sirard, and Chantale Jean from BMS-PRI, Candiac, Quebec, Analytical Department, for providing HPLC analysis.

## References

(1) (a) Bevilacqua, M. P.; Butcher, E.; Furie, B.; Gallatin, M.; Gimbrone, M.; Harlan, J.; Kishimoto, K.; Lasky, L.; McEver, R.; Paulson, J.; et al. Selectins: a Family of Adhesion Receptors. *Cell* **1991**, *67*, 233. (b) Nelson, R. M.; Dolich, S.; Aruffo, A.; Cecconi, O.; Bevilacqua, M. P. Higher-Affinity Oligosaccharide Ligands for E-Selectin. *J. Clin. Invest.* **1993**, *91*, 1157−1166 and refs 1−35 therein.

(2) Mulligan, M. S.; Paulson, J. C.; De Frees, S.; Zheng, Z.-L.; Lowe, J. B.; Ward, P. A. Protective Effects of Oligosaccharides in P-Selectin-Dependent Lung Injury. *Nature* **1993**, *364*, 149.

(3) (a) Phillips, M. L.; Nudelman, E.; Gaeta, F. C.; Perez, M.; Singhal, A. K.; Hakomori, S.; Paulson, J. C. ELAM-1 Mediates Cell Adhesion by Recognition of a Carbohydrate Ligand, Sialyl-Le$^x$. *Science* **1990**, *250*, 1130−1132. (b) Tiemeyer, M.; Swiedler, S. J.; Ishihara, M.; Moreland, M.; Schweingruber, H.; Hirtzer, P.; Brandley, B. K. Carbohydrate Ligands for Endothelial-Leukocyte Adhesion Molecule 1. *Proc. Natl. Acad. Sci. U.S.A.* **1991**, *88*, 1138−1142. (c) Walz, G.; Aruffo, A.; Kolanus, W. E.; Bevilacqua, M.; Seed, B. Recognition by ELAM-1 of the Sialyl-Le$^x$ Determinant on Myeloid and Tumor Cells. *Science* **1990**, *250*, 1132−1135.

(4) (a) Aruffo, A.; Kolanus, W.; Walz, G.; Fredman, P.; Seed, B. CD62/P-Selectin Recognition of Myeloid and Tumor Cell Sulfatides. *Cell* **1991**, *67*, 35−44. (b) Suzuki, Y.; Toda, Y.; Tamatani, T.; Wanatabe, T.; Suzuki, T.; Nakao, T.; Murase, K.; Kiso, M.; Hasegawa, A.; Tadano-Aritomi, K.; Ishizuka, I.; Miyasaka, M. Sulfated Glycolipids are Ligands for a Lymphocyte Homing Receptor, L-Selectin (LECAM-1), Binding Epitope in Sulfated Sugar Chain. *Biochem. Biophys. Res. Commun.* **1993**, *190*, 426−434. (c) Todderud, G.; Alford, J.; Millsap, K. A.; Aruffo, A.; Tramposch, K. M. PMN Binding to P-Selectin is Inhibited by Sulfatide. *J. Leukocyte Biol.* **1992**, *52*, 85.

(5) (a) Nair, X.; Todderud, G.; Davern, L.; Lee, D.; Aruffo, A.; Tramposch, K. M. Inhibition of Immune Complex-Induced Inflammation by a Small Molecular Weight Selectin Antagonist. *Mediators Inflammation* **1994**, *3*, 459−463. (b) Mulligan, M. S.; Miyasaka, M.; Suzuki, M.; Kawashima, H.; Iizuka, M.; Hasegawa, A.; Kiso, M.; Warner, R. L.; Ward, P. A. Anti-inflammatory Effects of Sulfatides in Selectin-Dependent Acute Lung Injury. *Int. Immunol.* **1995**, *7*, 1107−1113. (c) Kajihara, J.-I.; Guoji, Y.; Kato, K.; Suzuki, Y. Sulfatide, a Specific Sugar Ligand for L-Selectin, Blocks $CCl_4$-Induced Liver Inflammation in Rats. *Biosci. Biotech. Biochem.* **1995**, *59*, 155−157.

(6) Erbe, D. V.; Wolitzky, B. A.; Presta, L. G.; Norton, C. R.; Ramos, R. J.; Burns, D. K.; Rumberger, J. M.; Narasinga Rao, B. N.; Foxall, C.; Brandley, B. K.; Lasky, L. A. Identification of an E-selectin Region Critical for Carbohydrate Recognition and Cell Adhesion. *J. Cell Biol.* **1992**, *119*, 215−227.

(7) (a) Hollenbaugh, D.; Bajorath, J.; Stenkamp, R.; Aruffo, A. Interaction of P-selectin (CD62) and Its Cellular Ligand: Analysis of Critical Residues. *Biochemistry* **1993**, *32*, 2960−2966. (b) Bajorath, J.; Aruffo, A. Three-Dimensional Protein Models: Insights into Structure, Function, and Molecular Interactions. *Bioconjugate Chem.* **1994**, *5*, 173−181. (c) Erbe, D. V.; Watson, S. R.; Presta, L. G.; Wolitzky, B. A.; Foxall, C.; Brandley, B. K.; Lasky, L. A. P- and E-Selectin Use Common Sites for Carbohydrate Ligand Recognition and Cell Adhesion. *J. Cell Biol.* **1993**, *120*, 1227−1235.

(8) Graves, B. J.; Crowther, R. L.; Chandran, C.; Rumberger, J. M.; Li, S.; Huang, K.-S.; Presky, D. H.; Familetti, P. C.; Wolitzky, B. A.; Burns, D. K. Insight into E-Selectin/Ligand Interaction from the Crystal Structure and Mutagenesis of the lec/EGF Domains. *Nature* **1994**, *367*, 532−538.

(9) Bajorath, J.; Hollenbaugh, D.; King, G.; Harte, W., Jr.; Eustice, D. C.; Darveau, R. P.; Aruffo, A. The CD62/P-Selectin Binding Sites for Myeloid Cells and Sulfatides Are Overlapping. *Biochemistry* **1994**, *33*, 1332−1339.

(10) Zimmermann, P.; Bommer, R.; Bär, T.; Schmidt, R. R. Azidosphingosine Glycosylation in Glycosphingolipid Synthesis. *J. Carbohydr. Chem.* **1988**, *7*, 435−452.

(11) We also found in this case that tin(IV) chloride was a catalyst superior to boron trifluoride etherate giving higher yield of glycosylated product and also reducing the amount of O-acetylated sphingosine formed as a side product (see the Experimental Section).

(12) Zimmermann, P.; Schmidt, R. R. Synthese von erythro-Sphingosinen über die Azidoderivate. *Liebigs Ann. Chem.* **1988**, 663−667.

(13) Jeanloz, R. W.; Stoffyn, P. J. 2-Amino-2-Deoxy-α-D-Galactose Hydrochloride. *Methods in Carbohydrate Chemistry*; Academic Press: New York, 1962; Vol. 1, pp 221−227.

(14) Mori, K.; Nishio, H. Synthesis of (2S,3R,4E)-1-*O*-(*β*-D-Glucopyranosyl)-N-[24-(linoleoyloxy)tetracosanoyl]-4-sphingenine. The structure Proposed for the Esterified Cerebroside in the Epidermis of Guinea Pigs. *Liebigs Ann. Chem.* **1991**, 253−257.

(15) Lemieux, R. U.; Driguez, H. The Chemical Synthesis of 2-*O*-(α-L-Fucopyranosyl)-3-*O*-(α-D-Galactopyranosyl)-D-Galactose. The Terminal Structure of the Blood-Group B Antigenic Determinant. *J. Am. Chem. Soc.* **1975**, *97*, 4069−4075.

(16) Walz, G.; Aruffo, A.; Kolanus, W. E.; Bevilacqua, M.; Seed, B. Recognition by ELAM-1 of the Sialyl-Le$^x$ Determinant on Myeloid and Tumor Cells. *Science* **1990**, *250*, 1132−1135.

(17) Lemieux, R. U. The Origin of the Specificity in the Recognition of Oligosaccharides by Proteins. *Chem. Soc. Rev.* **1989**, *18*, 347−374.

(18) Mutagenesis studies have shown the importance of Arg 85 for the binding of related analogs. These results will be published in a following paper.

JM9606960