Studies on Selectin Blockers. 7. Structure−Activity Relationships of Sialyl Lewis X Mimetics Based on Modified Ser-Glu Dipeptides

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We have previously found that heterochiral fucodipeptides, L-Ser-D-Glu (**3a**) and D-Ser-L-Glu (**3b**), exhibited up to 20−100 times more potency than a sialyl Lewis X (sLe^X, **1)** and a 3′-sulfated Lewis X analogue (**2**) toward E-selectin binding and have also proposed, from molecular dynamics calculation, that their strong activities would depend on a possible formation of the type II and/or type II′ β-turn of compounds **3a**,**b** (Tsukida, T.; Hiramatsu, Y.; Tsujishita, H.; Kiyoi, T.; Yoshida, M.; Kurokawa, K.; Moriyama, H.; Ohmoto, H.; Wada, Y.; Saito, T.; Kondo, H. *J. Med. Chem.* **1997**, *40*, 3534−3541). To clarify our hypothesis, we synthesized several analogues of compounds **3a**,**b** and investigated their structure−activity relationships. As a result, it was indicated that the type II and/or type II′ β-turn conformation would be a comparatively tight form and would play important roles in favorable binding to E-selectin. These findings indicate that sLe^X mimetics with type II and type II′ β-turn dipeptides could be a useful methodology for the design of an active selectin blocker.

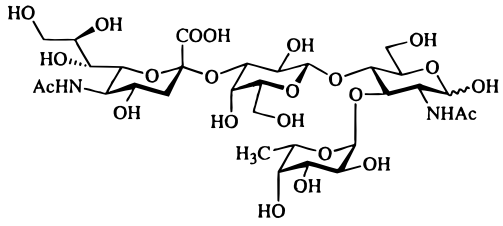
Introduction

A multistep series of adhesive events regulate inflammatory responses to infection or injury.[1] Selectins mediate the first adhesive step, which is characterized by rolling of leukocytes on endothelial cells, platelets, or other leukocytes.[2] Therefore, selectins are believed to be involved in the progression of the clinical manifestations of diseases, such as acute and/or chronic inflammation,[3] and have demonstrated a role in the inflammatory response. Since it has been reported that all selectins bind to sialyl Lewis X tetrasaccharide (sLe^X, **1**; Chart 1),[4] sLe^X-based drug design has attracted the interest of medicinal chemists. Development of carbohydrate-based therapy is, however, hindered by the complication that most proteins bind carbohydrates with weak affinity[5] and that the synthesis of complex oligosaccharides is a rather expensive and difficult process. Such a crucial problem makes sLe^X mimetics an attractive target for useful drug candidates.

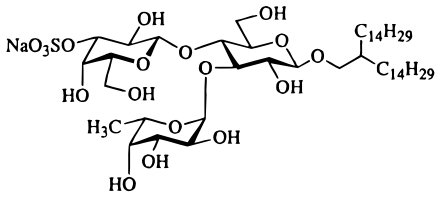
We have studied[6] the design and synthesis of sugar mimetics, to develop a methodology for sugar mimetics. Prediction and understanding of an active conformation of sugar is very important for the sugar mimetic study. Our previous studies[7] of molecular dynamics simulations of a 3′-sulfo Le^X (**2**; Chart 1)/E-selectin complex suggested the existence of three essential binding sites: (1) a fucose for the coordination to calcium, (2) a branched alkyl chain for the interaction with the hydrophobic region of E-selectin, and (3) a negatively charged group for the interaction with the basic residue of E-selectin. In addition, we have found an active scaffold, which can conserve the three essential groups to the desirable positions for the E-selectin binding, using a computational screening. Namely, we have proposed that the lactose unit of a 3′-sulfo Le^X derivative (**2**) could be replaced with a simple dipeptide, D-Ser-L-Glu (**3a**) or L-Ser-D-Glu (**3b**), characterized by a type II and/or type II′ β-turn formation (Figure 1).[6e] There is, however, little experimental evidence to support that the type II and/or type II′ β-turn conformation would be an active scaffold for the sLe^X mimics. To clarify the structure−activity relationships (SAR) of modified Ser-Glu dipeptides, we next investigated the SAR of compound **3** as illustrated in Figure 2.

In this paper, we describe the synthesis of Ser-Glu dipeptide derivatives and their in vitro inhibitory activities against E-, P-, and, L-selectin/sLe^X bindings.

Chart 1



sLe^x 1



sulfated Le^X 2

Results and Discussion

Chemistry. Our interest was to investigate the SAR of compounds **3** and to clarify the importance of type II and/or type II′ β-turn conformation as the active scaffold for the E-selectin binding. The SAR map of compounds **3** is illustrated in Figure 2.

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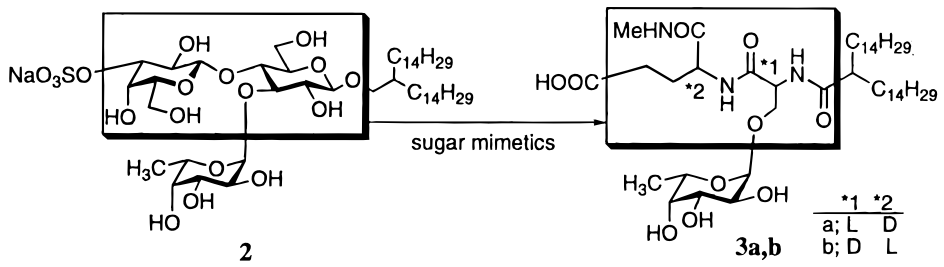


Figure 1. Successful sLe^X mimetics **2** and **3a**,**b**.

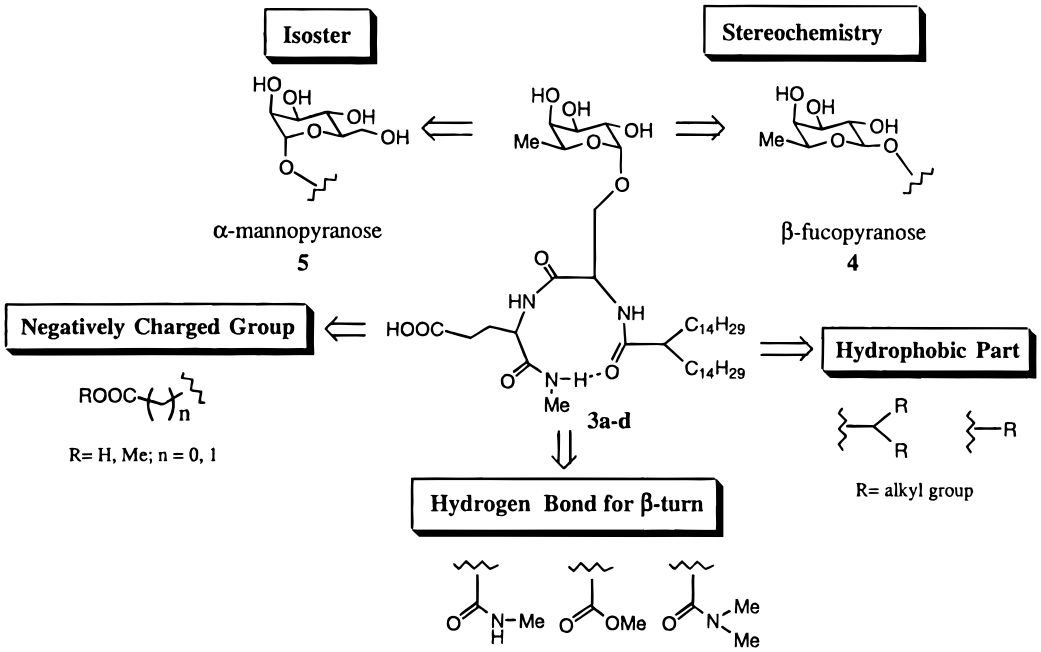


Figure 2. SAR map of compounds **3**-*5*.

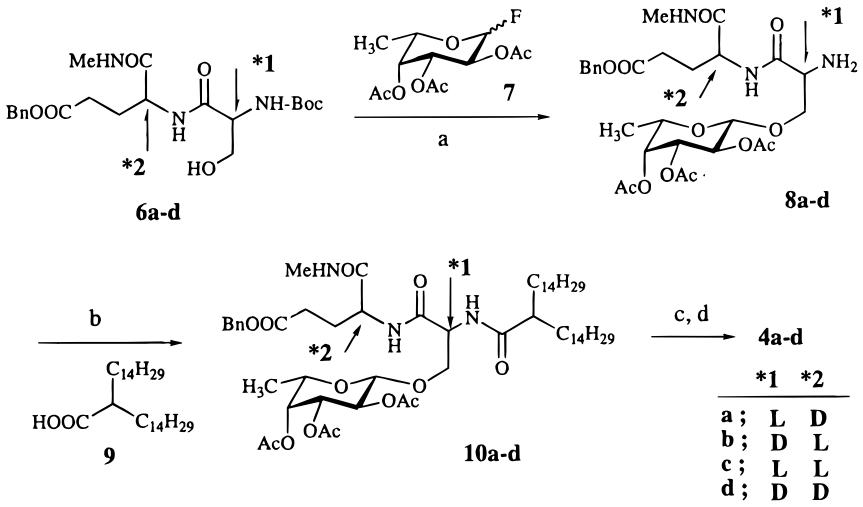
The construction of dipeptides units (**6a**−**d**) was carried out according to a previous paper.[6e] For the syntheses of compounds **4a**−**d**, the glycosylation of **6a**−**d** with 2,3,4-tri-*O*-acetyl fucose (**7**)[8] in the presence of $SnCl_2$/AgOTf as promoters yielded selectively *β*-glycosides **8a**−**d** in 65−75% yields. The condensation of **8a**−**d** with 1-tetradecylhexadecanoic acid (**9**) in the presence of WSC, 1-ethyl-3-[3-(dimethylamino)propyl]-carbodiimide hydrochloride, and HOBt, 1-hydroxy-1*H*-benzotriazole monohydrate, afforded compounds **10a**−**d**, in 58−62% yields. Finally, compounds **10a**−**d** were transformed, by removal of the protecting benzyl group under the general catalytic reduction conditions followed by treatment with 28% NaOMe in methanol, into the desired compounds **4a**−**d**, as shown in Scheme 1.

For the synthesis of the intermediates L-**13** and D-**13** for D-mannose derivatives **5a**−**d**, enantiomeric Ser units, a L-Ser unit (L-**11**) and a D-Ser unit (D-**11**), which were commercially available, were glycosylated with 1,2,3,4,6-penta-*O*-acetyl-D-mannose (**12**) in the presence of BF_3•OEt_2 as a promoter to afford the corresponding α-glycosides (L-**13**, D-**13**) stereoselectively. The deprotection of the Boc groups of the enantiomeric Glu units (L-**14**, D-**14**), which were synthesized according to a previous paper,[6e] with 4 N HCl in 1,4-dioxane at room temperature followed by coupling with the α-glycosides (L-**13**, D-**13**) in the presence of WSC and HOBt gave compounds **15a**−**d** in 60−98% yields. The deprotection of the Fmoc groups of **15a**−**d** with 20% morpholine in DMF at room temperature afforded the compounds **16a**−**d**, which were next coupled with **9** in the presence of WSC and HOBt for amide linkage to provide compounds **17a**−**d** in moderate yields. Finally, compounds **17a**−**d** were subjected to hydrogenolysis in the presence of a catalyst, 10% palladium−carbon, under hydrogen atmosphere, and then the acetyl groups were removed by treatment with 28% NaOMe in methanol to give the desired compounds **5a**−**d** in 78−84% yields, as shown in Scheme 2.

Compounds **18**−**21** and **33** were synthesized according to a previous paper,[6e] as shown in Scheme 3. First, the glycosylation of **6b**,**e**,**f** with 2,3,4-tri-*O*-benzylfucose donor **22** in the presence of $SnCl_2$/AgOTf as promoters and TMU as a weak base gave mainly α-glycosides **23**−**25**. The Boc group deprotection of **23**−**25** in TFA, followed by the coupling with carboxylic acids **9**, **26**, and **27** in the presence of WSC and HOBt, afforded compounds **28**−**32**, in 56−76% yields. Next, the compounds **28**−**32** were transformed, by the removal of the protecting benzyl group under hydrogen atmosphere, into the desired compounds **3b** and **18**−**21** in 83−94% yields. Compound **3b** was treated with 2 M $TMSCH_2N_2$/*n*-hexane in methanol−toluene to afford the methyl ester **33** quantitatively.

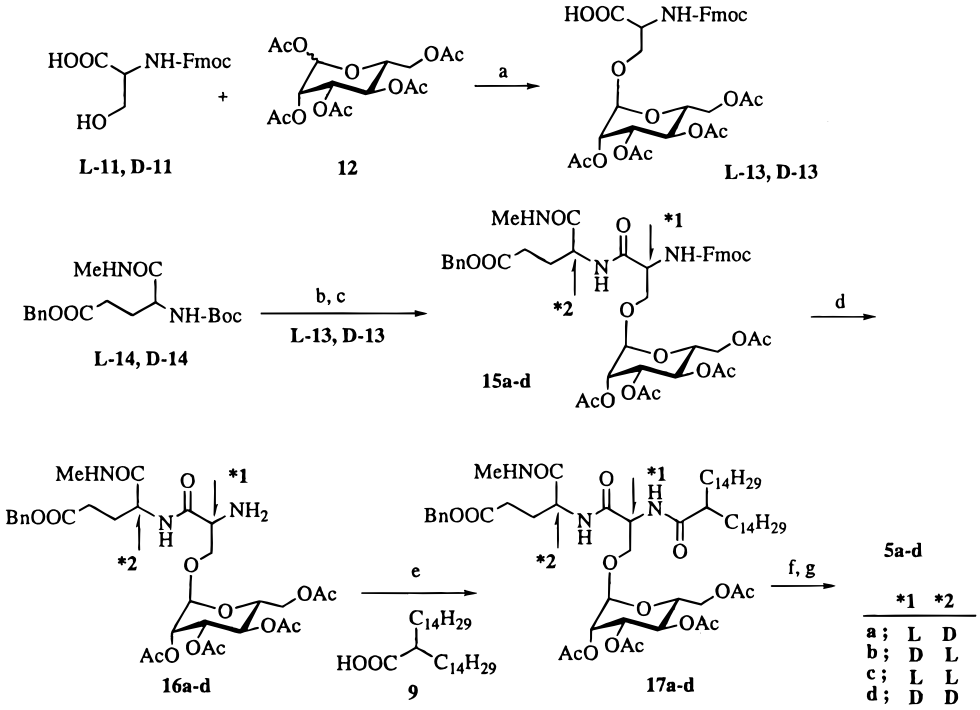
Biological Activities. The method using selectin-IgG chimeras reported by Foxall et al. was followed.[9] To explore the structure−activity relationships of compound **3**, we have studied the modification as illustrated

Scheme 1[a]



[a] Conditions: (a) $SnCl_2$, AgOTf, MS (4A)/CH_2Cl_2, 65−75%; (b) WSC, HOBt, 58−62%; (c) Pd/C/EtOH; (d) 28% NaOMe, 60−95%.

Scheme 2[a]

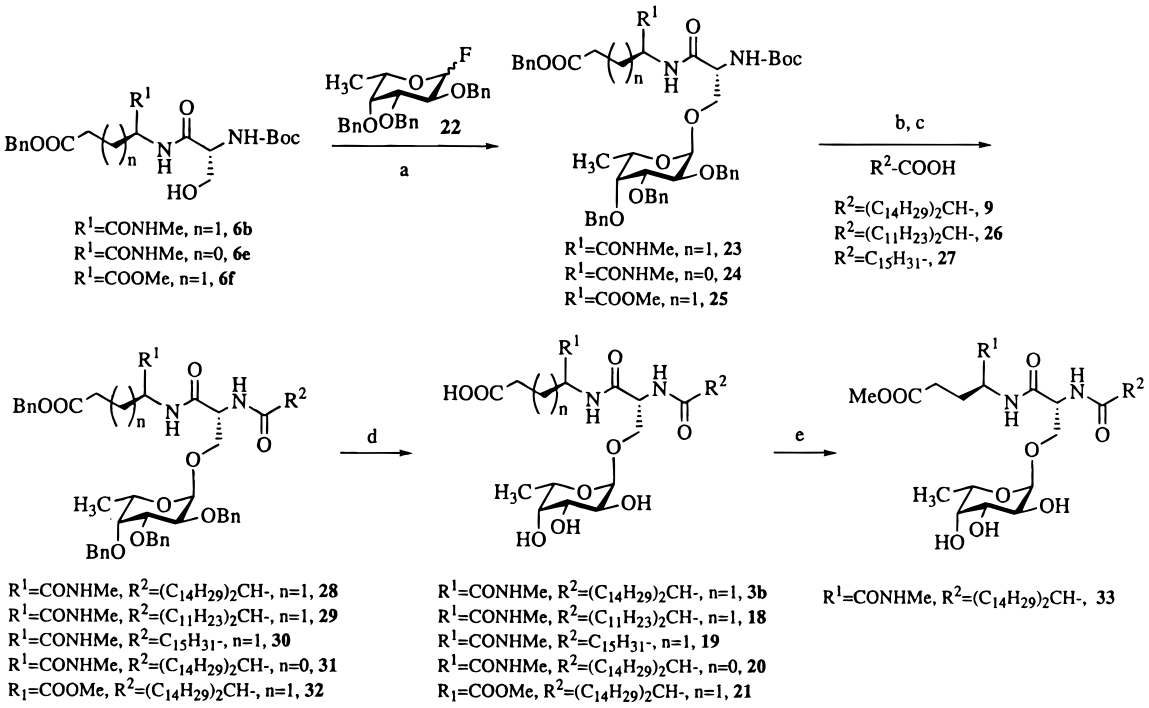


[a] Conditions: (a) $BF_3{\cdot}OEt_2$, $CHCl_3$, 45−63.5%; (b) 4 N HCl/1,4-dioxane; (c) **L-13**, **D-13**, WSC, HOBt, 60−98% from **L-14**, **D-14**; (d) 20% morpholine/DMF; (e) **9**, WSC, HOBt, 55−67%; (f) Pd/C/98% 1,4-dioxane; (g) 28% NaOMe/MeOH, 78−84% from **17a**−**d**.

in Figure 2: (1) stereochemistry and isostere, (2) hydrophobic part, (3) negatively charged group, (4) hydrogen bond for β-turn.

First, we focused on the stereochemistry and isostere of the L-fucose of compound **3**. The fucose residue was early recognized as an essential functionality for binding to selectins,[10] and it would have similar calcium-binding properties to that of the D-mannose in analogous mannose-binding proteins.[11] Currently, Kogan et al.[12] reported that the α-L-fucose unit could be replaced with an α-D-mannose in a study of selectin blockers. Therefore, we have also investigated the inhibitory activities of the D-mannose derivatives **5a**−**d**, against the E-, P-, and L-selectins, incorporated instead of the L-fucose of compounds **3a**−**d**. Toward the E-selectin, the L-Ser-D-Glu (**5a**) and the D-Ser-L-Glu (**5b**) showed potent inhibitory activities (IC_{50} values 3.5 μM for **5a** and 16 μM for **5b**), and the L-Ser-L-Glu (**5c**) and the D-Ser-D-Glu (**5d**), however, showed very weak activities (IC_{50} values of both **5c**,**d** were >1000 μM). The in vitro profiles of compounds **5a**−**d** were similar to those of compounds **3a**−**d** (IC_{50} values 13 μM for **3a**, 5.5 μM for **3b**, >1000 μM for **3c**, and >1000 μM for **3d**). Toward the P- and L-selectins, all dipeptides **5a**−**d** showed potent blocking activities, despite their different stereochemical features. These findings indicated that the α-D-mannose could function as an isostere of the α-L-fucose of compound **3** and that the heterochiral dipeptide backbones, the L-Ser-D-Glu and the D-Ser-L-Glu, which were characterized by type II and type II′ β-turns,[6e] could play important roles in favorable binding to E-selectin; in

Scheme 3[a]



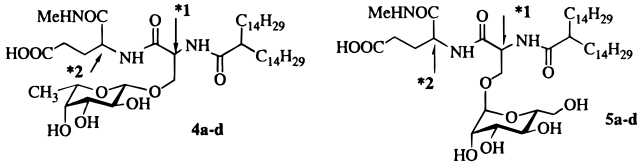
[a] Conditions: (a) $SnCl_2$, AgOTf, TMU, MS (4A)/$CHCl_3$; (b) TFA/$CHCl_3$; (c) WSC, HOBt, 56−76% from **23**, **24**, **25**; (d) 20% $Pd(OH)_2$/EtOH, 83−94%; (e) $TMSCH_2N_2$/MeOH−toluene, 95%.

addition, the ligand-binding site to E-selectin would be different from those to the P- and L-selectins.

On the other hand, it is known that a sLe^X, which is one of the natural ligands for selectin recognition,[4] has an α-linkage for the L-fucosyl bond. Recently, Wong et al.[13] reported that a β-fucosyl dipeptide showed inhibitory activity as well as the corresponding α-anomer against the E-selectin binding in a study of sLe^X mimetics. Thus, to study the stereochemistry−activity relationships concerning the L-fucose of compound **3**, we synthesized the corresponding β-anomers **4a**−**d** to the α-anomers **3a**−**d** and evaluated their inhibitory activities against E-, P-, and L-selectin bindings as shown in Table 1. As a result, regardless of the difference of the chirality of the dipeptide backbones, all compounds **4a**−**d** had very weak inhibitory activities (IC_{50} > 1000 μM) toward E-selectin binding. Namely, it was found that the α-configuration of the L-fucose of compound **3** was very important for E-selectin recognition. Our finding indicates that the compound **4** described here would have a comparatively tight conformation, such as the type II and type II′ β-turns, compared to the β-fucosyl dipeptide reported by Wong et al. Toward the P- and L-selectins, all of the dipeptides **4a**−**d** showed potent blocking activities.

Next, we investigated the modification of the hydrophobic part of compound **3b**, which was one of the most potent blockers against E-selectin. Compound **18**, including a shorter branched alkyl chain, 11-carbon length, compared to compound **3b** was 20−30 times less active than compound **3b** toward E- and P-selectins. In addition, compound **19** having a single alkyl chain showed significantly weak inhibitory activity to all selectins. To clarify the importance of the branched alkyl chain of compounds **5a**,**b** toward the inhibitory activity, we have studied the active forms of compounds

Table 1. Blocking Activity of Compounds **4a**−**d**, **5a**−**d**, **18**−**21**, **33**, **2**, and sLe^X



			IC_{50}, μM		
compd	*1	*2	E-selectin	P-selectin	L-selectin
4a	L	D	>100	0.3	0.8
4b	D	L	>100	0.3	1.6
4c	L	L	>1000	0.6	1.8
4d	D	D	>1000	0.3	0.7
5a	L	D	3.5	0.45	4
5b	D	L	16	0.42	3.1
5c	L	L	>1000	0.68	4.2
5d	D	D	>1000	0.38	4.4
18	D	L	160	15	12
19	D	L	>500	250−500	200
20	D	L	>500	3.6	3.8
21	D	L	>500	1.6	2.4
33			>500	37	>500
2			280	100	30
sLe^X			600	>1000	>1000

5a,**b**, like a micellar species, in solution. Namely, we have measured the UV absorbance to investigate light scattering changes on the concentration with varying concentrations of compounds **5a**,**b**. As a result, the critical micelle concentration (CMC) could not be seen at IC_{50} values 3.5 and 16 μM, respectively. These findings demonstrate that the branched alkyl chains with a moderate carbon length would be necessary for the strong bindings to all selectins.

Current sLe^X mimetic studies show that the sialic acid residue of sLe^X could be easily replaced by negatively charged groups, such as carboxylic acid,[14] sulfuric acid,[15] and phosphoric acid,[6a] and the negatively charged group

was essential for E-, P-, and L-selectins. We have also reported that the negatively charged group, a carboxylate of the Glu unit of **3a**,**b**, would be important for the ionic interaction with the basic residue Lys 111 in E-selectin by molecular dynamics simulation.[6e] To clarify this point, we have synthesized the compound **33** including a methyl carboxylate masked with a methyl group. As expected, compound **33** had very weak activity (IC_{50} > 500 μM) toward E-selectin. On the other hand, compound **20** containing a L-Asp unit instead of a L-Glu unit had markedly reduced inhibitory activity (IC_{50} > 500 μM) against E-selectin. Namely, this result indicates that there is a moderate position of the negatively charged group necessary for the E-selectin binding.

Finally, to clarify the importance of the possible β-turn conformation of compounds **3a**,**b**, we synthesized compound **21** lacking an amide proton necessary for the formation of β-turn and investigated the inhibitory activity against E-selectin. It was of interest that the inhibitory activity of compound **21** toward the E-selectin was dramatically decreased, IC_{50} > 500 μM.

In conclusion, we have investigated the SAR of compound **3** found currently using a computational screening, and we have found that a Ser-Glu dipeptide backbone, which is characterized by a type II and/or type II′ β-turn, could be a useful template for the design of sLe^X mimetics.

Experimental Section

Inhibition Assay of Selectin−sLe^X Binding. The construction of the selectin-immunoglobulin was carried out according to a previous paper.[16]

A solution of sLe^X pentasaccharide ceramide analogue in a 1:1 mixture of methanol and distilled water was pipetted into microtiter plate wells (96 wells; Falcon PRO-BIND) at 100 pmol/50 μL/well and was adsorbed by evaporating the solvent. The wells were washed twice with distilled water, blocked with 5% BSA (bovine serum albumin)−1 mM $CaCl_2$/50 mM imidazole buffer (pH 7.2) for 1 h at room temperature, and washed three times with 50 mM imidazole buffer (pH 7.2).

Separately, a 1:1 volumetric mixture of a 1:500 dilution in 1% BSA−1 mM $CaCl_2$/50 mM imidazole buffer (pH 7.2) of biotinylated goat $F(ab')^2$ anti-human IgG(g)/streptavidin-alkaline phosphatase (Zymed Lab Inc.) and a selectin-immunoglobulin fusion protein (selectin-Ig) was incubated at room temperature for 30 min to form a complex. The test compounds were dissolved in DMSO at 10 mM and finally diluted by 1 mM $CaCl_2$/50 mM imidazole buffer (pH 7.2) to final concentrations at 100, 50, 25, 12.5, 6.25, 3.13, 1.56, and 0.78 μM, respectively. Reactant solutions were prepared by incubating 30 μL of this solution at each concentration with 30 μL of the above complex solution for 30 min at room temperature. This reactant solution was then added to the above microtiter wells at 50 μL/well and incubated at 37 °C for 45 min. The wells were washed three times with 50 mM imidazole buffer (pH 7.2) and distilled water, respectively, followed by addition of *p*-nitrophenyl phosphate (1 mg/mL) and 0.01% $MgCl_2$ in 1 M diethanolamine (pH 9.8) at 50 μL/well. The reactant mixture was developed for 120 min at room temperature, and absorbance at 405 nm was measured. Percent binding was calculated by the following equation:

$$\% \text{ binding} = (X - C/A - C) \times 100$$

wherein X is the absorbance of wells containing the test compounds at each concentration, C is the absorbance of wells not containing the selectin-Ig and test compounds, and A is the absorbance of control wells not containing the test compounds. The results of inhibitory activities are presented in Table 1 as IC_{50} values, the concentrations of blockers necessary to cause 50% inhibition of the ligand binding to each of the selectins by the compound. The number of replicates is 2.

General Procedure for the Preparation of β-Glycosides 8a−d by Glycosylation of 6a−d with 2,3,4-Tri-*O*-acetylfucose Donor 7: [*O*-(2,3,4-Tri-*O*-acetyl-β-L-fucopyranosyl)-D-seryl]-L-glutamic Acid 1-Methylamide 5-Benzyl Ester (8b). A mixture of molecular sieves (4 Å, 1.0 g), AgOTf (1.41 g, 5.48 mM), and $SnCl_2$ (1.04 g, 5.48 mM) in CH_2Cl_2 (10 mL) was stirred for 0.5 h under argon atmosphere at room temperature and cooled to −20 °C. 2,3,4-Tri-*O*-acetyl-L-fucosyl fluoride (**7**) (1.20 g, 4.11 mM) in CH_2Cl_2 (3 mL) and compound **6b** (1.20 g, 2.74 mM) in CH_2Cl_2 (5 mL) were added to the mixture successively and stirred for 21 h while gradually returning to room temperature. The precipitate was filtered off, and the filtrate was concentrated in vacuo. The resulting residue was purified by thin-layer chromatography developing with 9:1 $CHCl_3$/methanol to give **8b** (1.24 g, 74.3%) as a syrup: ^{1}H NMR ($CDCl_3$) δ 1.2 (d, 3H, J = 6.4 Hz), 1.99 (s, 9H), 2.07 (s, 3H), 2.13 (s, 3H), 2.15−2.4 (m, 3H), 2.4−2.6 (m, 2H), 2.8 (d, 3H, J = 4.7 Hz), 3.49−3.62 (m, 1H), 3.7 (dd, 1H, J = 3.8, 13.6 Hz), 3.76−3.88 (m, 1H), 4.02−4.16 (m, 1H), 4.95−5.20 (m, 3H), 5.23 (d, 1H, J = 2.6 Hz), 6.78 (d, 1H, J = 4.7 Hz), 7.35 (s, 5H), 7.87 (d, 1H, J = 8.2 Hz). Anal. ($C_{28}H_{39}N_3O_{12}$) C, H, N.

[*O*-(2,3,4-Tri-*O*-acetyl-β-L-fucopyranosyl)-L-seryl]-D-glutamic acid 1-methylamide 5-benzyl ester (8a): yield 65.6% as a syrup; ^{1}H NMR ($CDCl_3$) δ 1.20 (d, 3H, J = 6.3 Hz), 1.98 (s, 9H), 2.03 (s, 3H), 2.08 (t, 1H, J = 2.7 Hz), 2.16 (s, 3H), 2.15−2.35 (m, 1H), 2.38−2.57 (m, 2H), 2.79 (d, 3H, J = 4.7 Hz), 3.56 (t, 1H, J = 5.1 Hz), 3.72−3.95 (m, 2H), 3.99 (dd, 1H, J = 3.8, 9.4 Hz), 4.44 (d, 1H, J = 7.6 Hz), 4.39−4.52 (m, 1H), 5.0 (dd, 1H, J = 3.3, 10.5 Hz), 5.04−5.18 (m, 3H), 5.23 (d, 1H, J = 3.3 Hz), 6.67 (d, 1H, J = 4.5 Hz), 7.28−7.40 (m, 5H), 8.0 (d, 1H, J = 8.6 Hz). Anal. ($C_{28}H_{39}N_3O_{12}$) C, H, N.

[*O*-(2,3,4-Tri-*O*-acetyl-β-L-fucopyranosyl)-L-seryl]-L-glutamic acid 1-methylamide 5-benzyl ester (8c): crude **8c** was used without further purification.

[*O*-(2,3,4-Tri-*O*-acetyl-β-L-fucopyranosyl)-D-seryl]-D-glutamic acid 1-methylamide 5-benzyl ester (8d): yield 68.1% as a syrup; ^{1}H NMR ($CDCl_3$) δ 1.18 (d, 3H, J = 6.4 Hz), 1.99 (s, 9H), 2.05 (s, 3H), 2.12 (s, 3H), 2.35−2.55 (m, 2H), 2.76 (d, 3H, J = 4.6 Hz), 3.5−3.66 (m, 1H), 3.74−3.96 (m, 3H), 4.37−4.55 (m, 1H), 4.51 (d, 1H, J = 7.6 Hz), 5.02 (dd, 1H, J = 3.4, 10.4 Hz), 5.10 (s, 2H), 5.21 (d, 1H, J = 3.2 Hz), 7.08 (q, 1H, J = 4.8 Hz), 7.25−7.38 (m, 5H), 7.93 (d, 1H, J = 8.4 Hz). Anal. ($C_{28}H_{39}N_3O_{12}$) C, H, N.

General Procedure for the Preparation of 10a−d: [*N*-(2-Tetradecylhexadecanoyl)-*O*-(2,3,4-tri-*O*-acetyl-β-L-fucopyranosyl)-D-seryl]-L-glutamic Acid 1-Methylamide 5-Benzyl Ester (10b). To a solution of **8c** (1.20 g, 1.97 mM) in DMF (50 mL) was added 2-tetradecylhexadecanoic acid (0.89 g, 1.97 mM), and the mixture was dissolved by heating and then cooled to room temperature. WSC (0.57 g, 2.96 mM) and HOBt (0.45 mg, 2.96 mM) were added to the solution. After the mixture stirred for 16.5 h, AcOEt (120 mL) was added to the solution, and the mixture was washed with 1 N HCl, saturated sodium hydrogen carbonate, and brine successively, dried ($MgSO_4$), and concentrated. The resulting residue was purified by thin-layer chromatography developing with 20:1 $CHCl_3$/methanol to give **10b** (1.20 g, 58.3%) as a syrup: ^{1}H NMR ($CDCl_3$) δ 0.8−0.95 (m, 6H), 0.96−1.68 (m, 60H), 1.99 (s, 3H), 2.04 (s, 3H), 2.10 (s, 3H), 2.40−2.64 (m, 2H), 2.75 (d, 3H, J = 4.7 Hz), 3.78 (dd, 1H, J = 3.3, 11.0 Hz), 3.83−4.05 (m, 2H), 4.4−4.67 (m, 2H), 4.59 (d, 1H, J = 7.7 Hz), 5.02 (dd, 1H, J = 3.3, 10.4 Hz), 5.06−5.2 (m, 3H), 5.25 (d, 1H, J = 3.2 Hz), 6.62 (d, 1H, J = 8.2 Hz), 6.7 (d, 1H, J = 4.8 Hz), 7.20−7.42 (m, 5H). Anal. ($C_{58}H_{97}N_3O_{13}$) C, H, N.

[*N*-(2-Tetradecylhexadecanoyl)-*O*-(2,3,4-tri-*O*-acetyl-β-L-fucopyranosyl)-L-seryl]-D-glutamic acid 1-methylamide 5-benzyl ester (10a): yield 61.8% as a syrup; ^{1}H NMR ($CDCl_3$) δ 0.8−1.00 (m, 6H), 1.19 (d, 3H, J = 6.4 Hz), 1.20−1.38 (m, 52H), 1.38−1.66 (m, 2H), 1.70 (s, 2H), 1.98 (s, 3H), 2.07 (s, 3H), 2.13 (s, 3H), 2.17−2.40 (m, 2H), 2.79 (d, 3H, J = 4.7 Hz), 3.74−3.92 (m, 2H), 3.99 (dd, 1H, J = 4.4, 9.4 Hz), 4.37−4.56

(m, 2H), 4.49 (d, 1H, J = 7.3 Hz), 4.95−5.2 (m, 4H), 5.2−5.3 (m, 1H), 6.44 (d, 1H, J = 5.6 Hz), 6.96 (d, 1H, J = 7.9 Hz), 7.35 (s, 5H). Anal. ($C_{58}H_{97}N_3O_{13}$) C, H, N.

[*N*-(2-Tetradecylhexadecanoyl)-*O*-(2,3,4-tri-*O*-acetyl-β-L-fucopyranosyl)-L-seryl]-L-glutamic acid 1-methylamide 5-benzyl ester (10c): yield 60% as a white crystal; mp 102−104 °C; ^{1}H NMR ($CDCl_3$) δ 0.85−0.9 (m, 6H), 1.19−1.3 (m, 55H), 1.38−1.57 (m, 2H), 1.70 (s, 2H), 1.99 (s, 3H), 2.08 (s, 3H), 2.11 (s, 3H), 2.51−2.59 (m, 2H), 2.84 (d, 3H, J = 4.7 Hz), 3.78−3.85 (m, 2H), 3.94 (dd, 1H, J = 4.6, 9.0 Hz), 4.41−4.54 (m, 2H), 4.47 (d, 1H, J = 7.2 Hz), 4.96−5.1 (m, 2H), 5.12 (s, 2H), 5.24−5.29 (m, 1H), 6.5 (d, 1H, J = 6.3 Hz), 6.72 (d, 1H, J = 4.7 Hz), 6.94 (d, 1H, J = 8.3 Hz), 7.34 (s, 5H). Anal. ($C_{58}H_{97}N_3O_{13}$) C, H, N.

[*N*-(2-Tetradecylhexadecanoyl)-*O*-(2,3,4-tri-*O*-acetyl-β-L-fucopyranosyl)-D-seryl]-D-glutamic acid 1-methylamide 5-benzyl ester (10d): yield 59.6% as a white crystal; mp 103−105 °C; ^{1}H NMR ($CDCl_3$) δ 0.80−0.95 (m, 6H), 1.05−1.75 (m, 55H), 1.99 (s, 3H), 2.05 (s, 3H), 2.11 (s, 3H), 2.2−2.42 (m, 1H), 2.43−2.63 (m, 2H), 2.74−2.8 (m, 1H), 2.84 (d, 3H, J = 4.7 Hz), 3.79 (dd, 1H, J = 8.5, 11.2 Hz), 3.86−3.97 (m, 1H), 3.98−4.08 (m, 1H), 4.37−4.52 (m, 1H), 4.50−4.73 (m, 1H), 4.63 (d, 1H, J = 7.7 Hz), 4.99 (dd, 1H, J = 3.2, 10.4 Hz), 5.04−5.07 (m, 3H), 5.25 (d, 1H, J = 2.7 Hz), 6.46 (d, 1H, J = 5.9 Hz), 6.65 (d, 1H, J = 4.8 Hz), 7.27−7.42 (m, 5H). Anal. ($C_{58}H_{97}N_3O_{13}$) C, H, N.

General Procedure for the Preparation of 4a−d: [*N*-(2-Tetradecylhexadecanoyl)-*O*-(β-L-fucopyranosyl)-D-seryl]-L-glutamic Acid 1-Methylamide (4b). To a solution of **10b** (0.25 g, 0.239 mM) in ethanol (30 mL) was added Pd/C (50 mg), and the mixture was stirred for 2 h under hydrogen atmosphere. The precipitate was filtered off, and the filtrate was concentrated in vacuo. The residue was dissolved in methanol (20 mL), 28% NaOMe/methanol (74 mg, 0.478 mM) was added to the solution, and this was stirred for 0.5 h at room temperature. DOWEX 50W-X8 (10 g) was added to the mixture, and this was stirred for 3 min and then added to $CHCl_3$ (10 mL). The precipitate was filtered off; the filtrate was concentrated in vacuo to give the desired compound **4b** (0.13 g, 64.6%) as a white powder: $[\alpha]_D$ −4° (c = 0.1, MeOH); mp gradually melted at 163 °C; ^{1}H NMR (DMSO-d_6) δ 0.8−0.9 (m, 6H), 0.95−1.55 (m, 52H), 1.6−1.8 (m, 1H), 1.8−2.08 (m, 1H), 2.16−2.36 (m, 3H), 2.58 (d, 3H, J = 4.3 Hz), 3.42−3.6 (m, 3H), 3.82−4.0 (m, 1H), 4.08 (d, 1H, J = 6.8 Hz), 4.1−4.28 (m, 1H), 4.27−4.5 (m, 2H), 4.69 (s, 1H), 4.83 (s, 1H), 7.8 (d, 1H, J = 4.6 Hz), 7.89 (d, 1H, J = 8.0 Hz), 8.0 (d, 1H, J = 7.3 Hz), 12.0 (s, 1H); MS spectrum 828 $(M + H)^+$. Anal. ($C_{45}H_{85}N_3O_{10}\cdot 1.5H_2O$) C, H, N.

[*N*-(2-Tetradecylhexadecanoyl)-*O*-(β-L-fucopyranosyl)-L-seryl]-D-glutamic acid 1-methylamide (4a): yield 94.6% as a white powder; $[\alpha]_D$ +5° (c = 0.1, MeOH); mp 198−199 °C; ^{1}H NMR (DMSO-d_6) δ 0.7−0.93 (m, 6H), 0.95−1.55 (m, 55H), 1.55−1.8 (m, 1H), 1.8−2.04 (m, 2H), 2.06−2.3 (m, 3H), 2.57 (d, 3H, J = 4.3 Hz), 3.4−3.68 (m, 2H), 3.7−3.89 (m, 1H), 4.0−4.24 (m, 2H), 4.13 (d, 1H, J = 6.9 Hz), 4.23−4.47 (m, 2H), 4.68 (s, 1H), 7.77 (d, 1H, J = 4.6 Hz), 7.99 (d, 1H, J = 6.7 Hz), 8.02 (d, 1H, J = 8.0 Hz), 12.1 (s, 1H); MS spectrum 828 $(M + H)^+$. Anal. ($C_{45}H_{85}N_3O_{10}\cdot 1.5H_2O$) C, H, N.

[*N*-(2-Tetradecylhexadecanoyl)-*O*-(β-L-fucopyranosyl)-L-seryl]-L-glutamic acid 1-methylamide (4c): yield 60.9% as a white powder; $[\alpha]_D$ −9° (c = 0.1, MeOH); mp gradually melted at 160 °C; ^{1}H NMR (DMSO-d_6) δ 0.82−0.87 (m, 6H), 1.13 (d, 3H, J = 6.4 Hz), 1.18−1.41 (m, 52H), 1.65−1.73 (m, 1H), 1.83−1.93 (m, 1H), 2.12−2.19 (m, 3H), 2.53 (d, 3H, J = 4.5 Hz), 3.34−3.58 (m, 3H), 3.68−3.75 (m, 1H), 4.06−4.15 (m, 2H), 4.38−4.48 (m, 2H), 4.70 (s, 1H), 7.54 (d, 1H, J = 4.7 Hz), 7.87−7.95 (m, 2H), 12.01 (bs, 1H); MS spectrum 828 $(M + H)^+$. Anal. ($C_{45}H_{85}N_3O_{10}\cdot 2H_2O$) C, H, N.

[*N*-(2-Tetradecylhexadecanoyl)-*O*-(-L-fucopyranosyl)-D-seryl]-D-glutamic acid 1-methylamide (4d): yield 65.5% as a white powder; $[\alpha]_D$ +6° (c = 0.1, MeOH); mp gradually melted at 147 °C; ^{1}H NMR (DMSO-d_6) δ 0.8−0.9 (m, 6H), 0.95−1.6 (m, 55H), 1.6−1.82 (m, 1H), 1.82−2.07 (m, 1H), 2.08−2.36 (m, 3H), 2.59 (d, 3H, J = 4.5 Hz), 3.46−3.85 (m, 3H), 3.94 (dd, 1H, J = 4.6, 9.8 Hz), 4.07 (d, 1H, J = 7.3 Hz), 4.12−4.3 (m, 1H), 4.3−4.66 (m, 2H), 4.67−4.8 (m, 1H), 7.56 (d, 1H, J = 4.7 Hz), 7.92 (d, 1H, J = 7.4 Hz), 7.98 (d, 1H, J = 8.2 Hz), 12.1 (s, 1H); MS spectrum 828 $(M + H)^+$. Anal. ($C_{45}H_{85}N_3O_{10}\cdot 1.5H_2O$) C, H, N.

General Procedure for the Preparation of L-13 and D-13 by Glycosylation of L-12 and D-12 with 1,2,3,4,6-Penta-*O*-acetyl-D-mannopyranose Donor 11: *N*-(9-Fluorenylmethyloxycarbonyl)-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-L-serine (L-13). To a mixture of *N*-(9-fluorenylmethyloxycarbonyl)-D-serine (0.9 g, 2.75 mM) and 1,2,3,4,6-penta-*O*-acetyl-D-mannopyranose (0.9 g, 3.64 mM) in $CHCl_3$ (36 mL) was added $BF_3\cdot OEt_2$ (2.6 mL), and the mixture was stirred for 21 h under nitrogen at room temperature. Concentrated, the residue was dissolved in AcOEt (90 mL), washed with water, dried ($MgSO_4$), and concentrated in vacuo. The resulting residue was purified by chromatography (SiO_2, gradient elution $CHCl_3$/methanol, 30:1 to 20:1) to give **L-13** (1.15 g, 63.5%) as a syrup: ^{1}H NMR ($CDCl_3$) δ 1.96, 2.03, 2.16 (3s, 12H), 3.9−4.2 (m, 3H), 4.2−4.3 (m, 2H), 4.3−4.8 (m, 3H), 4.88 (bs, 1H), 5.1−5.4 (m, 3H), 6.1 (bs, 1H), 7.2−7.5 (m, 5H), 7.8 (d, 2H, J = 7.4 Hz). Anal. ($C_{32}H_{35}NO_{14}$) C, H, N.

***N*-(9-Fluorenylmethyloxycarbonyl)-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-D-serine (D-13):** yield 45.0% as a syrup; ^{1}H NMR ($CDCl_3$) δ 1.98, 2.09, 2.14 (3s, 12H), 3.65−3.85 (m, 1H), 3.98 (bs, 1H), 4.05−4.3 (m, 4H), 4.3−4.7 (m, 3H), 4.83 (bs, 1H), 5.15−5.4 (m, 3H), 5.9 (bs, 1H), 7.2−7.45 (m, 5H), 7.61 (d, 2H, J = 6.4 Hz), 7.75 (d, 2H, J = 7.4 Hz). Anal. ($C_{32}H_{35}NO_{14}$) C, H, N.

General Procedure for the Preparation of 15a−d: [*N*-(9-Fluorenylmethyloxycarbonyl)-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-D-seryl]-L-glutamic Acid 1-Methylamide 5-Benzyl Ester (15b). To the **L-14** (575 mg, 1.64 mM) was added 4 N HCl/1,4-dioxane (3 mL), and the mixture was stirred for 15 min at room temperature. The mixture was concentrated, and the resulting residue and **D-13** (0.9 g, 1.37 mM) were dissolved in DMF (25 mL), added to Et_3N (180 mg, 1.78 mM), and then cooled to 0 °C. WSC (315 mg, 1.64 mM) and HOBt (252 mg, 1.64 mM) were added to the solution, and this was stirred for 18 h at room temperature. AcOEt (120 mL) was added, and the mixture was washed with 1 N HCl, saturated sodium hydrogen carbonate, and brine successively, dried ($MgSO_4$), and concentrated. The resulting residue was purified by thin-layer chromatography developing with 20:1 $CHCl_3$/methanol to give **15b** (767 mg, 62.9%) as a white crystal: ^{1}H NMR ($CDCl_3$) δ 1.98, 2.00, 2.10, 2.15 (4s, 12H), 1.9−2.7 (m, 4H), 2.78 (d, 3H, J = 4.8 Hz), 3.54 (dd, 1H, J = 4.8, 10.0 Hz), 3.97 (bs, 1H), 4.1−4.3 (m, 4H), 4.3−4.5 (m, 4H), 4.8 (s, 1H), 5.06 (d, 1H, J = 12.3 Hz), 5.12 (d, 1H, J = 12.3 Hz), 5.15−5.35 (m, 3H), 5.86 (d, 1H, J = 7.4 Hz), 6.36 (q, 1H, J = 4.8 Hz), 7.2−7.45 (m, 9H), 7.62 (d, 2H, J = 7.2 Hz), 7.76 (d, 2H, J = 7.3 Hz). Anal. ($C_{45}H_{51}N_3O_{16}$) C, H, N.

[*N*-(9-Fluorenylmethyloxycarbonyl)-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-L-seryl]-D-glutamic acid 1-methylamide 5-benzyl ester (15a): yield 97.5%; ^{1}H NMR ($CDCl_3$) δ 1.97, 2.00, 2.08, 2.15 (4s, 12H), 1.9−2.7 (m, 4H), 2.77 (d, 3H, J = 4.8 Hz), 3.9 (bs, 1H), 4.1−4.5 (m, 9H), 4.83 (bs, 1H), 5.0−5.2 (m, 3H), 5.3−5.4 (m, 3H), 5.8 (bs, 1H), 6.3 (bs, 1H), 7.3−7.45 (m, 9H), 7.61 (d, 2H, J = 7.2 Hz), 7.76 (d, 2H, J = 7.1 Hz), 8.00 (bs, 1H). Anal. ($C_{45}H_{51}N_3O_{16}$) C, H, N.

[*N*-(9-Fluorenylmethyloxycarbonyl)-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-L-seryl]-L-glutamic acid 1-methylamide 5-benzyl ester (15c): yield 60.7% as a crystal; ^{1}H NMR ($CDCl_3$) δ 1.97, 2.00, 2.08, 2.15 (4s, 12H), 1.9−2.7 (m, 4H), 2.77 (d, 3H, J = 4.8 Hz), 3.9−4.0 (m, 1H), 4.1−4.5 (m, 6H), 4.8 (bs, 1H), 5.0−5. (m, 2H), 5.2−5.4 (m, 3H), 5.7 (bs, 1H), 6.3 (bs, 1H), 7.2−7.5 (m, 9H), 7.61 (d, 2H, J = 7.2 Hz), 7.76 (d, 2H, J = 7.4 Hz). Anal. ($C_{45}H_{51}N_3O_{16}$) C, H, N.

[*N*-(9-Fluorenylmethyloxycarbonyl)-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-D-seryl]-D-glutamic acid 1-methylamide 5-benzyl ester (15d): yield 73.5% as a pale-yellow crystal; ^{1}H NMR ($CDCl_3$) δ 1.95, 1.97, 2.10, 2.16 (4s, 12H), 2.05−2.2 (m, 2H), 2.5−2.7 (m, 2H), 2.77 (d, 3H, J = 4.8 Hz), 3.53 (dd, 1H, J = 4.1, 8.9 Hz), 3.94 (bs, 1H), 4.1−4.3 (m,

4H), 4.3−4.5 (m, 3H), 4.84 (s, 1H), 5.04 (d, 1H, J = 12.2 Hz), 5.11 (d, 1H, J = 12.2 Hz), 5.23−5.3 (m, 2H), 5.72 (bs, 1H), 6.36 (bs, 1H), 7.1−7.4 (m, 9H), 7.62 (d, 2H, J = 6.6 Hz), 7.76 (d, 2H, J = 7.7 Hz). Anal. ($C_{45}H_{51}N_3O_{16}$) C, H, N.

General Procedure for the Preparation of 16a−d by the Fmoc Group Deprotection of 15a−d: [*O*-(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl)-D-seryl]-L-glutamic Acid 1-Methylamide 5-Benzyl Ester (16b). To **15b** (0.5 g, 0.56 mM) was added 20% morpholine/DMF (12 mL), and the solution was stirred for 1.5 h at room temperature. AcOEt (100 mL) was added, and this was washed with water twice, dried ($MgSO_4$), and concentrated in vacuo. The resulting residue was purified by thin-layer chromatography developing with 10:1 $CHCl_3$/methanol to give **16b** (347 mg, 92.5%) as a syrup: ^{1}H NMR ($CDCl_3$) δ 1.97, 2.03, 2.11, 2.14 (4s, 12H), 1.9−2.6 (m, 4H), 2.77 (d, 3H, J = 4.8 Hz), 3.45−3.55 (m, 1H), 3.62 (dd, 1H, J = 3.6, 9.5 Hz), 3.9−4.07 (m, 2H), 4.1−4.2 (m, 1H), 4.25 (dd, 1H, 5.2, 12.3 Hz), 5.15−5.35 (m, 3H), 5.86 (d, 1H, J = 7.4 Hz), 6.58 (q, 1H, J = 4.7 Hz), 7.2−7.4 (m, 5H), 8.03 (d, 1H, J = 8.3 Hz). Anal. ($C_{30}H_{41}N_3O_{14}$) C, H, N.

[*O*-(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl)-L-seryl]-D-glutamic acid 1-methylamide 5-benzyl ester (16a): crude **16a** was used without further purification.

[*O*-(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl)-L-seryl]-L-glutamic acid 1-methylamide 5-benzyl ester (16c): yield 70.1% as a syrup; ^{1}H NMR ($CDCl_3$) δ 1.98, 2.03, 2.10, 2.14 (4s, 12H), 2.0−2.25 (m, 2H), 2.25−2.65 (m, 2H), 2.78 (d, 3H, J = 4.7 Hz), 3.4−3.7 (m, 2H), 3.97 (dd, 1H, J = 2.3, 8.6 Hz), 4.11 (dd, 1H, J = 2.5, 12.3 Hz), 4.28 (dd, 1H, J = 5.5, 12.2 Hz), 4.3−4.5 (m, 1H), 4.8 (d, 1H, J = 1.4 Hz), 5.0−5.35 (m, 5H), 6.14 (bs, 1H), 7.3−7.4 (m, 5H), 7.9−8.1 (m, 2H). Anal. ($C_{45}H_{51}N_3O_{16}$) C, H, N.

[*O*-(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl)-D-seryl]-D-glutamic acid 1-methylamide 5-benzyl ester (16d): yield >100% DMF contained; ^{1}H NMR ($CDCl_3$) δ 1.95, 1.97, 2.10, 2.15 (4s, 12H), 2.0−2.2 (m, 2H), 2.35−2.62 (m, 2H), 2.78 (d, 3H, J = 5.0 Hz), 3.5−3.8 (m, 2H), 3.9−4.0 (m, 1H), 4.05−4.15 (m, 1H), 4.15 (d, 1H, J = 2.5 Hz), 4.25 (dd, 1H, J = 5.1, 12.3 Hz), 4.3−4.45 (m, 1H), 4.83 (s, 1H), 5.10 (d, 1H, J = 12.3 Hz), 5.16 (d, 1H, J = 12.3 Hz), 5.2−5.3 (m, 3H), 6.40 (bs, 1H), 7.3−7.4 (m, 5H).

General Procedure for the Preparation of 17a−d: [*N*-(2-Tetradecylhexadecanoyl)-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-D-seryl]-L-glutamic Acid 1-Methylamide 5-Benzyl Ester (17b). 16c (345 mg, 0.517 mM) and 2-tetradecylhexadecanoic acid (234 mg, 0.517 mM) were dissolved in DMF by heating and then cooled to room temperature. WSC (119 mg, 0.62 mM) and HOBt (95 mg, 0.62 mM) were added to the solution. After the mixture stirred for 18.5 h, AcOEt (120 mL) was added to the solution, and the mixture was washed with 1 N HCl, saturated sodium hydrogen carbonate, and brine successively, dried ($MgSO_4$), and concentrated. The resulting residue was purified by thin-layer chromatography developing with 25:1 $CHCl_3$/methanol to give **17b** (347 mg, 60.9%): ^{1}H NMR ($CDCl_3$) δ 0.85−1.0 (m, 6H), 1.1−1.6 (m, 52H), 1.96, 2.02, 2.11, 2.13 (4s, 12H), 1.9−2.6 (m, 4H), 2.78 (d, 3H, J = 4.8 Hz), 3.51 (dd, 1H, J = 5.3, 9.4 Hz), 4.02 (bs, 1H), 4.12−4.39 (m, 3H), 4.4−4.5 (m, 1H), 4.55−4.7 (m, 1H), 4.79 (s, 1H), 5.1 (d, 1H, J = 12.3 Hz), 5.15 (d, 1H, J = 12.3 Hz), 5.2−5.3 (m, 3H), 6.37 (q, 1H, J = 4.9 Hz), 6.48 (d, 1H, J = 7.0 Hz), 7.1 (d, 1H, J = 7.8 Hz), 7.35 (s, 5H). Anal. ($C_{60}H_{99}N_3O_{15}$) C, H, N.

[*N*-(2-Tetradecylhexadecanoyl)-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-L-seryl]-D-glutamic acid 1-methylamide 5-benzyl ester (17a): yield 62.0%; ^{1}H NMR ($CDCl_3$) δ 0.7−1.0 (m, 6H), 1.0−1.6 (m, 52H), 1.96, 2.01, 2.09, 2.13 (4s, 12H), 2.3−2.65 (m, 2H), 2.77 (d, 3H, J = 4.8 Hz), 3.7−4.0 (m, 1H), 4.10 (dd, 1H, 2.4, 12.2 Hz), 4.26 (dd, 1H, J = 5.1, 12.3 Hz), 4.3−4.5 (m, 2H), 4.85 (s, 1H), 5.0−5.35 (m, 5H), 6.38 (d, 1H, J = 7.1 Hz), 6.49 (d, 1H, J = 4.6 Hz), 7.20 (d, 1H, J = 7.9 Hz), 7.25−7.45 (m, 5H). Anal. ($C_{60}H_{99}N_3O_{15}$) C, H, N.

[*N*-(2-Tetradecylhexadecanoyl)-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-L-seryl]-L-glutamic acid 1-methylamide 5-benzyl ester (17c): yield 55.8% as a crystal; mp 139 °C; ^{1}H NMR ($CDCl_3$) δ 0.8−0.95 (m, 6H), 1.1−1.5 (m, 52H), 1.95, 2.02, 2.09, 2.13 (4s, 12H), 2.4−2.6 (m, 2H), 2.78 (d, 3H, J = 4.8 Hz), 3.8−3.9 (m, 2H), 3.98 (bs, 1H), 4.11 (dd, 1H, 2.4, 12.3 Hz), 4.27 (dd, 1H, J = 5.4, 12.3 Hz), 4.35−4.5 (m, 1H), 4.5−4.65 (m, 1H), 4.86 (d, 1H, J = 1.2 Hz), 5.09 (d, 1H, J = 12.3 Hz), 5.15 (d, 1H, J = 12.3 Hz), 5.2−5.32 (m, 3H), 6.25−6.45 (m, 2H), 7.3−7.4 (m, 5H). Anal. ($C_{60}H_{99}N_3O_{15}$) C, H, N.

[*N*-(2-Tetradecylhexadecanoyl)-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-D-seryl]-D-glutamic acid 1-methylamide 5-benzyl ester (17d): yield 67.0% as a pale-yellow crystal; ^{1}H NMR ($CDCl_3$) δ 0.85−0.9 (m, 6H), 1.0−1.7 (m, 52H), 1.93, 1.99, 2.11, 2.15 (4s, 12H), 2.05−2.25 (m, 2H), 2.46−2.65 (m, 2H), 2.78 (d, 3H, J = 4.6 Hz), 3.52 (dd, 1H, J = 5.1, 9.4 Hz), 3.97 (bs, 1H), 4.1−4.3 (m, 3H), 4.4−4.55 (m, 1H), 4.62 (bs, 1H), 4.83 (s, 1H), 5.08 (d, 1H, J = 12.3 Hz), 5.14 (d, 1H, J = 12.3 Hz), 5.2−5.35 (m, 3H), 6.3−6.5 (m, 2H), 7.3−7.4 (m, 5H), 7.53 (bs, 1H). Anal. ($C_{60}H_{99}N_3O_{15}$) C, H, N.

General Procedure for the Preparation of 5a−d: [*N*-(2-Tetradecylhexadecanoyl)-α-D-mannopyranosyl)-D-seryl]-L-glutamic Acid 1-Methylamide (5b). To a solution of **17b** (347 mg, 0.315 mM) in 98% 1,4-dioxane (30 mL) was added Pd/C (350 mg), and the mixture was stirred for 1.5 h under hydrogen atmosphere. The precipitate was filtered off, and the filtrate was concentrated in vacuo. The residue was dissolved in methanol (35 mL), 28% NaOMe/methanol (122 mg) was added to the solution, and this was stirred for 1.5 h at room temperature. DOWEX (1.0 g) was added to the mixture, and this was stirred for 3 min. The precipitate was filtered off, and the filtrate was concentrated under reduced pressure to give the desired compound **5b** (223 mg, 79.0%) as a white powder: $[\alpha]_D$ 23° (c = 0.1, MeOH); mp 203−206 °C; ^{1}H NMR (DMSO-d_6) δ 0.75−1.0 (m, 6H), 1.05−1.55 (m, 52H), 1.6−1.8 (m, 1H), 1.8−2.05 (m, 1H), 2.56 (d, 3H, J = 4.5 Hz), 3.2−3.8 (m, 8H), 4.1−4.25 (m, 1H), 4.25−4.4 (m, 1H), 4.4−4.5 (m, 1H), 4.5−4.7 (m, 2H), 7.76 (q, 1H, J = 4.7 Hz), 8.02 (d, 1H, J = 7.7 Hz), 12.0 (s, 1H). Anal. ($C_{45}H_{85}N_3O_{11}$) C, H, N.

[*N*-(2-Tetradecylhexadecanoyl)-α-D-mannopyranosyl)-L-seryl]-D-glutamic acid 1-methylamide (5a): yield 82.9% as a white crystal; mp 162−168 °C; ^{1}H NMR (DMSO-d_6) δ 0.75−0.95 (m, 6H), 1.1−1.6 (m, 52H), 1.6−1.8 (m, 1H), 1.85−2.05 (m, 1H), 2.1−2.35 (m, 3H), 2.57 (d, 3H, J = 4.5 Hz), 3.35−3.8 (m, 6H), 4.1−4.25 (m, 1H), 4.35−4.5 (m, 1H), 4.65 (d, 1H, J = 1.4 Hz), 7.75 (q, 1H, J = 4.5 Hz), 7.9−8.15 (m, 1H). Anal. ($C_{45}H_{85}N_3O_{11}$) C, H, N.

[*N*-(2-Tetradecylhexadecanoyl)-α-D-mannopyranosyl)-L-seryl]-L-glutamic acid 1-methylamide (5c): yield 84.0% as a white powder; mp 168 °C; ^{1}H NMR (DMSO-d_6) δ 0.75−0.9 (m, 6H), 1.0−1.55 (m, 52H), 1.55−2.0 (m, 2H), 2.0−2.3 (m, 3H), 2.56 (d, 3H, J = 4.5 Hz), 3.2−3.8 (m, 8H), 4.1−4.25 (m, 1H), 4.35−4.5 (m, 1H), 4.61 (s, 1H), 7.67 (q, 1H, J = 4.5 Hz), 7.80 (d, 1H, J = 7.9 Hz), 7.98 (d, 1H, J = 8.0 Hz). Anal. ($C_{45}H_{85}N_3O_{11}$) C, H, N.

[*N*-(2-Tetradecylhexadecanoyl)-α-D-mannopyranosyl)-D-seryl]-D-glutamic acid 1-methylamide (5d): yield 78.0% as a white powder; ^{1}H NMR (DMSO-d_6) δ 0.85−0.9 (m, 6H), 1.05−1.55 (m, 52H), 1.6−2.0 (m, 2H), 2.1−2.3 (m, 3H), 2.60 (d, 3H, J = 4.4 Hz), 3.3−3.7 (m, 8H), 4.15−4.3 (m, 2H), 4.5−4.6 (m, 1H), 4.62 (s, 1H), 7.71 (q, 1H, J = 4.4 Hz), 7.83 (d, 1H, J = 7.5 Hz), 7.95 (d, 1H, J = 7.9 Hz). Anal. ($C_{45}H_{85}N_3O_{11}$) C, H, N.

General Procedure for the Preparation of Dipeptide Glycosyl Acceptors 6a−f: *N*-(*tert*-Butoxycarbonyl)-D-seryl-L-glutamic Acid 1-Methylamide 5-Benzyl Ester (6b). To the *N*-(*tert*-butoxycarbonyl)-L-glutamic acid 1-methylamide 5-benzyl ester (10.0 g, 28.5 mM) was added 4 N HCl/1,4-dioxane (30 mL), and the solution was stirred for 0.5 h at room temperature. The mixture was concentrated, and the residue was dissolved in DMF (200 mL), added to Et_3N (5.4 mL), and then cooled to 0 °C. WSC (6.6 g, 34.2 mM) and HOBt (5.2 g, 34.2 mM) were added to the mixture, and this was stirred for 18 h at room temperature. The solvent was removed under reduced pressure, and the oily residue was dissolved in AcOEt (300 mL), washed with 0.1 N HCl, saturated sodium hydrogen carbonate, and brine, dried (Mg-

SO_4), and concentrated. The precipitate was filtered, and recrystallization from AcOEt/*n*-hexane gave **6b** (10.3 g, 82.5%) as a white crystal: $[\alpha]_D$ −5° (*c* = 0.1, $CHCl_3$); mp 127−128 °C; ^{1}H NMR (DMSO-d_6) δ 1.38 (s, 9H), 1.65−1.85 (m, 1H), 1.90−2.15 (m, 1H), 2.30−2.40 (m, 2H), 2.58 (d, 3H, *J* = 4.6 Hz), 3.54 (t, 2H, *J* = 5.6 Hz), 3.85−4.00 (m, 1H), 4.13−4.29 (m, 1H), 4.88 (t, 1H, *J* = 5.6 Hz), 5.07 (s, 2H), 6.82 (d, 1H, *J* = 6.9 Hz), 7.30−7.45 (m, 5H), 7.77 (d, 1H, *J* = 4.6 Hz), 8.03 (d, 1H, *J* = 8.3 Hz). Anal. ($C_{21}H_{31}N_3O_7$) C, H, N.

***N*-(*tert*-Butoxycarbonyl)-D-seryl-L-aspartic acid 1-methylamide 5-benzyl ester (6e):** yield 94.3%, contained DMF; ^{1}H NMR ($CDCl_3$) δ 1.44 (s, 9H), 2.65−2.80 (m, 1H), 2.75 (d, 3H, *J* = 4.8 Hz), 3.15 (dd, 1H, *J* = 4.9, 17.2 Hz), 3.70−3.85 (m, 1H), 3.90−4.15 (m, 2H), 4.75−4.90 (m, 1H), 5.10 (d, 1H, *J* = 12.2 Hz), 5.15 (d, 1H, *J* = 12.2 Hz), 5.63 (bs, 1H), 6.91 (bs, 1H), 7.30−7.45 (m, 5H), 7.52 (d, 1H, *J* = 8.0 Hz).

***N*-(*tert*-Butoxycarbonyl)-D-seryl-L-glutamic acid 1-methyl 5-benzyl diester (6f):** yield 84.7% as a syrup; ^{1}H NMR ($CDCl_3$) δ 1.45 (s, 9H), 1.95−2.15 (m, 1H), 2.15−2.35 (m, 1H), 2.40−2.55 (m, 2H), 3.55−3.70 (m, 1H), 3.72 (s, 3H), 4.00−4.25 (m, 2H), 4.55−4.70 (m, 1H), 5.12 (s, 2H), 5.57 (d, 1H, *J* = 7.3 Hz), 7.25−7.45 (m, 5H). Anal. ($C_{21}H_{30}N_2O_8$) C, H, N.

General Procedure for the Preparation of 23−25 by Glycosylation of 6b,e,f with 2,3,4-Tri-*O*-benzylfucose Donor 22: [*N*-(*tert*-Butoxycarbonyl)-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-D-seryl]-L-glutamic Acid 1-Methylamide 5-Benzyl Ester (23). A mixture of molecular sieves (4 Å, 2.0 g), AgOTf (0.59 g, 2.28 mM), and $SnCl_2$ (0.43 g, 2.28 mM) in $CHCl_3$ (15 mL) was stirred for 5 h under nitrogen atmosphere at room temperature and cooled to −40−50 °C. TMU (0.66 g, 5.70 mM), 2,3,4-tri-*O*-benzyl-L-fucosyl fluoride (**22**) (1.00 g, 2.28 mM) in $CHCl_3$ (1 mL), and compound **6b** (0.50 g, 1.14 mM) in $CHCl_3$ (3 mL) were added to the mixture successively and stirred for 1 h at the same temperature and for 20 h while gradually returning to room temperature. The precipitate was filtered off, and the filtrate was concentrated. The residue was purified by thin-layer chromatography developing with 1:1 AcOEt/cyclohexane to give **23** (0.60 g, 62.0%) as a white crystal: $[\alpha]_D$ −59° (*c* = 0.1, $CHCl_3$); mp 77−81 °C; ^{1}H NMR ($CDCl_3$) δ 1.13 (d, 3H, *J* = 6.5 Hz), 1.43 (s, 9H), 1.7−2.1 (m, 1H), 2.1−2.3 (m, 1H), 2.3−2.6 (m,2H), 2.67 (d, 3H, *J* = 4.8 Hz), 3.5−3.7 (m, 2H), 3.8−4.0 (m, 3H), 4.0−4.25 (m, 1H), 4.25−4.45 (m, 1H), 4.5−5.0 (m, 7H), 5.0−5.2 (m, 2H), 5.5 (bs, 1H), 6.07 (bs, 1H), 7.1−7.45 (m, 20H). Anal. ($C_{48}H_{59}N_3O_{11}$) C, H, N.

[*N*-(*tert*-Butoxycarbonyl)-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-D-seryl]-L-aspartic acid 1-methylamide 5-benzyl ester (24): yield 84.0% as a crude syrup; ^{1}H NMR ($CDCl_3$) δ 1.13 (d, 3H, *J* = 6.4 Hz), 1.43 (s, 9H), 2.63 (d, 3H, *J* = 4.8 Hz), 3.55−3.70 (m, 2H), 3.70−4.00 (m, 3H), 4.00−4.20 (m, 2H), 4.55−5.00 (m, 8H), 5.10 (s, 2H), 7.20−7.45 (m, 20H).

[*N*-(*tert*-Butoxycarbonyl)-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-D-seryl]-L-glutamic acid 1-methyl 5-benzyl diester (25): crude **25** was used without further purification.

General Procedure for the Preparation of 28−32: [*N*-(2-Tetradecylhexadecanoyl)-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-D-seryl]-L-glutamic Acid 1-Methylamide 5-Benzyl Ester (28). To a solution of **23** (0.5 g, 0.59 mM) in CH_2Cl_2 (10 mL) was added TFA (10 mL) at 0 °C, and the mixture was stirred for 2 h at room temperature. Concentrated, the residue was dissolved in AcOEt (100 mL), washed with saturated sodium carbonate, and dried ($MgSO_4$), and the solvent was removed in vacuo. The residue was dissolved in DMF (50 mL), and 2-tetradecylhexadecanoic acid (294 mg, 0.65 mM) was added to the solution. The mixture was dissolved by heating and then cooled to room temperature. WSC (170 mg, 0.89 mM) and HOBt (136 mg, 0.89 mM) were added to the solution. After the mixture was stirred for 20 h, AcOEt (100 mL) was added to the solution, washed with 1 N HCl, saturated sodium hydrogen carbonate, and brine successively, dried ($MgSO_4$), and concentrated. The residue was purified by thin-layer chromatography developing with 25:1 $CHCl_3$/methanol to give **28** (456 mg, 65.0%) as a white crystal: $[\alpha]_D$ −44° (*c* = 0.1, $CHCl_3$); mp 118−120 °C; ^{1}H NMR ($CDCl_3$) δ 0.8−0.95 (m, 6H), 1.12 (d, 3H, *J* = 6.5 Hz), 1.15−1.7 (m, 52H), 1.75−1.92 (m, 1H), 1.92−2.1 (m, 1H), 2.1−2.3 (m, 2H), 2.3−2.6 (m, 2H), 2.66 (d, 3H, *J* = 4.8 Hz), 3.45−3.65 (m, 2H), 3.78−3.95 (m, 3H), 4.08 (dd, 1H, *J* = 4.2,10.2 Hz), 4.15−4.25 (m, 2H), 4.25−4.4 (m, 1H), 4.6−5.0 (m, 7H), 5.05 (d, 1H, *J* = 11.9 Hz), 5.1 (d, 1H, *J* = 12.3 Hz), 6.0−6.1 (m, 1H), 6.47 (d, 1H, *J* = 6.7 Hz), 7.15−7.4 (m, 20H). Anal. ($C_{73}H_{109}N_3O_{10}$) C, H, N.

[*N*-(2-Undecyltridecanoyl)-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-D-seryl]-L-glutamic acid 1-methylamide 5-benzyl ester (29): yield 56.2% as a white crystal; mp 127−128 °C; ^{1}H NMR ($CDCl_3$) δ 0.8−0.95 (m, 6H), 1.12 (d, 3H, *J* = 6.5 Hz), 1.20−1.75 (m, 40H), 1.9−2.1 (m, 1H), 2.1−2.3 (m, 1H), 2.3−2.6 (m, 2H), 2.66 (d, 3H, *J* = 4.8 Hz), 3.45−3.70 (m, 2H), 3.75−3.95 (m, 3H), 4.08 (dd, 1H, *J* = 3.5, 9.9 Hz), 4.25−4.50 (m, 2H), 4.55−5.0 (m, 7H), 5.05 (d, 1H, *J* = 12.5 Hz), 5.10 (d, 1H, *J* = 12.3 Hz), 6.52 (d, 1H, *J* = 5.8 Hz), 7.15−7.50 (m, 20H). Anal. ($C_{67}H_{97}N_3O_{10}$) C, H, N.

[*N*-Palmityl-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-D-seryl]-L-glutamic acid 1-methylamide 5-benzyl ester (30): yield 58.0% as a white crystal; mp 118−120 °C; ^{1}H NMR ($CDCl_3$) δ 0.8−0.95 (m, 6H), 1.12 (d, 3H, *J* = 6.5 Hz), 1.15−1.40 (m, 24H), 1.45−1.75 (m, 2H), 1.8−1.95 (m, 1H), 2.1−2.3 (m, 3H), 2.3−2.6 (m, 2H), 2.67 (d, 3H, *J* = 3.2 Hz), 3.55 (dd, 1H, *J* = 8.5, 11.1 Hz), 3.60−3.65 (m, 1H), 3.80−3.95 (m, 3H), 4.08 (dd, 1H, *J* = 2.9, 10.3 Hz), 4.25−4.45 (m, 2H), 4.55−4.95 (m, 7H), 5.05 (d, 1H, *J* = 12.3 Hz), 5.10 (d, 1H, *J* = 12.3 Hz), 6.10 (bs, 1H), 6.52 (d, 1H, *J* = 6.4 Hz), 7.15−7.40 (m, 20H). Anal. ($C_{59}H_{81}N_3O_{10}$) C, H, N.

[*N*-(2-Tetradecylhexadecanoyl)-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-D-seryl]-L-aspartic acid 1-methylamide 5-benzyl ester (31): yield 75.7% as a white crystal; mp 128−129 °C; ^{1}H NMR ($CDCl_3$) δ 0.8−0.95 (m, 6H), 1.12 (d, 3H, *J* = 6.5 Hz), 1.15−1.60 (m, 52H), 1.85−2.1 (m, 1H), 2.63 (d, 3H, *J* = 4.7 Hz), 2.75−3.0 (m, 2H), 3.52 (dd, 1H, *J* = 7.7, 11.0 Hz), 3.59 (d, 1H, *J* = 1.6 Hz), 3.75−3.95 (m, 3H), 4.06 (dd, 1H, *J* = 3.6, 10.1 Hz), 4.30−4.45 (m, 1H), 4.55−5.0 (m, 7H), 5.10 (s, 2H), 6.45−6.6 (m, 2H), 7.20−7.45 (m, 20H). Anal. ($C_{72}H_{107}N_3O_{10}$) C, H, N.

[*N*-(2-Tetradecylhexadecanoyl)-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-D-seryl]-L-glutamic acid 1-methyl 5-benzyl diester (32): yield 75.7% as a syrup; ^{1}H NMR ($CDCl_3$) δ 0.8−0.95 (m, 6H), 1.10 (d, 3H, *J* = 6.5 Hz), 1.2−1.65 (m, 52H), 1.75−2.1 (m, 2H), 2.1−2.3 (m, 1H), 2.3−2.55 (m, 2H), 3.45 (dd, 1H, *J* = 9.3, 11.2 Hz), 3.57 (d, 1H, *J* = 1.8 Hz), 3.66 (s, 3H), 3.75−3.9 (m, 2H), 3.86 (dd, 1H, *J* = 5.7, 11.5 Hz), 4.06 (dd, 1H,*J* = 3.7, 10.1 Hz), 4.4−4.55 (m, 1H), 4.55−5.0 (m, 7H), 5.04 (d, 1H, *J* = 12.5 Hz), 5.09 (d, 1H, *J* = 12.5 Hz), 6.50 (d, 1H, *J* = 6.3 Hz), 7.20−7.40 (m, 20H). Anal. ($C_{73}H_{108}N_2O_{11}$) C, H, N.

General Procedure for the Preparation of 3b and 18−21: [*N*-(2-Tetradecylhexadecanoyl)-*O*-(α-L-fucopyranosyl)-D-seryl]-L-glutamic Acid 1-Methylamide (3b). To a solution of **28** (80 mg, 0.067 mM) in ethanol (50 mL) was added 20% $Pd(OH)_2$/C (80 mg), and the mixture was stirred for 4 h under hydrogen (3−4 atmospheric) pressure. The precipitate was filtered off, and the filtrate was concentrated in vacuo. The residue was crystallyzed with water to give **3b** (46 mg, 82.5%) as a white crystal: $[\alpha]_D$ −62° (*c* = 0.1, MeOH); mp 179−183 °C; ^{1}H NMR (DMSO-d_6) δ 0.75−0.9 (m, 6H), 1.06 (d, 3H, *J* = 6.4 Hz), 1.1−1.55 (m, 52H), 1.6−1.8 (m, 1H), 1.8−2.1 (m, 1H), 2.1−2.3 (m, 3H), 2.58 (d, 3H, *J* = 4.5 Hz), 3.4−3.6 (m, 3H), 3.6−3.85 (m, 2H), 4.1−4.3 (m, 1H), 4.34 (d, 1H, *J* = 4.5 Hz), 4.4−4.55 (m, 1H), 7.45 (d, 1H, *J* = 4.1 Hz), 7.97 (d, 1H, *J* = 7.0 Hz), 8.05 (d, 1H, *J* = 8.0 Hz). Anal. ($C_{45}H_{85}N_3O_{10}$) C, H, N.

[*N*-(2-Undecyltridecanoyl)-*O*-(α-L-fucopyranosyl)-D-seryl]-L-glutamic acid 1-methylamide (18): yield 84.3% as a white powder; mp 168−170 °C dec; ^{1}H NMR (DMSO-d_6) δ 0.75−0.95 (m, 6H), 1.05 (d, 3H, *J* = 6.4 Hz), 1.0−1.55 (m, 40H), 1.6−1.8 (m, 1H), 1.8−2.1 (m, 1H), 2.1−2.3 (m, 3H), 2.57 (d, 3H, *J* = 4.5 Hz), 3.6−3.85 (m, 3H), 4.1−4.3 (m, 1H), 4.3−4.55 (m, 2H), 4.40 (d, 1H, *J* = 4.5 Hz), 4.64 (s, 1H), 7.79 (q, 1H, *J* = 4.6 Hz), 8.04 (d, 1H, *J* = 7.3 Hz), 8.09 (d, 1H, *J* = 8.4 Hz); MS spectrum 766 $(M + Na)^+$. Anal. ($C_{39}H_{73}N_3O_{10}$) C, H, N.

[*N*-Palmityl-*O*-(α-L-fucopyranosyl)-D-seryl]-L-glutamic acid 1-methylamide (19): yield 83.0% as a white powder; mp 155−158 °C dec; ^{1}H NMR (DMSO-d_6) δ 0.75−0.95 (m, 3H), 1.05 (d, 3H, J = 6.5 Hz), 1.1−1.35 (m, 24H), 1.4−1.55 (m, 2H), 1.6−1.8 (m, 1H), 1.85−2.05 (m, 1H), 2.05−2.3 (m, 4H), 2.58 (d, 3H, J = 4.5 Hz), 3.4−3.7 (m, 5H), 3.75 (q, 1H, J = 6.6 Hz), 4.1−4.25 (m, 1H), 4.25−4.6 (m, 4H), 4.64 (s, 1H), 7.78 (q, 1H, J = 4.6 Hz), 7.98 (d, 1H, J = 7.1 Hz), 8.14 (d, 1H, J = 8.2 Hz), 12.05 (bs, 1H); MS spectrum 654 $(M + Na)^+$. Anal. ($C_{31}H_{57}N_3O_{10}$) C, H, N.

[*N*-(2-Tetradecylhexadecanoyl)-*O*-(α-L-fucopyranosyl)-D-seryl]-L-aspartic acid 1-methylamide (20): yield 86.7% as a pale-yellow powder; mp 60−63 °C dec; ^{1}H NMR (DMSO-d_6) δ 0.75−0.95 (m, 6H), 1.05 (d, 3H, J = 6.4 Hz), 1.1−1.5 (m, 52H), 2.1−2.3 (m, 2H), 3.3−3.8 (m, 5H), 4.3−4.5 (m, 2H), 4.5−4.6 (m, 1H); MS spectrum 836 $(M + Na)^+$. Anal. ($C_{44}H_{83}N_3O_{10}$) C, H, N.

[*N*-(2-Tetradecylhexadecanoyl)-*O*-(α-L-fucopyranosyl)-D-seryl]-L-glutamic acid 1-methyl ester (21): yield 93.7% as a pale-yellow powder; mp 40−41 °C dec; ^{1}H NMR (DMSO-d_6) δ 0.75−0.95 (m, 6H), 1.05 (d, 3H, J = 6.4 Hz), 1.1−1.55 (m, 52H), 1.65−1.85 (m, 1H), 1.85−2.1 (m, 1H), 2.1−2.3 (m, 3H), 3.35−3.65 (m, 5H), 3.62 (s, 3H), 3.73 (q, 1H, J = 6.6 Hz), 4.2−4.4 (m, 1H), 4.39 (d, 1H, J = 4.4 Hz), 4.5−4.65 (m, 1H), 4.65 (s, 1H), 7.89 (d, 1H, J = 8.3 Hz), 8.27 (d, 1H, J = 7.7 Hz), 12.12 (s, 1H); MS spectrum 851 $(M + Na)^+$. Anal. ($C_{45}H_{84}N_2O_{11}$) C, H, N.

[*N*-(2-Tetradecylhexadecanoyl)-*O*-(α-L-fucopyranosyl)-D-seryl]-L-glutamic Acid 1-Methylamide 5-Methyl Ester (33). To a solution of **3b** (100 mg, 0.12 mM) in methanol−toluene (1:1, 10 mL) was added 2 M $TMSCH_2N_2$/*n*-hexane (0.18 mL, 0.36 mM), and the mixture was stirred for 30 min at room temperature. Concentrated under reduced pressure, the resulting precipitate was collected with Et_2O to give **33** (96 mg, 95.0%) as a pale-yellow powder: mp 100−102 °C; ^{1}H NMR (DMSO-d_6) δ 0.75−0.95 (m, 6H), 1.06 (d, 3H, J = 6.4 Hz), 1.1−1.6 (m, 52H), 1.65−1.85 (m, 1H), 1.85−2.1 (m, 1H), 2.15−2.4 (m, 4H), 2.57 (d, 3H, J = 4.4 Hz), 3.4−3.8 (m, 5H), 3.57 (s, 3H), 4.1−4.3 (m, 1H), 4.4−4.55 (m, 1H), 4.65 (s, 1H), 7.81 (q, 1H, J = 4.4 Hz), 8.02 (d, 1H, J = 7.2 Hz), 8.08 (d, 1H, J = 8.2 Hz); MS spectrum 864 $(M + Na)^+$. Anal. ($C_{46}H_{87}N_3O_{10}$) C, H, N.

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